MOTIVATION-COGNITION INTERACTION: FROM NEUROCOGNITIVE MODELS TO CLINICAL APPLICATIONS

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MOTIVATION-COGNITION INTERACTION: FROM NEUROCOGNITIVE MODELS TO CLINICAL APPLICATIONS

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EDITORIAL
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Editorial: Motivation-Cognition Interaction: From Neurocognitive Models to Clinical Applications

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Editorial on the Research Topic

Motivation-Cognition Interaction: From Neurocognitive Models to Clinical Applications

In a recent definition (Botvinick and Braver, 2015), motivational-cognition interactions have been defined in terms of "the invigorating impact, on both behavior and cognition, of prospective reward (both extrinsic reward, such as money, and intrinsic reward tied to the satisfaction of self-relevant behavioral goals, and including negative rewards, i.e., punishments)" (Botvinick and Braver, 2015). This definition captures the idea that incentives, both positive and negative, consequently induce motivational states, which in turn lead to dynamic changes in cognitive processing and therefore behavior.

The last two decades have witnessed a sharp rise in the number of publications on the topic of motivation-cognition interactions. One reason for this increase is the availability of human functional neuroimaging methods (such as fMRI, PET, and fNIRS), which have led to an improved understanding of the neural correlates of motivation-cognition interaction mechanisms. Specifically, these methods have suggested the critical role played by dopaminergic modulation of both cortical and subcortical structures, especially the prefrontal cortex, the anterior cingulate and the parietal cortex (Westbrook and Braver, 2016). Another contributing factor is the growing awareness of the potential role of dysfunctional motivation-cognition interaction mechanisms in the development of abnormal behaviors in several clinical conditions, such as Parkinson's disease, Schizophrenia, and Eating Disorders. Indeed, the study of these and others clinical conditions can also illuminate understanding of healthy brain function.

This Special Research Topic covers several of the different paradigms, methodologies and conditions that have been brought to bear on motivation-cognition interactions, from cognitive neuroscience, cognitive and clinical neuropsychology, to clinical psychology and psychiatry. The aim of this collection is to put together the newest evidence that has been emerging from this exciting research field, which highlights the important link between basic and clinical research, and ultimately points to the invaluable role of an interdisciplinary approach. The articles that have been collected under this topic comprise 14 contributions, which include 11 original research articles and 3 brief research reports. We encourage interested researchers to give the collected articles a thorough reading, in order to gain a complete understanding of how basic neurocognitive models of motivation-cognition interaction can be directed toward different clinical applications.

A first section of papers presents new research on healthy participants. Many of these papers yield important new insights into the nature of motivation-cognition interactions. Massar et al. provide evidence regarding the importance of considering both task type and effort levels, when

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assessing punishment (loss aversion) effects on cognitive performance. Likewise, Crawford et al. suggest the importance of considering the type of incentive, in that they found robust effects of both monetary and liquid incentives on cognitive performance and self-reported affect and motivation, but weaker motivational and affective effects for social incentives. A number of papers compared motivation-cognition interactions among younger and older adults. Interestingly, Jang et al. provided evidence for the demotivating/distracting effects of loss incentives, respectively, in the two age-groups. Bowen et al. also tested both younger and older adults, but focused on reward anticipation, to demonstrate that these incentives bolster memory in a relatively automatic, rather than strategic, fashion. In contrast, Di Rosa et al. highlight the role of anxiety among both age groups, in producing potential distracting effects of reward motivational incentives. Le et al. utilized functional neuroimaging (fMRI) to examine the neural basis of aging effects on reward motivation, observing clear evidence of age-related reductions in activity in a rewarded Go/NoGo task, that mediated the observed behavioral changes. Zhuang et al. focused on intra-individual variability, demonstrating that hormonal changes during the menstrual cycle influenced impulsivity and both activity and connectivity in frontostriatal circuits. Schiff et al. also examined intra-individual variability, finding a significant effect of fasting on the motivational modulation, by food-reward stimuli, of attentional and cognitive control mechanisms. Taken together, this first set of papers demonstrate the need to consider variables that have previously received less attention in motivation studies, such as the kind of motivational incentive being (social vs. monetary vs. food; positive vs. negative), inter-individual variability in psychological variables such as trait anxiety, and as well non-psychological intra-individual variables, such as hormonal levels or the hours from the last meal. Additionally, these papers clearly show the importance of investigating how aging can impact these mechanisms, since younger and older adults have been found to respond differently to different kinds of incentive manipulations.

A second set of papers illustrate the utility of applying motivation-cognition interaction models to the study of clinical populations. Two studies were conducted on eating disorders. In Chami et al. the researchers demonstrated the efficacy of food-specific inhibitory control training, in patients with bulimia nervosa and binge eating disorder, using an innovative paradigm based on principles related to motivation-cognitive control interaction mechanisms. In Cardi et al. the researchers analyzed the role of motivation in a self-help intervention for patients with anorexia nervosa, showing its role in predicting drop-outs, alliance with the therapist, psychological distress and the ability to change. Two studies provided new evidence on motivation-cognition mechanisms in schizophrenia. Kreis et al. reported the presence of a reduced effort investment in patients with schizophrenia, but also indicated the lack of a direct link between objective and subjective measures of effort. ten Velden Hegelstad et al. did not find any relation between motivation and memory performance in patients with psychosis, suggesting that the primary deficit may be cognitive rather than motivational in nature. Taken together, these two works clearly indicate the need to additional investigate this clinical condition, and moreover highlight the need of further investigation about the feasibility of using subjective vs. objective measures of effort. Last but not least, two original contributions concern the study of patients with mild cognitive impairment (MCI) and with Alzheimer's disease (AD). Using resting state fMRI, Wang et al. examined the effect of a music-based intervention on the intrinsic connectivity of the auditory and the reward neural systems, reporting on the presence of dysfunctional within and between-network connectivity in AD patients, when compared with individual with MCI and with healthy controls. Yin et al. analyzed data from the Chinese Longitudinal Healthy Longevity Survey, reporting a significant association between social support and rewarding activities, like children's visit, in reducing the risk of cognitive impairment among older adults.

To conclude, we are pleased to note that the Special Research Topic offers a diverse set of fourteen engaging papers, each of which addresses in its own way the theme of this issue: Motivation-Cognition interaction. We thank the Frontiers in Psychology Editorial team for their commitment to the project over the past months, the many reviewers who kindly helped us, the researchers whose work is published here and, most importantly, the participants who took part in their studies.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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ORIGINAL RESEARCH
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Social Support and the Incidence of Cognitive Impairment Among Older Adults in China: Findings From the Chinese Longitudinal Healthy Longevity Survey Study

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Objective: Social support shows a protective effect against cognitive impairment in older adults. However, the longitudinal relationship between the distinct sources of social support and the incidence of cognitive impairment remains unclear. This study aims to investigate the association between different sources of social support and the incidence of cognitive impairment among older adults in China.

Method: We used longitudinal data (2005–2014) from the Chinese Longitudinal Healthy Longevity Survey (CLHLS, 2005–2014, mean follow-up years 5.32 ± 2.64). In total, 5897 participants (aged 81.7 ± 9.7 years, range 65–112 years, 49.0% male) were enrolled. Cognitive impairment was measured by the Mini-Mental State Examination (MMSE). Social support included support from family and friends (marital status; contacts with family and friends; children's visits; siblings' visits, sick care; money received from and money given to children) and the availability of support from social community (social service and social security). We calculated subdistribution hazard ratios (SHR) of cognitive impairment by establishing Cox regression models, adjusting for residence, gender, age, education, participation in physical exercise, activities of daily living, smoking, drinking, negative psychological well-being, baseline cognitive function, occupation, leisure activities, and diseases.

Results: During a 9-year follow-up, 1047 participants developed cognitive impairment. Participants who were married had a 16.0% lower risk of developing cognitive impairment compared to the widowed older adults after controlling for all covariates, but the protective effect of being married was no longer significant ($p = 0.067$) when additional adjustment was made for all types of social support. Children's visits were significantly associated with the risk of cognitive impairment after controlling for all types of social support and covariate variables (SHR = 0.808, 95% confidence interval, 0.669–0.975, $p = 0.026$).

Conclusion: Children's visits were consistently associated with a lower incidence of cognitive impairment in Chinese older adults.

Keywords: social support, older adults, cognitive impairment, Chinese Longitudinal Healthy Longevity Survey, China

INTRODUCTION

Social support plays an important role in late life. Previous studies have shown that social support is a strong predictor of health-related quality of life, mental health, and everyday function (1, 2). Social support has been defined as "the support accessible to an individual through social ties to other individuals, groups, and the larger community" (3). It is often divided into emotional and instrumental support (2). Emotional support usually refers to the provision of caring, empathy, trust, and love (4), and instrumental support refers to the provision of tangible goods, services, or aid (4, 5).

Accumulating evidence demonstrates a protective effect of social support against cognitive decline in older adults (6, 7). MacArthur Studies of Successful Aging found that baseline social support predicted cognitive function 7.5 years later (7). A meta-analysis reported that social support associated with global cognition and memory performance in healthy older adults (6).

Although the association between social support and cognitive function is consistently observed in older adults, the longitudinal relationship between the distinct dimensions of social support and the risk of cognitive impairment remains unclear. Many studies failed to distinguish different types of social support. For example, Andrew & Rockwood used a composite "social vulnerability index" to reflect social support (8), which included emotional, instrumental, informational support from close family members, relatives, friends, and someone others. However, the protective effects of social support may differ by the types of social support. A longitudinal study reported that emotional social support showed greater protective effects on cognitive decline than instrumental support (9). As the importance of different social support sources may vary in older adults, it is meaningful to investigate the independent impact of specific sources of social support on cognitive function. For older adults, interactions with close family members (especially those who live with them) are likely to be the most influential support resources (10). Previous studies have highlighted the effect of marital status on late-life cognition. Widowhood and being single are found to be significant predictors of cognitive impairment (11–15). A cross-sectional study in China reported that family support but not support from friends was related to cognitive function (16).

In addition, the importance of different social relationships may vary in different cultural contexts. English and Carstensen (17) suggested that as social contacts of older adults decreased, the relations with their spouses and other family members comprised an important part of their social networks. Previous studies claimed that the Chinese social network structure differed from that of Western countries, as the Chinese older adults were more likely to live with their children, and their social interactions were more family-centered (18). Social support, especially emotional support from children, is one of the most important factors affecting mental health in Chinese older adults (19). Therefore, it is important to consider how various sources of social support have different impacts on cognition in Chinese contexts.

The purpose of this study is to examine the relationship between specific sources of social support and the risk of cognitive impairment in a population-based sample of Chinese older adults. We hypothesized that the protective influence of social support on the risk of cognitive impairment would differ by support sources, and support from close family members (spouses and children) would have a greater effect than other support sources.

METHODS

Study Population

Data were obtained from the Chinese Longitudinal Healthy Longevity Survey (CLHLS, http://opendata.pku.edu.cn/dataverse/CHADS). The CLHLS study was approved by the Research Ethics Committees of Duke University and Peking University. All participants provided written informed consent. The CLHLS was initiated in 1998 and follow-up surveys were conducted in 2000, 2002, 2005, 2008, 2011, and 2014. The details of the study design and data collection of CLHLS were fully described previously (20). Initially, the CLHLS project only included the oldest-old adults aged 80 and over in 22 provinces in mainland China. From 2002 onwards, the CLHLS included younger older adults aged 65–79. The present study sample included 2005–2014 longitudinal datasets. The baseline (2005) interview enrolled 8175 participants, and 300 participants who lived in nursing homes were excluded from the analysis. Then, we excluded the participants with cognitive impairment at baseline based on MMSE score, resulting in a sample of 5930 participants. In addition, 33 participants who claimed to have dementia and 14 participants who were diagnosed with dementia by the hospital were also excluded. A sample of 5897 participants with normal cognitive status was included in the analysis. **Figure 1** illustrates the flowchart of participants from baseline to the follow-up. The main reasons for the loss to follow-up were changes in home addresses and reluctance to participate due to transportation difficulties and unfavorable weather (21).

Social Support

Social support included emotional and instrumental support from family and friends and the availability of support outside the family. Specifically, social support from family and friends

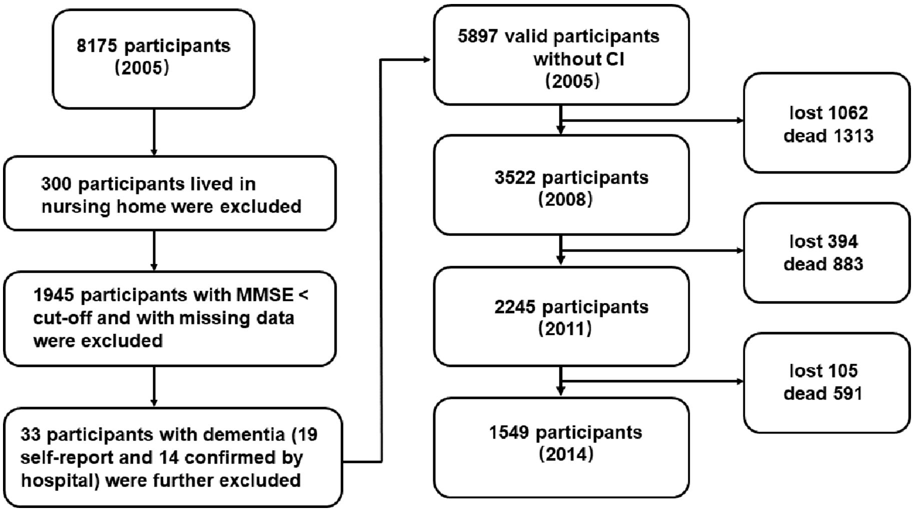

FIGURE 1 | The flowchart of the study sample from 2005 to 2014. “Lost” means the data was lost in the follow-up surveys; “dead” means the participant was dead in the follow-up surveys.

included contacts with family members and friends, children's frequent visit, siblings' frequent visit, sick care (whether family members provided care when participants were in sick), money received (whether participants received money from children), and money given (whether participants gave money to their children). In addition, marital status (married and living together; married but separated; widowed; divorced; never married) as a mixed variable was also included in the analysis.

Contacts with close family members, relatives, friends, and others were measured through three questions: “the first three people you talk to when you need to tell something about yourself,” “the first three people you ask for help when you have problems/difficulties,” and “the first three people to whom you talk most frequently in daily life.” The score of contacts with close family members, relatives, friends, and others was rated according to the answers to the three questions. If the first person was the spouse, the item “spouse” scored 3; if the second person was the spouse, the item “spouse” scored 2; otherwise, the score was 1. Items like “children,” “daughter/son-in-law,” “friends,” “other relatives,” and so on were scored under the same rule as “spouse.” Composite scores were calculated separately for each item (ranging from 3 to 9). A higher score indicated closer contact. Children's and siblings' personal information (names, gender, age, relations, alive or not, and current residence) was collected, and participants were asked whether their children and siblings visited them frequently (yes or no) to evaluate the children's visits and siblings' visits. Children's visits and siblings' visits were then recoded into dichotomous variables (whether or not children/siblings visited the participant frequently). The money received from children was measured through three questions: “how much did you receive from your son(s) or daughter(s)-in-law last year?” “how much did you receive from your daughter(s) or son(s)-in-law last year?” and “how much did you receive from your grandchild(ren) last year?” Then, money received was recoded into a trichotomous variable (yes/no/unknown). The money given to children was measured in the same way. Sick care was assessed by the question “who took care of you when you were sick?” and answers were classified into four categories: none, spouse, children, others (friends, neighbors, or nurses). Then sick care was also recoded into a trichotomous variable (yes/no/unknown).

The availability of social support outside the family included the perceived availability of social services from community and social insurance. The availability of social service was assessed by asking whether a series of services (personal care, house call physicians, psychological consulting, daily shopping, social and recreation activities, legal aid, healthcare education, and mediation of neighborhood disputes) were available in the community. The availability of social insurance was assessed by asking participants whether he or she had a series of social insurance, including retirement wage, pension, private old-age insurance, public free medical services, the cooperative medical scheme, basic medical insurance, severe disease insurance, and life insurance. All answers were classified into three categories: yes, no, and unknown (**Table 1**). Then, the availability of social service and social insurance were respectively recoded into composite dichotomous variables (whether at least one social service/insurance was available).

Cognitive Impairment

Cognitive impairment was measured by the Mini-Mental State Examination (MMSE) (22). The higher the score (0–30), the greater the cognitive ability of the participant. As most of the Chinese older adults had no formal education, several items of MMSE were simplified to make them more practical. The serial 7 subtraction was simplified to serial 3 subtraction, and reading and writing a sentence was replaced by verbally naming as many kinds of food as possible in one minute (23). As over half of the

TABLE 1 | The measurement of the availability of social security and social service.

Measurements	N		
	Yes	No	Unknown
Social security availability			
Do you have retirement wage at present?	1385	4511	1
Do you have pension at present?	278	5619	0
Do you have private old age insurance at present?	49	5848	0
Can you access to public free medical services at present?	486	5411	0
Can you access to the cooperative medical scheme at present?	614	5283	0
Do you have basic medical insurance at present?	636	5261	0
Do you have severe disease insurance at present?	256	5641	0
Do you have life insurance at present?	67	5830	0
Social service availability			
Is personal care service available in your community?	128	5765	4
Is house call physician available in your community?	573	5320	4
Is psychological consulting service available in your community?	311	5583	3
Is daily shopping service available in your community?	254	5639	4
Is social and recreation service available in your community?	719	5174	4
Is legal aid service available in your community?	480	5412	5
Is healthcare education service available in your community?	634	5258	5
Is neighborhood dispute mediation available in your community?	1260	4633	4

participants (54%) received no formal education in the present study, we used education-based MMSE cutoff points to define cognitive impairment: < 18, participants with no formal education; < 21, participants with 1–6 years of education; and <25, participants with more than 6 years of education (24, 25).

Covariables

Several control variables were adjusted in Cox models, including gender, age, residence (rural, town, city), education (years of schooling), participation in physical exercise (yes/no), activities of daily living (ADL), smoking (yes/no), drinking (yes/no), negative well-being (3–15), baseline MMSE, occupation (labor/intellectual), leisure activities, and physical diseases (yes/no).

ADL ability was measured through the Katz Index of Activities of Daily Living scale (Cronbach's $\alpha = 0.87$) (26). An index of negative well-being was used to control the potential influence of depressive symptoms, as no direct measure of depressive symptoms was included in the CLHLS questionnaire (25, 27). The index was measured by three items about neuroticism ("I often feel fearful or anxious"), loneliness ("I often feel lonely or isolated"), and perceived loss of self-worth ("The older I get, the more useless I feel"). Participants answered on a five-point Likert scale, with "1" for "does not describe me at all" and "5" for "describes me very well." The sum score on three items was the score of negative well-being, with a higher score indicating worse psychological well-being. It is the recommended measurement of depressive symptoms in CLHLS database book (27). Participation in physical exercise was measured by one question: "Do you regularly participate in physical exercise (yes or no)?" Occupation was measured by one question: "What was your primary occupation before age 60?" Nine alternative answers were offered in the questionnaire: (1) professional or technical (personnel/doctors/teachers), (2) governmental, institutional or managerial personnel, (3) staff/service worker/industrial worker, (4) self-employer, (5) agriculture, forestry, animal husbandry, fishery, (6) housewife, (7) military personnel, (8) unemployed, (9) others. Among these answers, (1) and (2) were defined as "intellectual work"; (3), (5), (6), and (7) were defined as "labor work"; (4), (8), and (9) were defined as "others." Physical diseases were measured by the question of whether participants have suffered any physical diseases, including hypertension, diabetes, heart disease, stroke and cerebrovascular disease, bronchitis, emphysema, asthma and pneumonia, pulmonary tuberculosis, cataracts, glaucoma, cancer, prostate tumor, gastric or duodenal ulcer, Parkinson's disease, bedsore, arthritis, and so on. The measurement of disease was then recoded as a dichotomous variable. In addition, the measurement of leisure activities included participants' engagement in housework, gardening, reading, playing cards/mahjong, raising pets/animals, watching TV/listening to the radio, and social activities. The answers were the frequencies of the eight activities: "almost every day," "not daily, but at least once a week," and "not weekly, but at least once a month," "not monthly, but sometimes," and "never." For each activity, "never" scored 0, and "almost every day" scored 4. The total score of eight leisure activities was also calculated.

Analysis

Cox models were established to estimate the subdistribution hazard ratio (SHR) and the 95% confidence interval of cognitive impairment was associated with social support. SPSS 23.0 for Windows (SPSS Inc., Chicago, IL, USA) was used to collate, recode and analyze the dataset. The final event was defined as cognitive impairment. The time of the incident was defined as the time from the 2005 investigation to the diagnosis of cognitive impairment.

First, all variables were separately included in regression models, adjusting for gender and age (**Table 3**). As the univariate analyses showed that contacts with spouse/children/children-in-law/friends/other relatives were not significantly associated with the risk of cognitive impairment, they were not included in further analyses.

Then, all types of social support (marital status, children's visits, siblings' visits, money given, and money received, sick care, the availability of social service and social security) entered regression models separately, controlling for all covariate variables. When children's visits and siblings' visits were examined, children alive and siblings alive were adjusted in the model respectively; when money given and money received were examined, children alive was also controlled; when sick care was examined, children alive and marital status were additionally adjusted in the model.

Finally, all types of social support entered the Cox regression simultaneously, controlling for all covariates, including gender, age, residence, education, negative well-being, ADL, drinking, smoking, exercise, MMSE baseline, disease, and leisure activities.

TABLE 2 | Sample characteristics.

	CI rate (%)	Study population (n = 5897)	Status at follow-up			
			Not CI (n = 1116)	CI (n = 1047)	Dead (n = 2266)	Lost (n = 1468)
Age						
65–74	11.8%	1689 (28.6%)	675	199	375	440
75–84	20.0%	1957 (33.2%)	375	392	674	516
85–94	21.3%	1557 (26.4%)	59	331	791	376
95–112	18.0%	694 (11.8%)	7	125	426	136
Gender						
Female	20.2%	3009 (51.0%)	555	607	1056	791
Male	15.2%	2888 (49.0%)	561	440	1210	677
Education						
0 years	20.0%	3172 (53.9%)	533	633	1308	698
1–6 years	14.3%	2023 (34.2)	438	290	781	514
6+ years	17.7%	702 (11.9)	145	124	177	256
Residence						
Rural	19.2%	3301 (56.0%)	695	634	1387	585
City	15.3%	1284 (21.8%)	184	196	363	541
Town	16.5%	1312 (22.2%)	237	217	516	342
Marital status						
Widowed	20.5%	3253 (55.3%)	403	667	1394	789
Married	14.6%	2448 (41.5%)	669	358	783	638
Separated	9.0%	145 (2.4%)	33	13	69	30
Divorced	16.0%	25 (0.4%)	4	4	11	6
Never married	19.2%	26 (0.4%)	7	5	9	5
ADL						
Impaired (> 6)	18.7%	791 (13.3%)	17	146	420	199
Normal (6)	17.6%	5115 (86.7%)	1099	901	1846	1269
Physical exercise						
Yes	16.5%	2289 (38.7%)	385	377	875	652
No	18.6%	3608 (61.3%)	731	670	1391	816
Smoking						
Yes	15.1%	2204 (37.4%)	396	332	933	543
No	19.4%	3693 (62.6%)	720	715	1333	925
Drinking						
Yes	17.6%	1887 (31.9%)	323	332	798	434
No	17.8%	4010 (68.1%)	793	715	1468	1034
Negative well-being						
3–8	17.2%	4637 (78.3%)	918	796	1726	1177
9–15	19.6%	1293 (21.7%)	198	251	540	291
Children's visit						
Yes	17.4%	4997 (84.7%)	1005	867	1874	1251
No	20.0%	900 (15.3%)	111	180	392	217
Children alive						
Yes	17.7%	5649 (95.8%)	1089	1001	2157	1402
No	18.5%	248 (4.2%)	27	46	109	66
Siblings' visit						
Yes	15.6%	1992 (33.8%)	554	310	639	489
No	18.9%	3905 (66.2%)	562	737	1627	979
Siblings alive						
Yes	16.6%	3388 (57.4%)	846	563	1112	867
No	19.3%	2509 (42.6%)	270	484	1154	601
Money given						
Yes	15.8%	1574 (26.6%)	377	249	523	425
No	18.4%	4192 (71.1%)	716	773	1697	1006
Unknown	19.1%	131 (2.2%)	23	25	46	37
Money received						
Yes	18.1%	5015 (85.0%)	939	910	1979	1187
No	14.7%	726 (12.4%)	151	107	232	236
Unknown	19.2%	156 (2.6%)	26	30	55	45
Sick care						
Yes	17.4%	5577 (94.6%)	1075	970	2148	1384
No	24.8%	129 (2.2%)	26	32	45	26

(Continued)

TABLE 2 | Continued

	CI rate (%)	Study population (n = 5897)	Status at follow-up			
			Not CI (n = 1116)	CI (n = 1047)	Dead (n = 2266)	Lost (n = 1468)
Unknown	23.6%	191 (3.2%)	15	45	73	58
Social security						
Yes	15.2%	2256 (38.3%)	430	343	697	786
No	19.3%	3641 (61.7%)	686	704	1569	682
Social service						
Yes	17.0%	1911 (32.4%)	341	325	652	593
No	18.1%	3986 (67.6%)	775	722	1614	875
Disease						
Yes	17.9%	3245 (55.0%)	592	582	1238	833
No	17.5%	2652 (45.0%)	524	465	1028	635
Occupation						
Labor	18.3%	5034 (85.4%)	950	923	2000	1166
Intellectual	13.7%	652 (11.1%)	127	89	185	251
Others	16.6%	211 (3.5%)	39	35	81	56
Baseline MMSE						
18–20	24.5%	314 (5.3%)	21	77	145	71
21–24	24.3%	913 (15.5)	85	222	406	200
25–30	16.0%	4670 (79.2%)	1010	748	1715	1197

Married: married and living with the spouse; Separated: married and not living with the spouse.
CI, cognitive impairment; ADL, activities of daily living, MMSE, Mini-Mental State Examination.

RESULTS

Out of 5897 participants at baseline, 1047 (17.8%) developed cognitive impairment (mean follow-up years 5.12 ± 2.32), 2266 (38.4%) were dead at the follow-up (mean follow-up years 4.57 ± 2.22), 1468 (24.9%) were lost to follow-up (mean follow-up years 3.83 ± 1.69), and 1116 (18.9%) maintained normal cognitive status (mean follow-up years 9.06 ± 0.32) at the end of the survey. **Table 2** presented the characteristics of the participants.

When gender and age were adjusted, the univariate Cox regression showed that marital status, children's visits, sibling's visits, siblings alive, money given, and the availability of social insurance were significantly related to the risk of cognitive impairment, separately (**Table 3**). However, after adjusting for all covariate variables, only marital status and children's visits had significant impacts on the incidence of cognitive impairment (**Table 4**).

When all covariates were controlled, the univariate Cox regression showed that participants who were married had a 16.0% lower risk of developing cognitive impairment compared to the widowed older adults (SHR = 0.840, 95% confidence interval 0.722–0.976, p = 0.023; **Table 4**). However, when all types of social support and covariates were included in the regression, the protective effect of being married was no longer significant (p = 0.067; **Table 5**).

Children's visits had a stable impact on the incidence of cognitive impairment in univariate and multivariate analyses (**Tables 4**, **5**). Participants who were frequently visited by their children had a 19.2% lower risk of developing cognitive impairment compared to those who were not (SHR = 0.808, 95% confidence interval, 0.669–0.975, p = 0.026) even after controlling for all other types of social support and covariate variables.

DISCUSSION

In the present study, the association between social support and cognitive impairment was investigated in a representative population-based sample of Chinese older adults during a 9-year follow-up. We found that emotional support from children (children's visits) was consistently associated with a lower incidence of cognitive impairment in older adults.

With aging, the social contact of older adults decreases, and the relations with spouse and family members are a major part of their social networks (17). Thus, we hypothesized that family relations were one of the major factors that influenced cognitive function in older adults. Stable marital relationships and good relationships with children and relatives ensured daily care, family comfort, and social support for older adults (28). However, those who are widowed, divorced, or living alone lack spiritual and marital support, which may cause loneliness, insecurity, and negative attitude toward life (29), leaving them vulnerable to psychological and cognitive pathology (30).

The results partially supported the hypothesized association between family relations and the risk of cognitive impairment in Chinese older adults. Children's visits were constantly associated with a decreased risk of cognitive impairment in both univariate and multivariate analyses. Being married showed a protective effect against cognitive impairment in the univariate Cox regression compared with being widowed, but this protective effect failed to survive after controlling for other types of social support (p = 0.067). The result is consistent with some previous studies which found widowed older adults did not have a higher risk of cognitive impairment or dementia compared to their married counterparts (14, 31). The results also showed that older adults who were married but not living with their spouse had a lower risk of

TABLE 3 | The univariate Cox analysis of all variables (demographic variables and social support) oncognitive impairment.

Demographic variables			Social support		
	SHR (95% CI)	***p***		**SHR (95% CI)**	***p***
Age	1.084 (1.077–1.091)	**<0.001**	Marital status	Reference (widowed)	
Gender	0.786 (0.695–0.889)	**<0.001**	Married	0.790 (0.682–0.916)	0.002
Residence	Reference (rural)		Separated	0.379 (0.218–0.658)	**<0.001**
City	0.889 (0.756–1.045)	0.155	Divorced	0.756 (0.282–2.025)	0.578
Town	0.925 (0.793–1.080)	0.325	Never married	1.555 (0.641–3.771)	0.329
Education	0.989 (0.971–1.008)	0.271	Children's visit	0.766 (0.652–0.900)	**<0.001**
Negative well-being	1.077 (1.049–1.106)	**<0.001**	Children alive	0.824 (0.613–1.108)	0.201
ADL	1.135 (1.084–1.190)	**<0.001**	Siblings' visit	0.844 (0.734–0.972)	0.018
Drinking	1.244 (1.080–1.434)	0.003	Siblings alive	0.865 (0.758–0.986)	0.030
Smoking	0.974 (0.838–1.132)	0.730	C_spouse	0.984 (0.966–1.001)	0.068
Exercise	0.979 (0.861–1.112)	0.742	C_children	1.007 (0.985–1.030)	0.540
Disease	1.124 (0.995–1.270)	0.061	C_children in law	1.016 (0.987–1.045)	0.290
Occupation	Reference (labor)		C_relatives	0.998 (0.950–1.048)	0.923
Intellectual	0.862 (0.689–1.079)	0.195	C_friends	1.011 (0.977–1.044)	0.549
Others	0.920 (0.655–1.291)	0.629	Money given	Reference (no)	
Baseline MMSE	0.925 (0.907–0.943)	**<0.001**	Yes	0.820 (0.710–0.948)	0.007
Leisure activities	0.956 (0.945–0.967)	**<0.001**	Unknown	1.050 (0.705–1.564)	0.811
			Money received	Reference (no)	
			Yes	1.163 (0.950–1.424)	0.143
			Unknown	1.358 (0.906–2.038)	0.139
			Sick care	Reference (no)	
			Yes	0.718 (0.504–1.021)	0.065
			Unknown	1.259 (0.798–1.987)	0.322
			Social security	0.864 (0.756–0.987)	0.031
			Social service	1.026 (0.899–1.170)	0.706

All variables were included in model separately, after controlling for gender, age.

Married: married and living with the spouse; Separated: married and not living with the spouse; C_spouse: contacts with spouse; C_children: contacts with children; C_children in law: contacts with children-in-law; C_relatives: contacts with relatives; C_friends: contacts with friends and neighbors. Money given: whether participants gave money to their children or not in the past year; Money received: whether participants received money from their children or not in the past year. Sick care: whether family members' care is available or not when participants are in sick.

SHR, subdistribution hazard ratio; 95% CI, 95% confidence interval.

cognitive impairment compared to the widowed participants even when all types of social support and covariates were adjusted. As the number of participants who were married but not living with their spouse was relatively small (n = 145, 2.4% of the sample), the finding should be interpreted with great caution.

The main finding of the present study suggests the importance of emotional support from children in maintaining cognitive ability in Chinese older population. In general, the old parents in China lean on their children for financial support more or less. Numbers of studies found that both the provision and receipt of social support played an important role in cognitive function in older adults (32–35). Interestingly, the current study found that those participants who gave money to their children had the same risk of cognitive impairment as those who did not; also, there was no difference in the risk of cognitive impairment between participants who received money from their children and those who did not. Consistent with a previous study, Ellwardt et al. found that instrumental support did not buffer cognitive decline (9). The result might indicate that both the provision and receipt of instrumental support of children was not a vital factor in cognitive decline.

According to Berkman's theoretical model, social support refers to a person's perception of support availability in their social network (2), which does not emphasize the difference between specific resources of social support. However, different resources of social support probably play different roles in cognitive impairment. For example, a survey on Chinese older adults reported that emotional support from children is one of the most important factors in affecting mental health (19). Zhu, Hu, and Efird also found that compared to support from friends and important others, support from family was the most important indicator of older adults' cognitive function (16). However, previous studies in America reported opposite results. Brown et al. and Ficker et al. found that it was friends' support rather than family's support that had a greater impact on cognitive function of older adults (36, 37). Zhu et al. proposed that these contradictory results could be explained from the perspective of cultural differences (16).

In Chinese family culture, the social networks of older adults are more family-centered, which stresses the contact between older parents and other family members. In addition, traditional Chinese culture advocates filial piety, which is the reflection of the blood ties between parents and children in families. The traditional filial morality contributes to the development of personal morals and Chinese children are expected to take good care of and respect their parents when they are old. For many old Chinese parents, children are their important spiritual pillar and the contacts with children bring them a lot of happiness. The essence of filial piety is love, which implies gratefulness, respect, generosity, happiness, and selflessness.

TABLE 4 | The univariate Cox analysis of social support on cognitive impairment.

Social support	SHR (95% CI)	*p*
Marital status	Reference (widowed)	
Married	0.840 (0.722–0.976)	0.023
Separated	0.419 (0.241–0.728)	0.002
Divorced	0.666 (0.247–1.799)	0.423
Never married	1.403 (0.577–3.415)	0.455
Children's visit	0.798 (0.664–0.960)	0.017
Siblings' visit	0.906 (0.765–1.072)	0.250
Money give	Reference (no)	
Yes	0.895 (0.773–1.036)	0.138
Unknown	0.932 (0.593–1.465)	0.761
Money receive	Reference (no)	
Yes	1.088 (0.883–1.340)	0.430
Unknown	1.170 (0.745–1.837)	0.496
Sick care	Reference (no)	
Yes	0.776 (0.541–1.113)	0.168
Unknown	1.154 (0.719–1.852)	0.553
Social security	0.987 (0.849–1.148)	0.867
Social service	1.071 (0.936–1.226)	0.318

The variables were included in model separately, after controlling for gender, age, residence, negative well-being, ADL, drink, smoking, education, exercise, baseline MMSE, occupation, disease, and leisure activities. When children's visit and siblings' visit were examined, children alive and siblings alive was additional adjusted in the model respectively; when money given to and money received from children were examined, children alive was also controlled; when sick care was examined, children alive and marital status were additional adjusted in the model. For marital status, Married maps married and living with the spouse; Separated maps married and not living with the spouse.

TABLE 5 | The multivariable Cox analysis of all variables on cognitive impairment.

	SHR (95%CI)	*p*
Gender	0.876 (0.739–1.039)	0.128
Age	1.066 (1.058–1.075)	**<0.001**
Residence	Reference (rural)	
City	0.932 (0.769–1.130)	0.475
Town	0.918 (0.782–1.078)	0.296
Education	1.023 (0.993–1.041)	0.056
Negative well–being	1.038 (1.009–1.068)	0.009
ADL	1.064 (1.010–1.121)	0.019
Drinking	1.261 (1.085–1.465)	0.002
Smoking	0.906 (0.772–1.064)	0.230
Exercise	1.028 (0.895–1.182)	0.692
Baseline MMSE	0.944 (0.924–0.965)	**<0.001**
Disease	1.107 (0.976–1.255)	.114
Occupation	Reference (labor)	
Intellectual	0.995 (0.752–1.315)	0.971
others	0.961 (0.682–1.354)	0.821
Leisure activities	0.972 (0.958–0.985)	**<0.001**
Marital status	Reference (widowed)	
Married	0.867 (0.744–1.010)	0.067
Separated	0.432 (0.248–0.752)	0.003
Divorced	0.599 (0.217–1.656)	0.323
Never married	1.023 (0.376–2.781)	0.964
Children's visit	0.808 (0.669–0.975)	0.026
Children alive	1.099 (0.747–1.619)	0.631
Siblings' visit	0.909 (0.767–1.077)	0.269
Siblings alive	0.991 (0.845–1.163)	0.912
Money given	Reference (no)	
Yes	0.895 (0.771–1.039)	0.144
Unknown	0.608 (0.264–1.403)	0.244
Money received	Reference (no)	
Yes	1.119 (0.905–1.384)	0.300
Unknown	1.592 (0.737–3.440)	0.237
Sick care	Reference (no)	
Yes	0.795 (0.550–1.148)	0.220
Unknown	1.168 (0.724–1.885)	0.525
Social security	1.003 (0.858–1.171)	0.972
Social service	1.071 (0.932–1.230)	0.332

All variables were included into model together. For marital status, Married maps married and living with the spouse; Separated maps married and not living with the spouse.

Numbers of studies have found that filial piety was closely associated with subjective happiness, depression, and life satisfaction (37–39). The result of the present study is in line with the expectations, and evidence suggests only children's visits, not "being married and living with the spouse," can predict the cognitive decline in older adults. Social service, social security, or instrumental support from children cannot always predict older adults' cognitive decline, which confirmed the irreplaceable role of emotional support from children.

There are some limitations in the present study. Cognitive function was solely assessed by the MMSE, without clinical evaluation or other cognitive tests. The MMSE is a brief measure of global cognitive function, which might not be sensitive enough to screen the early stage of cognitive impairment or detect changes in cognitive function. Similarly, the measurement of social support was recoded according to the existing variables in the CLHLS questionnaire, and hence, there were unavoidable repetitions in the contents of these variables. For example, contacts with children overlapped with children's visits to some extent. However, the current analysis distinguished between the various resources of social support according to existing variables, which made a difference compared to previous studies. In addition, the measurements of social service and social security were used to assess the perceived availability of social service/security, which was not exactly the same as received social service/security. Perceived availability of social support and received social support are considered as related but different sub-constructs.

CONCLUSION

In Chinese older adults, emotional support from children (children's visits) was consistently associated with a lower incidence of cognitive impairment after adjusting for all types of social support and covariates.

DATA AVAILABILITY STATEMENT

The CLHLS datasets are publicly available at the Peking University Open Research Data on CLHLS (http://opendata.pku.edu.cn/dataverse/CHADS). The dataset is publicly accessible to scholars for non-profit purposes. A signed data user agreement is required before data can be obtained.

ETHICS STATEMENT

The study is a secondary analysis of the data from the CLHLS (http://opendata.pku.edu.cn/dataverse/CHADS), a collaborative project conducted by Duke University and Peking University. The CLHLS study was approved by the Research Ethics Committees of Duke University and Peking University. All participants provided written informed consent.

AUTHOR CONTRIBUTIONS

SY: study design, analysis of the raw data, interpretation of data, revision of the manuscript. QY: further data analysis, revision of the manuscript. JX: revision of the manuscript. TL: further data analysis, interpretation of data, draft and revision of the manuscript. XZ: developed the research question, interpretation of data, revision of the manuscript. All authors contributed to and have approved the final manuscript.

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The Feasibility of Using Guided Self-Help in Anorexia Nervosa: An Analysis of Drop-Out From the Study Protocol and Intervention Adherence

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The implementation of online technologies to promote wellbeing is increasingly becoming a worldwide priority. This study includes secondary analyses of data and examined drop-out rates in an online guided self-help intervention for patients with anorexia nervosa. Specifically, rates of drop-out at end of treatment (i.e., 6 weeks assessment), as well as intervention adherence (minimum of four of six online guided sessions) and differences between completers and drop-outs were examined. Motivation to change and associated patient variables were assessed as predictors of drop-out using structural equation modeling. Ninety-nine patients were randomized to the intervention arm of the trial. Data were available for 82 individuals, 67 of whom completed the 6 weeks assessment and attended a minimum of four online sessions. No significant differences were found between completers and drop-outs at baseline. At the end of the first week of participation, drop-outs from the 6 weeks assessment or the intervention reported less satisfaction with their work with the mentor delivering online guidance. Greater confidence in own ability to change and higher controlled motivation (willingness to change due to pressure from others) predicted lower drop-out rates from the 6 weeks assessment. Stronger alliance with the therapist at the treatment center and lower psychological distress were associated with greater autonomous motivation (self-directed motivation) and importance and ability to change. Data demonstrate that a novel online guided self-help intervention for patients with anorexia nervosa is feasible. Early satisfaction with the program and external pressure to change have a protective role against drop-out rates.

Clinical Trial Registration: www.ClinicalTrials.gov, identifier NCT02336841.

Keywords: anorexia nervosa, drop-out, intervention, motivation, online, trial

INTRODUCTION

The World Health Organization (WHO) has established the use of online technologies to support wellbeing (eHealth) as a priority (World Health Organization, 2016). This challenge has been embraced by mental health professionals and researchers, as demonstrated by a large increase in the utilization of technological aids in the prevention and treatment of mental health issues

(Zhang and Ho, 2015). One of the main advantages of developing and implementing online mental health programmes is that they can be more easily disseminated to, and received by patients, compared to standard face-to-face therapies. This is particularly relevant for mental illnesses that are difficult to identify, for which access to specialized services is challenging and that are marked by high levels of stigmatization and shame. At the same time, concerns have been raised regarding the high drop-out rates from online interventions (on average 31%) among people with psychological disorders (Melville et al., 2010) and recent studies have highlighted the need for more research on patient individual factors associated with drop-out (Fernández-Álvarez et al., 2017). The aim of this paper is to examine dropout from a novel online guided self-help intervention in anorexia nervosa.

Patients with eating disorders are difficult to identify and treat, despite the burden that the illness poses on the individual, their families and the society (Aardoom et al., 2016). Only a subgroup of individuals receives appropriate treatment (Hart et al., 2011), whilst others struggle with barriers such as poor availability of specialized services and high levels of shame and fear of criticism related to the illness (Cachelin and Striegel-Moore, 2006; Becker et al., 2010). In recent years, there has been a large increase in the use of computerized interventions for patients with eating disorders, especially for prevention and to treat symptoms of loss of control over-eating and purging using cognitive-behavioral principles and techniques (Aardoom et al., 2013; Schlegl et al., 2015). Most of these interventions include self-help materials and different forms of guidance delivered by health professionals or lay people and are overall associated with reduced eating disorder psychopathology (medium effect size) and binge abstinence (small effect size) (Traviss-Turner et al., 2017). However, drop-out rates from manualized self-help interventions for eating disorders vary greatly across studies (ranging between 1 and 88%; Beintner et al., 2014), and intervention- and person-related variables associated with early drop-out from study protocols and interventions are largely unknown (e.g., Barakat et al., 2019).

Data on the efficacy and acceptability of online treatments are particularly scarce in anorexia nervosa. This might be justified by cautiousness and concerns regarding the use of non-traditional forms of therapy (e.g., regular and intensive face-to-face contact with a mental health professional) with individuals at risk of medical complications (Wilson and Zandberg, 2012). However, more recent findings from a systematic review and meta-analysis on task-sharing interventions in anorexia nervosa (Albano et al., 2019) suggest that guided self-help in this condition is associated with lower drop-out rates from the study protocol than a comparison condition (either waiting list or inpatient/outpatient treatment protocols). Based on this evidence, as well as the high rates of patients who do not complete or relapse from treatment and their strong ambivalence toward change (Schmidt and Treasure, 2006; Fassino et al., 2009; DeJong et al., 2012) we suggest that the use of online guided self-help to complement standard care in anorexia nervosa is worth exploring.

We developed a 6 weeks online guided self-help intervention for patients with anorexia nervosa (*Recovery*MANTRA) and compared the efficacy of adding this intervention to Treatment As Usual (TAU; standard care consisting of medical monitoring and psychological support) against TAU alone in a randomized controlled trial (i.e., SHARED) of patients with anorexia nervosa assessed for outpatient treatment (Cardi et al., 2015). Findings indicated that patients receiving *Recovery*MANTRA in addition to TAU reported higher confidence in own ability to change (p = 0.02, small effect size), greater alliance with the therapist at the outpatient service (p = 0.005, small to medium effect size) and trend-level greater reductions in anxiety (p = 0.06, small effect size) at 6 weeks, compared to a control group (Cardi et al., 2019). *Recovery*MANTRA challenges positive beliefs about the illness and other maintaining factors, including cognitive rigidity, emotion regulation difficulties, isolation and food restriction (Schmidt and Treasure, 2006; Treasure and Schmidt, 2013). It focuses on the use of behavior change techniques and weekly online support from mentors (i.e., recovered individuals, carers of people with lifetime eating disorders) and graduate psychology students trained in motivation interviewing (Cardi et al., 2015). The greatest emphasis of *Recovery*MANTRA is on empowering individuals by increasing their motivation and confidence to change (Cardi et al., 2015). This is consistent with the assumptions of self-determination theory that underpins the intervention and also with the evidence that a patient's motivation to change predicts outcome and drop-out in eating disorders (Vall and Wade, 2015; Thaler et al., 2016). Patient autonomous motivation to change before treatment (i.e., motivation to change due to a patient's intrinsic motivation), in particular, appears related to lower levels of eating disorder symptoms at the end of treatment (Mansour et al., 2012; Thaler et al., 2016) or to faster improvement in these symptoms (Carter and Kelly, 2015). On the other hand, controlled motivation (i.e., motivation to change due to pressure from others or the desire to avoid negative feelings, such as shame and guilt) has not been found to predict treatment outcomes (Mansour et al., 2012; Carter and Kelly, 2015; Thaler et al., 2016).

This study conducted secondary analyses of data from the SHARED trial (as published in Cardi et al., 2015, 2019) and examined drop-out rates (i.e., non-completion of end-of-intervention assessment measures) and intervention adherence rates (adherence defined as attendance of a minimum of four of six sessions) to establish the acceptability of delivering *Recovery*MANTRA to patients. The drop-out and completer groups were compared in terms of baseline socio-demographic and clinical variables and eating behaviors, usage of the self-help materials and perceived quality of the relationship with the online mentor at the end of the first week of project participation. Baseline motivation to change among patients (i.e., autonomous motivation, controlled motivation, importance to change and confidence in own ability to change) and related patient variables were considered to predict drop-out from the 6 weeks assessment and drop-out from the intervention.

Based on a number of studies available in the literature on the use of technology-based interventions in eating disorders (Schlegl et al., 2015), no differences in clinical (i.e., illness severity) or demographic (i.e., age, years of education) variables between those who did and did not drop-out were expected at baseline. However, it was hypothesized that there would be differences between groups in terms of perceived quality of the relationship with the mentor within the first week of receiving *Recovery*MANTRA (for a review on the importance of considering process measures earlier on when delivering technology-based interventions; see Kelders et al., 2012). In particular, it was expected for completers to report greater satisfaction with the mentor allocated to them and their work together. Based on past findings in the eating disorder literature (Mansour et al., 2012; Carter and Kelly, 2015; Thaler et al., 2016), it was also predicted that higher levels of autonomous motivation to change and higher levels of importance and confidence in one's own ability to change would be associated with lower rates of drop-out from the end-of-intervention assessment and from *Recovery*MANTRA.

MATERIALS AND METHODS

Participants

This longitudinal study was part of a multi-center, two-armed trial comparing the effects of treatment as usual (TAU) complemented by guided self-help (*Recovery*MANTRA) to the effects of TAU alone on clinical outcomes of patients with anorexia nervosa assessed for outpatient treatment (Cardi et al., 2015, 2019). The purpose of this study was to investigate drop-out rates from completing the assessment measures at the end of the intervention (i.e., drop-out from the assessment) as well as drop-out from *Recovery*MANTRA (i.e., drop-out from the intervention defined as attendance of less than four out of six online guided sessions) in the group of individuals randomized to receive *Recovery*MANTRA in addition to TAU. This group was composed of 99 individuals, aged 16 or over and with a diagnosis of anorexia nervosa or atypical/partial anorexia nervosa according to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (American Psychiatric Association, 2013; definition of atypical anorexia nervosa as follows: fulfillment of all diagnostic criteria, except the weight criterion or amenorrhea or fat phobia; definition of partial anorexia nervosa, as follows: having features of the illness, but missing at least two of the four diagnostic criteria, Thomas et al., 2009). Participants were recruited between April 2015 and December 2016 from 22 eating disorder outpatient services across the United Kingdom. The investigation was carried out in accordance with the latest version of the Declaration of Helsinki and the study design was reviewed by an appropriate ethical committee (Research Ethics Committee of London-Brent, project reference number: 14-LO-1347). Informed consent of the participants was obtained after the nature of the procedures had been fully explained. Exclusion criteria were: (a) life-threatening anorexia nervosa as defined in the NICE guidelines, (b) insufficient knowledge of English, and (c) severe mental or physical illness needing treatment in its own right (e.g., psychosis or diabetes mellitus). Due to missing data on key baseline variables, 17 subjects were excluded from the analyses. The final sample included 82 subjects and their clinical and sociodemographic characteristics are shown in **Table 1**.

Measures

Participants completed a baseline assessment consisting of the following measures:

Demographic and clinical survey, to collect information on age, gender, ethnicity, years of education, employment and social status, duration of illness, time of illness onset, diagnosis and first treatment received, previous hospital admissions, psychiatric comorbidity and medication and self-reported body mass index (BMI).

Autonomous and Controlled Motivations for Treatment Questionnaire (ACMTQ; Zuroff et al., 2007), a 12-item self-report questionnaire which consists of two six-item subscales assessing autonomous motivation and controlled motivation for treatment. Participants are asked to rate the extent to which they agree with each statement using a seven-point rating scale. The ACMTQ showed good/acceptable internal consistency in this study (Cronbach's α values: 0.89 and 0.71 for autonomous and controlled motivation subscales, respectively).

Importance and confidence in own ability to change were assessed using two self-developed single-items Likert scales ranging from 1 ("not important at all"/"not confident at all") to 10 ("extremely important"/"extremely confident in my ability to change"). This questionnaire is available in **Supplementary Material**.

Eating Disorder Examination Questionnaire (EDE-Q; Fairburn and Beglin, 1994), a 36-item self-report measure of eating disorder symptoms. The EDE-Q has been widely validated in clinical and non-clinical groups (Mond et al., 2004) and shows good reliability and validity. Items are rated on a six-point Likert scale, where higher scores indicate a greater level of eating pathology. For the purpose on the present study, only the total score was used (Cronbach's α:0.92).

Depression, Anxiety and Stress Scales (DASS-21; Lovibond and Lovibond, 1995) is a 21-item self-report measure of patients' psychological distress over the past 7 days. Items are scored on a four-point Likert scale. It includes three subscales (i.e., anxiety, depression, and stress), but only the total score was considered in this study (Cronbach's α:0.91).

Work and Social Adjustment Scale (WSAS; Mundt et al., 2002), a five-item self-report scale designed to assess patients' perceptions of impairment in everyday functioning resulting from a given problem. The scale evaluates functioning in the following domains: work, home management, social and private leisure activities, and close relationships. Scores for each item range from 0 to 8 and higher scores reflect more severe functional impairment. The WSAS demonstrated acceptable internal consistency in this study (Cronbach's α:0.73).

Alliance with therapist delivering TAU at the outpatient treatment centre was evaluated using five self-developed visual analogs scales [ranging from 0 (never) to 7 (always)] assessing patients' feelings that the therapist understood them, could be trusted, and that they worked toward mutually agreed and relevant goals. A mean score of the five scales was calculated to reflect overall alliance and used in this study (Cronbach's α: 0.92). This questionnaire is available in **Supplementary Material**.

TABLE 1 | Participants' demographics and clinical variables.

		Drop-out from the assessment				**Drop-out from the intervention**			
	Total group (n = 82)	**Completers (n = 67)**	**Drop-outs (n = 15)**	**Test and *p*-values**	**Cohen's d ES**	**Completers (n = 70)**	**Drop-outs (n = 12)**	**Test and *p*-values**	**Cohen's d ES**
	Mean (*SD*)	**Mean (*SD*)**	**Mean (*SD*)**	**Completer vs. Drop-out groups**		**Mean (*SD*)**	**Mean (*SD*)**	**Completer vs. Drop-out groups**	
BASELINE VARIABLES									
Age	26.57 (8.29)	27.03 (8.86)	24.53 (4.67)	$t(80) = 1.05$ $p = 0.294$	0.35	26.81 (8.73)	25.17 (4.99)	$t(80) = 0.63$ $p = 0.528$	0.23
Years of education	15.78 (2.59)	15.87 (2.54)	15.33 (2.87)	$t(72) = 0.66$ $p = 0.514$	0.20	15.85 (2.50)	15.33 (3.28)	$t(72) = 0.55$ $p = 0.581$	0.18
Body mass index	16.09 (1.41)	16.06 (1.41)	16.24 (1.43)	$t(80) = -0.45$ $p = 0.652$	0.13	16.06 (1.42)	16.24 (1.39)	$t(80) = -0.40$ $p = 0.690$	0.13
Duration of illness	6.75 (7.80)	7.22 (8.33)	4.67 (4.35)	$t(80) = 1.15$ $p = 0.255$	0.38	7.04 (8.20)	5.08 (4.75)	$t(80) = 0.80$ $p = 0.426$	0.29
Eating Disorder Examination Questionnaire	4.01 (1.14)	3.91 (1.13)	4.43 (1.13)	$t(80) = -1.61$ $p = 0.112$	0.46	3.92 (1.10)	4.53 (1.26)	$t(80) = -1.75$ $p = 0.084$	0.52
Depression Anxiety and Stress Scales	59.71 (23.49)	58.15 (21.99)	66.67 (29.13)	$t(80) = -1.27$ $p = 0.206$	0.33	57.89 (21.78)	70.33 (30.75)	$t(80) = -1.72$ $p = 0.090$	0.47
Work and Social Adjustment Scale	19.91 (7.86)	19.85 (7.60)	20.20 (9.21)	$t(80) = -0.15$ $p = 0.877$	0.04	19.90 (7.58)	20.00 (9.70)	$t(80) = -0.04$ $p = 0.968$	0.01
Importance to change	7.85 (2.19)	7.76 (2.22)	8.27 (2.09)	$t(80) = -0.81$ $p = 0.422$	0.24	7.81 (2.20)	8.08 (2.19)	$t(80) = -0.39$ $p = 0.697$	0.12
Confidence in own ability to change	5.19 (2.34)	5.32 (2.31)	4.60 (2.47)	$t(80) = 1.09$ $p = 0.279$	0.30	5.34 (2.29)	4.33 (2.57)	$t(80) = 1.39$ $p = 0.169$	0.41
Autonomous Motivation	4.84 (0.98)	4.83 (1.02)	4.86 (0.81)	$t(80) = -0.08$ $p = 0.937$	0.03	4.86 (1.01)	4.72 (0.82)	$t(80) = 0.44$ $p = 0.662$	0.15
Controlled Motivation	4.63 (0.91)	4.69 (0.93)	4.36 (0.78)	$t(80) = 1.29$ $p = 0.202$	0.38	4.63 (0.96)	4.60 (0.61)	$t(80) = 0.13$ $p = 0.900$	0.04
Alliance with therapist	4.84 (1.30)	4.92 (1.26)	4.49 (1.46)	$t(80) = 1.14$ $p = 0.256$	0.31	4.95 (1.24)	4.17 (1.45)	$t(80) = 1.98$ $p = 0.051$	0.58
Cognitive and behavioral flexibility	3.51 (1.06)	3.50 (0.97)	3.53 (1.43)	$t(80) = -0.11$ $p = 0.913$	0.02	3.53 (1.00)	3.37 (1.38)	$t(80) = 0.46$ $p = 0.645$	0.13
VARIABLES AT WEEK 1									
Confidence in own ability to change week 1	2.53 (1.02)	2.62 (1.01)	2.00 (0.89)	$t(76) = 1.88$ $p = 0.064$	0.65	2.59 (1.01)	2.00 (0.93)	$t(76) = 1.56$ $p = 0.123$	0.61
Hope week 1	2.53 (1.03)	2.60 (1.00)	2.00 (1.09)	$t(76) = 1.81$ $p = 0.074$	0.57	2.57 (1.00)	2.00 (1.19)	$t(76) = 1.50$ $p = 0.138$	0.52
Restriction week 1	0.75 (1.05)	0.72 (1.01)	0.92 (1.26)	$t(78) = -0.65$ $p = 0.519$	0.17	0.71 (1.01)	1.00 (1.33)	$t(78) = -0.65$ $p = 0.529$	0.25
Purging week 1	0.30 (0.75)	0.19 (0.63)	0.85 (1.07)	$t(78) = -2.13$ $p = 0.052$	0.61	0.21 (0.66)	0.90 (1.10)	$t(78) = -1.92$ $p = 0.084$	0.76
Use of self−help materials week 1	1.68 (0.47)	1.65 (0.48)	1.80 (0.42)	$t(60) = -0.98$ $p = 0.344$	0.33	1.67 (0.47)	1.71 (0.49)	$t(60) = -0.22$ $p = 0.828$	0.08
Comfortable working with mentor week 1	5.04 (1.68)	5.19 (1.61)	4.00 (1.87)	$t(70) = 2.03$ $p = 0.046$	0.68	5.17 (1.62)	3.67 (1.86)	$t(70) = 2.14$ $p = 0.036$	0.86
Agreed goals with mentor week 1	4.82 (1.74)	5.06 (1.60)	3.30 (1.89)	$t(71) = 3.15$ $p = 0.002$	1.00	4.94 (1.69)	3.71 (1.98)	$t(71) = 1.80$ $p = 0.077$	0.67

Demographic and clinical variables are expressed as means and standard deviations (SDs). Means and SDs are presented for the entire sample, as well as for completers and drop-outs, separately.

Cognitive and behavioral flexibility were assessed using four self-developed visual analog scales (ranging from 0 – never, to 7 – always) measuring the patient's attention to details and use of rigid behaviors. This questionnaire is available in **Supplementary Material**.

These measures, except for the demographic and clinical survey, were repeated at 6 weeks. Additionally, patients completed daily assessments of importance and confidence in their ability to change and hope (all measured using visual analogue scales ranging from 1 "not at all" to 5 "extremely"). They also completed weekly measures of frequency of eating disorder behaviors (restriction, purging, over-exercising, on a Likert scale ranging from 0: “0 days,” to 3: “6–7 days”), usage of self-help materials (workbook and video-clips, on a Likert scale ranging from 1 “0 days” to 5 “6–7 days”) and alliance with their mentor for the online sessions (i.e., ease of working with the mentor and degree to which they both agreed on the goals for the sessions, measured on a Likert scale ranging from 1 “never” to 7 “always”).

Procedure

Participants were recruited within a month from their first assessment session at the outpatient service. They completed the online baseline measures listed above on the study’s website and were then randomized, based on treatment centre and illness severity (i.e., Body Mass Index < 16 or ≥ 16 kg/m^2) to one of two study conditions: *Recovery*MANTRA plus TAU, or TAU alone. Participants in both groups completed an online assessment at 6 weeks and at 6- and 12-month follow-up (Cardi et al., 2015).

*Recovery*MANTRA and Treatment as Usual (TAU)

Participants allocated to the *Recovery*MANTRA + TAU group, had access to online self-help materials (workbook and video-clips) and weekly 1 h, individual, synchronous text-based chat sessions with a peer mentor or mentor. The aim of the guidance was to help participants to understand and familiarize with the contents provided by the self-help materials effectively and purposefully, in order to supplement their TAU. Peer mentors and mentors were respectively individuals recovered from an eating disorder and students and were trained in the use motivational interviewing strategies.

The exact content of TAU varied between the recruitment centers, but overall consisted of psychoeducation, individual or group psychotherapy, nutritional support, and medical monitoring.

Statistical Analyses

Demographic and clinical variables were described using means and standard deviations or percentages. The baseline and week 1 differences between groups were investigated using independent samples *t*-tests. Bivariate (Pearson) correlations coefficients between variables were computed. A structural equation model (SEM) was tested to analyze the relationships between baseline patient variables, motivation to change and drop-out from end of 6 weeks assessment or the intervention. SEM consists of a set of multivariate techniques that are confirmatory rather than exploratory in testing model fit (Byrne, 2011). It allows simultaneous and comprehensive estimation of the hypothesized relations among multiple independent and dependent variables in the model using the estimated covariance matrix generated on the basis of the observed covariance matrix of the measured variables. Model testing was performed using Mplus 6.0 (Muthén and Muthén, 1998–2012). A theoretical representation of the tested model is shown in **Figure 1**. Skewness and kurtosis were assessed and the Weighted Least Squares Mean and Variance adjusted (WLSMV) estimator was used as the method of parameter estimation. The following indices were considered to evaluate the overall model goodness fit: χ^2-test statistics (χ^2/df ratios < 3 indicate models with reasonable fit, Schermelleh-Engel et al., 2003), the comparative fit index (CFI, with values between 0.80 and 0.89 indicating adequate but marginal fit and values of $\geq$0.95 indicating better fit, Hu and Bentler, 1999) and the root-mean-square error of approximation (RMSEA, with values of $\leq$0.05 indicating close fit, and < 0.08 indicating reasonable fit) (Hoyle and Panther, 1995; MacCallum et al., 1996).

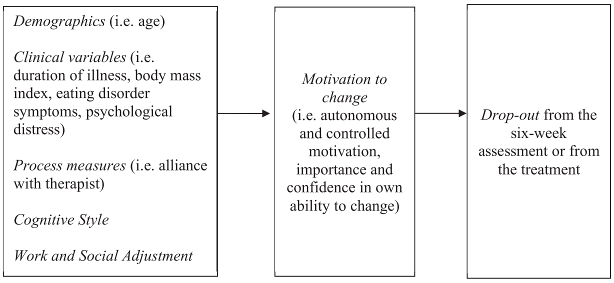

FIGURE 1 | Theoretical model. This figure describes hypothesized relationships between the variables investigated.

RESULTS

Demographic and Clinical Characteristics

Most participants were female (80/82) and from a white ethnic background (75/82). The mean age was 26.57 years (*SD* = 8.29). Almost half of the sample (41/82) was employed (part-time or full-time) and were not in a relationship (43/82). The mean body mass index (BMI) was 16.09 kg/m^2 (*SD* = 1.41). On average, patients had been ill for 7 years (*SD* = 7.80). A subgroup reported psychiatric comorbidity ($n = 19$), a previous hospital admission ($n = 20$) or the use of psychiatric medication ($n = 34$). Twenty-three participants (28%) reported purging symptoms. Demographic and clinical variables are described in **Table 1**.

Pearson correlations coefficients are shown in **Table 2**. At baseline, greater alliance with the therapist delivering TAU and lower psychological distress were related to higher autonomous motivation ($p < 0.01$) and importance and confidence in own ability to change ($p < 0.01$). Patients with lower BMI also reported higher importance to change ($p < 0.05$). However, this finding needs to be interpreted cautiously, considering that BMI was self-reported (as opposed to being measured by a clinician).

Completion of 6-Week Assessment and Guided Sessions

Rates of completion of the online assessments and attendance of the six guided sessions are shown in **Figure 2**. Sixty-seven participants completed the 6 weeks assessment, of whom all attended at least four guided sessions ($n = 2$ patients attended four sessions; $n = 6$ attended five sessions; $n = 59$ attended six sessions). Fifteen participants did not complete the 6 weeks questionnaires.

TABLE 2 | Pearson correlation coefficients of the study's variables.

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Age	–												
2. Alliance with therapist	0.237*	–											
3. Work and Social Adjustment Scale	−0.006	−0.129	–										
4. Depression Anxiety and Stress Scales	−0.173	−0.223*	0.537**	–									
5. Cognitive style	0.083	0.174	−0.195	−0.146	–								
6. Duration of illness	0.623**	0.216	0.091	−0.010	0.080	–							
7. Body mass index	−0.142	−0.039	−0.130	−0.018	0.038	−0.141	–						
8. Eating Disorder Examination Questionnaire	−0.070	−0.175	0.348**	0.652**	−0.229*	0.125	0.039	–					
9. Autonomous motivation	−0.066	0.398**	−0.003	−0.304**	0.054	−0.090	−0.094	−0.150	–				
10. Controlled motivation	0.018	0.198	0.165	0.007	−0.058	−0.007	−0.192	−0.016	0.372**	–			
11. Importance to change	0.028	0.343**	0.080	−0.292**	0.054	0.067	−0.271*	−0.136	0.577**	0.123	–		
12. Confidence in own ability to change	−0.012	0.395**	−0.275*	−0.501**	0.164	−0.108	0.020	−0.290**	0.515**	−0.026	0.460**	–	
13. Dropped-out from the assessment	−0.117	−0.127	0.017	0.141	0.012	−0.127	0.051	0.177	0.009	−0.142	0.090		–
14. Dropped-out from the intervention	−0.071	−0.216	0.005	0.188	−0.052	−0.089	0.045	0.192	−0.049	−0.014	0.044	−0.153	0.875**

*$p < 0.05$; **$p < 0.01$.

Among those, 12 completed less than four sessions (n = 3 patients attended no sessions, n = 1 completed one session, n = 6 completed two sessions, n = 2 completed three sessions, n = 1 completed four sessions, n = 1 completed five sessions, n = 1 completed six sessions).

Forty-nine participants (59.8%) received online support from graduate psychology students and 33 participants (40.2%) received online support from people with lived experience of eating disorders (recovered individuals or carers of people with lifetime eating disorders). The type of mentor did not impact on levels of drop-out.

Baseline Differences Between Completers and Drop-Outs

Overall, there were no statistically significant differences in terms of demographic and clinical characteristics between the group of individuals who completed the 6 weeks assessment or the intervention and those who did not (**Table 1**). There was a trend (p = 0.05, medium effect size) for those who did not complete the intervention to report lower alliance with their therapist at the outpatient clinic (**Table 1**).

Differences Between Groups at the End of the First Week of Participation in the Program

Patients who did not complete the end-of-intervention measures felt less comfortable working with their mentors ($p < 0.05$, medium effect size) and showed lower levels of agreement with them on the goals for the sessions ($p < 0.01$, large effect size) at the end of their first week of participation. There were also trends for participants who dropped out to report more episodes of purging (p = 0.05, medium effect size) and to have lower confidence in their ability to change (p = 0.06, medium effect size).

Participants who completed less than four online sessions felt less comfortable working with their mentor at the end of the first week of their participation in the program ($p < 0.05$, large effect size).

Structural Equation Modeling

Figure 3 shows the hypothesized model of the relationships among age, clinical impairment (eating disorder symptoms, body mass index, duration of illness, psychological distress), cognitive style, alliance with the therapist at the outpatient center, social and work adjustment, autonomous and controlled motivation for treatment, importance and confidence in own ability to change at baseline and drop-out from the assessment and from the intervention. The model showed a good fit to the data considering the following parameters: χ^2 = 15.573, df = 18, χ^2/df = 0.86, CFI = 1.000, RMSEA = 0.000, RMSEA 90% CI = 0.000–0.084. The standardized parameter estimates in **Table 3** indicated that the alliance with the therapist delivering TAU at the outpatient service at baseline was associated with all aspects of patient motivation to change (i.e., autonomous motivation, ability and importance to change and a trend toward significance for controlled motivation, p = 0.06). Patients reporting more psychological distress showed lower importance ($p < 0.01$) and

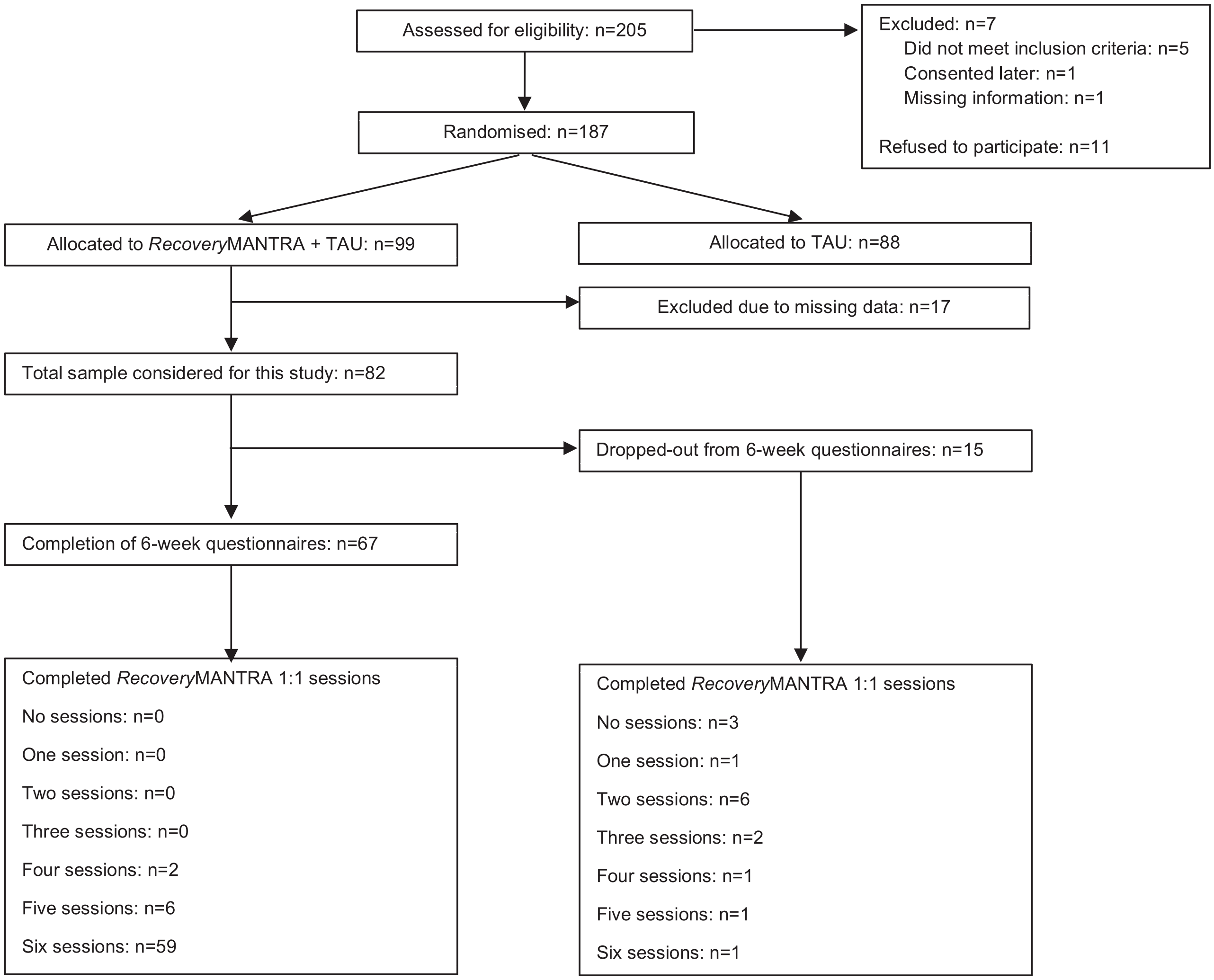

FIGURE 2 | Study flow-chart. This figure describes the process of assessing, randomizing and assessing participants and includes number of participants who completed the 6 weeks assessments and the *Recovery*MANTRA intervention sessions.

confidence in their ability to change ($p < 0.001$) and lower autonomous motivation ($p < .05$), whilst those with lower body mass index reported greater importance to change ($p < 0.05$). A trend toward significance indicated that greater work and social adjustment was associated with higher importance to change ($p = 0.06$). Higher controlled motivation and greater confidence in one's own ability to change predicted lower drop-out from the 6 weeks assessment ($p < 0.05$). Finally, a trend toward significance ($p = 0.06$) was found for greater confidence in one's own ability to change to predict lower drop-out from the treatment.

DISCUSSION

The aim of this study was to assess the feasibility of using a novel, online guided self-help program for patients with anorexia nervosa who had been assessed for outpatient treatment by examining drop-out rates. Rates of drop-out from the completion of the end-of-intervention assessment (end of intervention, at 6 weeks), rates of intervention adherence (defined as attendance of a minimum of four of six guided online sessions) and differences in baseline demographic (i.e., age, years of education) and clinical (i.e., illness severity) variables between drop-out and completers were explored. Differences between groups were also examined at the end of the first week of participation in the project, in relation to eating behavior, usage of self-help materials and satisfaction with the guidance provided. Finally, the relationship between motivation to change and drop-out was investigated. The hypotheses were that: (i) those who completed the end-of-intervention assessment or completed a minimum of four of six guided sessions would not be significantly different in demographic or clinical variables at baseline, compared to those who did not complete the assessment or the intervention, (ii) completers would show greater engagement with the guided self-help intervention and satisfaction with their mentor at the end of the first week, compared to non-completers,

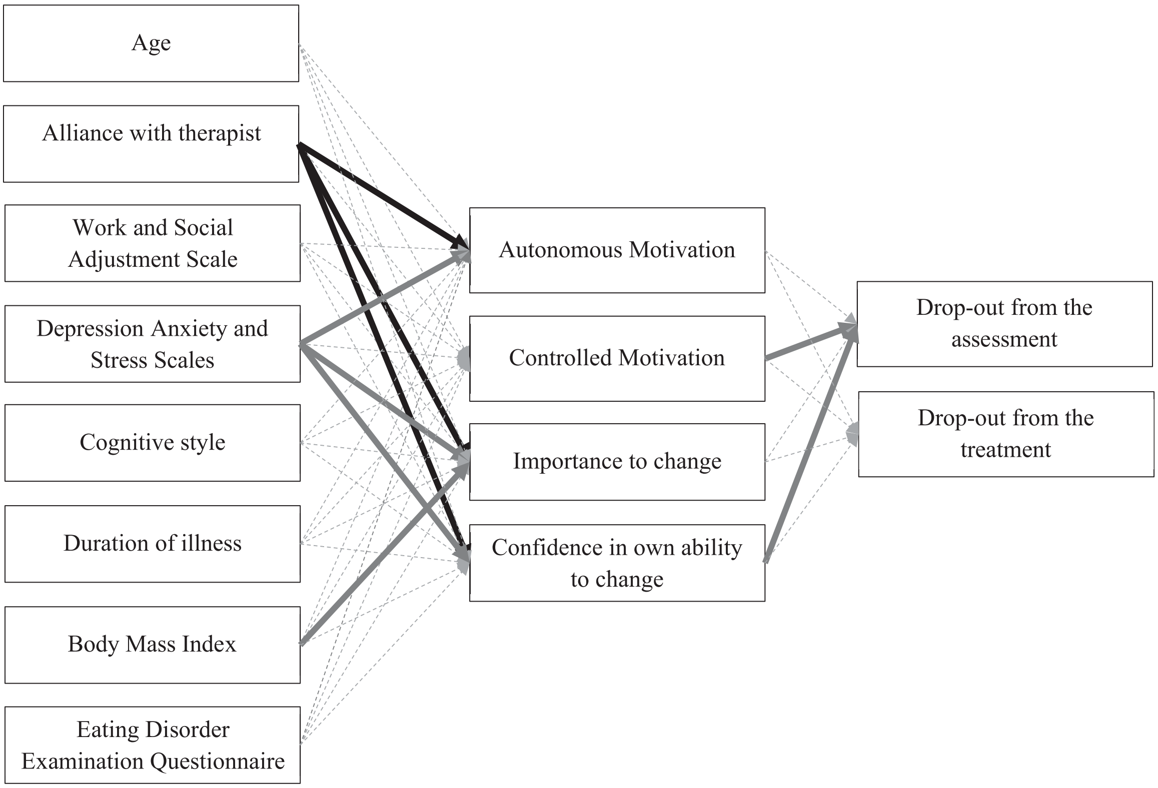

FIGURE 3 | Structural equation model. This model describes the relationships between patient demographic and clinical variables, self-reported motivation and drop-out from the 6 weeks assessments and *Recovery*MANTRA intervention. Errors are omitted from the diagram. Significant positive parameters are represented by black solid lines. Significant negative parameters are represented by gray solid lines. Non-significant parameters are represented by gray dashed lines. For clarity, correlations between variables are omitted from the diagram: autonomus motivation is not significantly correlated to controlled motivation ($p < 0.001$), importance to change ($p < 0.01$) and confidence in ability to change ($p < 0.01$); moreover, importance to change is correlated to confidence in ability to change ($p < 0.01$) and drop-out from the assessment is correlated to drop-out from the treatment ($p < 0.001$).

TABLE 3 | Standardized coefficients of the structural equation model.

	Autonomous motivation		**Controlled motivation**		**Importance to change**		**Confidence in own ability to change**		**Drop-out from the assessment**		**Drop-out from the treatment**	
	β	**R^2**	**β**	**R^2**	**β**	**R^2**	**β**	**R^2**	**β**	**R^2**	**β**	**R^2**
		0.293		0.148		0.281		0.448		0.273		0.199
Age	−0.15 (ns)		−0.01 (ns)		−0.17 (ns)		−0.08 (ns)		–		–	
Alliance with the therapist	0.39***		0.27 ($p = 0.055$)		0.28**		0.40***		–		–	
Work and Social Adjustment Scales	0.22 (ns)		0.24 (ns)		0.28 ($p = 0.062$)		0.08 (ns)		–		–	
Depression Anxiety and Stress Scales	−0.47*		−0.08 (ns)		−0.51**		−0.56***		–		–	
Cognitive style	0.04 (ns)		−0.07 (ns)		0.05 (ns)		0.08 (ns)		–		–	
Duration of illness	−0.18 (ns)		−0.08 (ns)		−0.01 (ns)		−0.16 (ns)		–		–	
Body Mass Index	−0.09 (ns)		−0.18 (ns)		−0.25*		−0.03 (ns)		–		–	
Eating Disorder Examination Questionnaire	0.21 (ns)		−0.03 (ns)		0.20 (ns)		0.11 (ns)		–		–	
Autonomous motivation	–		–		–		–		0.34 (ns)		0.19 (ns)	
Controlled motivation	–		–		–		–		−0.34*		−0.07 (ns)	
Importance to change	–		–		–		–		0.32 (ns)		0.36 (ns)	
Confidence in own ability to change	–		–		–		–		−0.46*		−0.46 ($p = 0.056$)	

Description of standardized coefficients of the variables included in the structural equation model. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

(iii) greater autonomous motivation to change at baseline would be associated with lower drop-out from the completion of the end-of-intervention measures and from the intervention.

Our results support the first hypothesis in that no baseline differences in socio-demographic or clinical variables were found between those who did and did not complete the 6-week assessment and between those who did and did not complete a minimum four guided sessions. This finding aligns with several studies examining drop-out from the use of technology-based interventions in patients with anorexia nervosa or bulimia nervosa (Schlegl et al., 2015). Results also support the second hypothesis, as patient- and treatment-related variables during the very first week of receiving the intervention differed between the completer and non-completer groups. Patients who dropped out (from assessment or the intervention) showed less satisfaction with their relationship with the mentor. Moreover, those who did not complete the end of intervention assessment showed a trend toward more frequent purging behaviors. These findings confirm the importance of considering patient- and early process-related variables when delivering technology-based interventions (Kelders et al., 2012) and are consistent with the literature indicating that low treatment credibility and poor early alliance with the therapist are associated with premature termination of treatment (Jordan et al., 2017). The poorer quality of the relationship with the mentor found in the group of non-completers is particularly important when considering the specific characteristics of *Recovery*MANTRA. The emphasis of the intervention is placed on increasing the patient's confidence in their own ability to change by providing compassionate mentorship and promoting the use of the recovery narratives (i.e., video-clips) (Cardi et al., 2015). The poor agreement on the goals for the online sessions and the weak alliance with the mentor are likely to jeopardize the intervention's outcomes. The greater frequency of purging behaviors at the end of the first week among those who did not complete the end-of-intervention measures also suggests that these behaviors might interfere with patients' ability or willingness to adhere to the program. It is also possible that the materials offered were not specific enough to support patients with tackling these symptoms. Patients with anorexia nervosa presenting episodes of binging and purging have shown poorer emotion regulation skills when coping with negative emotions than patients presenting restrictive behaviors (Rowsell et al., 2016) and higher frequency of purging behaviors has been associated with worse treatment outcomes overall (Vall and Wade, 2015).

Current findings offer mixed results with regard to the third study hypothesis. As expected, patients reporting greater confidence in their own ability to change were less likely to drop-out from the assessment or the intervention. However, controlled motivation predicted drop-out from the assessment in an unexpected direction, with greater controlled motivation being associated with lower drop-out. This finding does not align with what has been previously found in the literature. Three studies in particular have investigated the role of autonomous and controlled motivation to change in patients with eating disorders (Mansour et al., 2012; Carter and Kelly, 2015; Thaler et al., 2016). These studies found that greater autonomous motivation for treatment predicted lower levels of eating disorder symptoms, or a faster improvement in these symptoms at the end of treatment (Mansour et al., 2012; Carter and Kelly, 2015; Thaler et al., 2016). The current work differs from those past studies in at least three ways: (i) it did assess drop-out, rather than treatment outcomes, (ii) it examined the predictive role of patient motivation over a shorter period of time and (iii) it examined a technology-based as opposed to standard face-to-face treatment for patients with anorexia nervosa. These differences might explain the divergence of the findings and also highlight that autonomous and controlled motivation to change are likely to have a complex role in treatment processes and outcomes for patients with anorexia nervosa, considering the high ambivalence toward change among this patient group (Schmidt and Treasure, 2006). Controlled motivation indicates an individual's proneness to change due to expectations or pressure from others. Patients' tendency to align with expectations from others at the beginning of treatment could have a protective role against non-adherence to treatment. This would validate models of treatment that encourage the involvement of close others in the care of adults with anorexia nervosa, such as the New Maudsley Approach (Treasure et al., 2016).

Clinical Implications and Limitations

Sixty-seven out of 82 participants completed the 6 weeks assessment in this study, and they also attended a minimum of four out of six online guided sessions with a mentor. Across both groups (those who did and did not complete the 6 weeks assessment) 70 participants completed at least four guided sessions, of whom 59 participants completed all the six sessions offered. These rates of completion compare very favorably to the findings of a systematic review of 26 technology-based studies in eating disorders that reported mean compliance to treatment (defined as attendance to all treatment sessions) at 57.6% (ranging from 18.4 to 95.5%; Schlegl et al., 2015). Our rates also compare favorably to the finding that 20–40% for patients with anorexia nervosa do not complete standard, psychotherapy-based interventions (DeJong et al., 2012). Based on this evidence, it seems plausible to state that technology-based guided self-help for anorexia nervosa is acceptable and is not associated with lower adherence than standard treatment. A recent study also found that an online, guided self-help intervention designed to prevent relapse from intensive treatment was beneficial in the aftercare of inpatients with anorexia nervosa (Schmidt et al., 2017). However, these findings cannot generalize to the use of standalone online interventions to replace standard treatment or as only form of support after care in anorexia nervosa.

The finding that non-completers report lower satisfaction with their online mentor after the first week of participation in the program highlights the importance of attending early to the quality of the working alliance and the need to ensure that the work of the mentors is closely and regularly monitored, especially when guidance is delivered by non-professionals. Our research group supervised mentors once a week and trained them in the use of motivational interviewing techniques (Cardi et al., 2015). A greater emphasis on early fidelity to the intervention and use of the self-help materials might improve overall satisfaction with the mentorship among those who (are likely to) drop-out from the intervention. In our study, we contacted participants who were not completing the online sessions and assessments a maximum of four times (once/week for 3 weeks and once more after 20 days). Those who dropped out soon after the completion of the baseline questionnaires and never started the online sessions did not reply to any of our emails. Those who dropped-out after the first or first two online sessions and who also provided feedback to us expressed worries about confidentiality (n = 1), difficulties due to work commitments (n = 1), perceived lack of availability of the mentor (n = 1), a preference for face-to-face therapy (n = 1), and being too ill (n = 1) to continue with the project. This suggests that treatment preferences, beliefs about the illness and difficulties with synchronous guidance play a role in early drop-out from online interventions. Type and extent of previous treatments could also predict early drop-out from these interventions.

CONCLUSION

To conclude, the findings of this study indicate that online guided self-help offered to patients with anorexia nervosa who have been assessed to receive outpatient treatment is acceptable and feasible. To a certain degree, a patient's tendency to adhere to treatment because of external pressure or expectations from others seems to play a protective role in completing the online intervention. More work is needed on monitoring patients' clinical symptoms and expectations and satisfaction with the program during the earlier phases of their participation to reduce the risk of drop-out.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The study involved human participants and was reviewed and approved by the Research Ethics Committee of London-Brent, project reference number: 14-LO-1347. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

VC and JT contributed to study's conceptualization, investigation, data curation, funding acquisition, project administration, and writing up of the manuscript. GA contributed to project admin, investigation, data curation, formal analysis, and writing up of the manuscript. LS and GL contributed to conceptualization, data curation, formal analysis, and writing up of the manuscript. SA, US, and PM contributed to conceptualization, investigation, funding acquisition, and writing up of the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2020.00707/full#supplementary-material

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Exploring Changes in Event-Related Potentials After a Feasibility Trial of Inhibitory Training for Bulimia Nervosa and Binge Eating Disorder

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In a feasibility trial comparing two forms of combined inhibitory control training and goal planning (i.e., food-specific and general) among patients with bulimia nervosa (BN) and binge eating disorder (BED), we found evidence of symptomatic benefit, with stronger effects among participants receiving a food-specific intervention. The aim of the present study was to examine changes in behavioral outcomes and event-related potentials (ERPs; N2 and P3 amplitudes) from baseline to post-intervention that might suggest the mechanisms underpinning these effects. Fifty-five participants completed go/no-go tasks during two electroencephalography (EEG) sessions, at baseline and post-intervention. The go/no-go task included "go" cues to low energy-dense foods and non-foods, and "no-go" cues to high energy-dense foods and non-foods. Datasets with poor signal quality and/or outliers were excluded, leaving 48 participants ($N = 24$ BN; $N = 24$ BED) in the analyses. Participants allocated to the food-specific, compared to the general intervention group, showed significantly greater reductions in reaction time to low energy-dense foods, compared to non-foods, by post-intervention. Commission errors significantly increased from baseline to post-intervention, regardless of stimulus type (food vs. non-food) and intervention group (food-specific vs. general). There were no significant changes in omission errors. P3 amplitudes to "no-go" cues marginally, but non-significantly, decreased by post-intervention, but there was no significant interaction with stimulus type (high energy-dense food vs. non-food) or intervention group (food-specific vs. general). There were no significant changes in N2 amplitudes to "no-go" cues, N2 amplitudes to "go" cues, or P3 amplitudes to "go" cues from baseline to post-intervention. Training effects were only marginally captured by these event-related potentials. We discuss limitations to the task paradigm, including its two-choice nature, ease of completion, and validity, and give recommendations for future research exploring ERPs using inhibitory control paradigms.

Keywords: event-relate potentials, binge eating disorder, bulimia nervesa, change process, ERPs

INTRODUCTION

Rationale

The number of individuals receiving an eating disorder diagnosis has been increasing since the 1980s (Currin et al., 2005). This is particularly evident for binge eating disorder (BED), which has been increasing significantly in the new millennium (Micali et al., 2013). In order to improve the quality of current treatments for bulimia nervosa (BN) and BED it is essential to gain a better understanding of mechanisms that underpin binge-eating behavior.

Impulsivity is considered to be a risk factor for binge eating (Nasser et al., 2004). Reviews of cross-sectional research indicate that individuals with BED (Leombruni et al., 2014; Wu et al., 2016) and BN (Waxman, 2009; Vaz-Leal et al., 2015) show increased general (trait) impulsivity and eating-related impulsivity (Schag et al., 2013, 2019; Kessler et al., 2016; Giel et al., 2017). Furthermore, longitudinal studies conducted among individuals with BED have suggested that impulsivity is an impediment to treatment success (Meule and Platte, 2015; Manasse et al., 2017; Treasure et al., 2018).

As a multidimensional construct, impulsivity is thought to consist of two main components: decreased inhibitory control and increased reward sensitivity (Dawe and Loxton, 2004). Accordingly, impairments in inhibitory control have consistently been linked to increased eating disorder psychopathology (Svaldi et al., 2014; Manasse et al., 2016). Reward sensitivity, on the other hand, can be measured using behavioral tasks that explore implicit cognition, such as attentional biases (Deluchi et al., 2017). Stimuli that are highly motivationally relevant are likely to bias attention, in such a way where attention is directed toward a particular class of stimuli. Among individuals with binge eating behavior and/or obesity, attentional biases toward food cues, indicated by quicker reaction times to foods as opposed to non-foods during visual probe tasks, have been consistently reported (Castellanos et al., 2009; Nijs et al., 2010; Werthmann et al., 2011; Nijs and Franken, 2012; Jansen et al., 2015; Deluchi et al., 2017). Furthermore, this attentional bias may reflect difficulty disengaging from food stimuli, and greater reward while processing them (Leehr et al., 2018). It is hypothesized that this bias may, in turn, prevent individuals with binge eating behaviors from engaging in effective down-regulation of impulses toward food (Deluchi et al., 2017).

Event-related potentials (ERPs), derived from EEG recordings, offer the possibility of exploring cognitive processes within neural circuits (Luck, 2014). The N2, a negative fronto-central ERP observed ∼200–300 ms after stimulus presentation, has been used as a measure of inhibitory control and/or conflict monitoring (Falkenstein et al., 1999; Folstein et al., 2008; Watson and Garvey, 2013). The N2, localized to the anterior cingulate cortex (Lange et al., 1998; Liotti et al., 2000) is thought to reflect inhibitory control because it is enhanced to "no-go" compared to "go" stimuli (Enriquez-Geppert et al., 2010). In food-related tasks, N2 amplitudes are more negative when participants with binge eating behaviors are asked to inhibit to food, as opposed to non-food stimuli (Wolz et al., 2017) and this is particularly relevant to high energy-dense, as opposed to low-energy dense foods (Carbine et al., 2018). Nonetheless, there is uncertainty as to whether enhanced activation of N2 in response to high energy-dense food is a specific feature of binge-type eating disorders (Leehr et al., 2018; Chami et al., 2019), as it has also been reported among individuals in the higher BMI ranges (Carbine et al., 2018).

The P3 is an ERP with a positive peak that is elicited ∼300–600 ms after stimulus presentation (Albert et al., 2013). Its functional significance varies depending on the task at hand and it can reflect various cognitive processes, including target identification (Luck, 2014), working memory/context updating (Carbine et al., 2018), motivated attention (Schienle et al., 2008), or inhibitory control (Blackburne et al., 2016). Given that P3 responses are elicited in response to several cognitive processes, several variants have been described (see Polich, 2007 for an in-depth review). For instance, the P3a is often enhanced within fronto-central electrodes, and its generators are localized in cingulate, frontal, and right parietal areas (Volpe et al., 2007). It has been particularly relevant to inhibitory tasks (e.g., stroop task, stop-signal Tasks, or oddball paradigms; Polich, 2007; Blackburne et al., 2016). It has been thought to reflect a later stage that involves inhibition of the motor system (Dimoska et al., 2006), which may be particularly relevant to disinhibited eating behavior (i.e., binge eating; Smith et al., 2018). Exploring the *P3a* among participants with healthy, overweight, and obese BMIs, amplitudes were enhanced when the task involved inhibiting to high energy-dense, as opposed to low-energy dense foods (Carbine et al., 2018). In contrast, the *P3b* is more enhanced over parietal electrodes, and its generators are localized in bilateral, parietal, limbic, cingulate, and temporo-occipital regions (Volpe et al., 2007). It has been particularly relevant when exploring motivational relevance and salience (Herrmann et al., 2000). In line with this, several studies have reported enhanced P3b amplitudes toward food, as opposed to neutral non-food stimuli across all weight groups (Nijs et al., 2008, 2010; Hill et al., 2013; Hofmann et al., 2015). Due to the value of food for survival, food stimuli may represent natural "intrinsic targets," even in the absence of specific experimental demands.

Recent evidence suggests that neural mechanisms underlying these executive functions can be trained, and that inhibitory control may be conceptualized as a muscle than can be strengthened with exercise (Benikos et al., 2013; Blackburne et al., 2016; Jones et al., 2016). Go/no-go training is one of the methods that has been used to train inhibitory control toward food cues (Lawrence et al., 2015; Allom et al., 2016; Jones et al., 2016). This training requires a rapid response to "go" stimuli, and inhibition to "no-go" stimuli (Lawrence et al., 2015). It is hypothesized that repeatedly pairing inhibitory responses to specific cues can strengthen the association between the cue and the behavioral goal (Houben and Jansen, 2011; Turton et al., 2016). This has been evidenced by several treatment trials, which have also found that using food-specific go/no-go trainings, as opposed to a general go/no-go tasks (i.e., with non-food stimuli) is more effective at decreasing unhealthy eating behaviors among individuals who overeat (Houben and Jansen, 2011; Veling et al., 2011; Lawrence et al., 2015).

To our knowledge, only one published study on disordered eating (Blackburne et al., 2016) has used ERPs as a means of assessing treatment outcomes. Within the study, participants with BMIs in the obese range who received food-specific inhibitory control training exhibited enhanced "no-go" P3 (i.e., P3a) amplitudes post-intervention, while those allocated to the waitlist control showed the opposite effect. The authors have interpreted this as an improvement in inhibitory control processing (Blackburne et al., 2016).

Aims and Hypotheses

Aims

Recent evidence from a feasibility trial in our laboratory has found that an intervention combining go/no-go training and implementation intentions is associated with reductions in binge eating frequency among individuals with bulimia nervosa and BED (Chami et al., 2019). According to the Medical Research Council's (MRC) guidelines, a key element of the development and evaluation process is to understand change processes underlying intervention efficacy (Craig and Petticrew, 2013). In line with this, the primary aim of the present research was to examine behavioral (i.e., reaction times, omission errors, and commission errors) and event-related potential (i.e., N2 and P3) changes from baseline to post-intervention. Within this study, an omission error was defined as an error during "go" trials (a "no-go" response when the task requires a "go" response) and a commission error was defined as an error during "no-go" trials (a "go" response when the task requires a "no-go" response). Moreover, the research aims to explore whether participants receiving a *food-specific intervention*, as opposed to a general intervention, would show additional changes in reaction time, omission errors, commission errors, N2, and P3 amplitudes in response to food cues from baseline to post-intervention. To explore the relationship between ERPs and core binge-type eating disorder symptomatology, the research also aims to explore correlations between changes in binge eating frequency (Chami et al., submitted) and changes in N2 and P3 amplitudes to high energy-dense foods. Since the timing and onset of N2 and P3 can vary as a function of processing speed and training, we explore their respective latencies too.

Hypotheses

Behavioral

We hypothesized that reaction time and omission errors to "go" cues (i.e., low energy-dense food and non-food) and commission errors to "no-go" cues (i.e., high energy-dense food and non-food) will decrease from baseline to post-intervention. These effects will be more pronounced for food cues, and among individuals receiving a food-specific intervention.

N2 and P3

In response to "no-go" cues, we hypothesized that mean "no-go" N2 amplitudes will increase from baseline to post-intervention, indicative of improved inhibitory control, and that mean "no-go" P3 amplitudes will decrease from baseline to post-intervention, indicative of reduced motivated attention. The opposite pattern is expected for "go" cues. Again, these effects will be more pronounced to food cues, and among individuals receiving a food-specific intervention. Finally, we predict that the training effects on binge eating will correlate with "no-go" N2 and P3 amplitudes to high energy-dense foods.

MATERIALS AND METHODS

Participants

Participants with bulimia nervosa ($N = 40$) and BED ($N = 38$) were recruited through eating disorder charity websites, social media, flyers, and participant identification centers that supported the study. They were then randomly allocated to a food-specific or general intervention, which included both go/no-go training and goal planning (please refer to clinicaltrials.gov ID NCT03126526 for details of methodology; Chami et al., in submission). Within this manuscript, only participants who attended and completed both baseline and post-intervention EEG sessions were included ($N = 55$).

Eligibility required that participants met criteria for bulimia nervosa or BED according to the *Structured Clinical Interview for DSM-V*, had a Body Mass Index (BMI) of at least 18.5, were between the ages of 18 and 60, did not have a visual impairment that could not be repaired with eyewear, a neurological impairment, an alcohol or drug dependence, or psychosis.

Assessment

Self-Report Measures

Eligibility clearance. The Structured Clinical Interview for DSM-V (SCID-5; First, 2014), a semi-structured interview for making a DSM-V diagnosis, was used to confirm diagnosis among participants with bulimia nervosa and BED, and to ensure no history of any psychiatric disorder among healthy control participants. All other eligibility criteria (i.e., age, neurological impairment, visual impairment, and BMI) were assessed with a short interview.

Binge eating frequency. Item 13 of the eating disorder examination questionnaire (EDE-Q; Fairburn, 2008) was used as a standalone outcome to assess binge eating frequency (*Over the last 28 days, how many times have you eaten what other people would regard as an unusually large amount of food?*).

Behavioral Measures

Food-specific go/no-go task. The present study used the food-specific go/no-go task, as implemented by Lawrence et al. (2015). During each trial within the task, one of 36 pictures was laterally presented (equiprobable on the left- or right- side) on a 19-inch computer screen for 1250 ms, with a 1250 ms inter-stimulus interval. Participants were seated at a 20-inch distance from the screen. The stimuli consisted of 9 low-energy dense food pictures (e.g., fruits, vegetables, and rice cakes), 9 high-energy dense foods food pictures (e.g., chocolate, cake, and crisps), and 18 non-food pictures (i.e., clothing items). Some of the

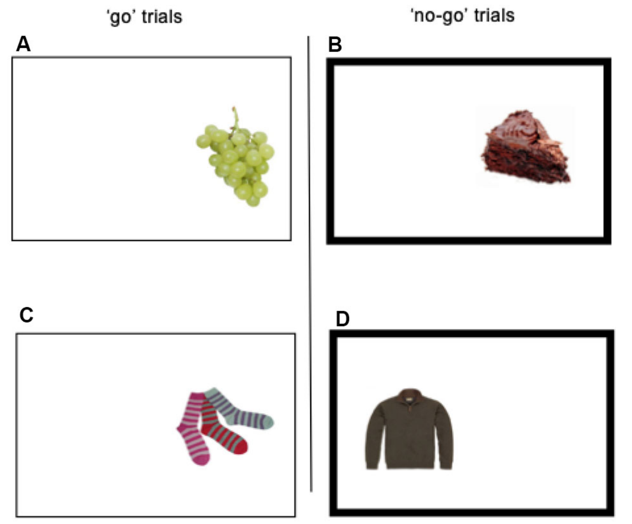

FIGURE 1 | Picture **(A)** represents the presentation of a healthy food on the right side of the rectangle on screen. For this condition, participants were required to press the letter "m" as quickly as possible ("go" trial). The same applies to the condition picture **(C)**. Picture **(B)** represents the presentation of a palatable food on the right side of the rectangle on screen. For this condition, participants were required not to respond, because the border of the rectangle is bold ("no-go" trial). The same applies to the condition in picture **(D)**.

food pictures had been previously used by fMRI studies of cue-reactivity, and they had been rated as pleasant (Beaver et al., 2006; Lawrence et al., 2012). A non-bold frame surrounding the picture and bold frame surrounding the picture, respectively, identified the "go" and "no-go" trials (see **Figure 1**). Non-bold frames remained on the screen during inter-trials. During "go" trials, participants were required to press "c" or "m" on the keyboard depending on the location of the picture on the screen ("c" for left and "m" for right). During the "no-go" trials, participants had to withhold their response. High-energy dense food pictures were always paired with "no-go" signals, resulting in 54 "no-go" trials, while the healthy food pictures were always paired with "go" signals, resulting in 54 go trials. The non-food pictures were equally likely to be paired with "go" and "no-go" frames. Each of the 36 pictures (9 + 9 + 18) was presented once per block, and participants completed 6 blocks per training session. The lack of "go" trials to high-energy dense food and "no-go" trials to healthy foods was due to the intervention that followed the session (Chami et al., in progress). Participants were provided with feedback regarding accuracy (error rate) and speed (mean reaction time) between blocks. Participants were instructed to respond as quickly and as accurately as possible. Food and non-food pictures were visually matched for size, color, and visual complexity (see **Figure 1**).

EEG

EEG was recorded continuously throughout the experimental tasks using BrainVision Recorder, and amplified with two 32-channel BrainAmp DC amplifiers (Brain Products GmbH, Munich, Germany) An actiCAP 64Ch standard cap was equipped after the 10–20 system (Jasper, 1958). FCz was used as the reference electrode, and AFz was used as the ground electrode. Impedances were kept below 15 KOhm for all the electrodes. Recording was performed with a sample rate of 500 Hz and an online bandpass filter between 0.1 and 100 Hz.

Offline, EEG data pre-processing was done using EEGLab (Delorme and Makeig, 2004) and comprised of the following steps: down-sampling to 256 Hz, manually removing bad channels, adding a zero channel and converting to average reference, high pass filtering at 1 Hz, which has been shown to be optimal for Independent Component Analysis (ICA), conducting ICA decomposition (AMICA; Palmer et al., 2012), identifying components for removal, extracting eye-blink, lateral eye movement, and facial muscle (e.g., jaw clenching) components, low pass filtering at 30 Hz, interpolating the removed channels, manually removing artifacts, segmenting the data into −500 ms pre-stimulus 1250 ms post-stimulus epochs, manually removing epochs with commission or omission errors, and baseline correcting (−500 ms–0 ms). Datasets from 4 participants were excluded from ERP analysis due to poor signal quality, leading to abnormal recordings. Moreover, 3 participants with N2 and P3 outliers were detected ($Z > |3.0|$) and case-wise excluded from all EEG analyses.

Primarily driven by previous EEG studies using the go/no-go task (e.g., Carbine et al., 2018), we had planned to examine P3 amplitudes in fronto-central regions. In the present data, however, a P3-like local maxima was found over parietal electrodes between 300 and 600 ms. This finding indicated that, despite the inhibitory nature of the task we had adopted, the unchallenging nature of it may have led to a "salience-related" response, thus evoking P3b amplitudes (Polich, 2007). Our analyses of P3 amplitudes thus focused on attentional allocation and biases. P3 latencies were extracted as the time when the amplitude reached 50% of its peak amplitude. The electrodes that were identified for extraction were in the parietal region (P5, P3, P1, Pz, P2, P4, and P6; see **Figure 2**).

Similarly, based on previous literature (Carbine et al., 2018) and our topography (see **Figure 2**), N2 amplitudes and

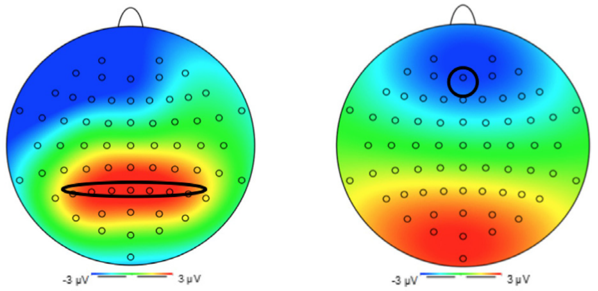

FIGURE 2 | Topography 1: P3 at electrode Pz. Topography 2: N2 at electrode Fz.

latencies were extracted from a frontal electrode (Fz). The N2 amplitude was extracted as the mean amplitude at electrode Fz occurring 200–350 ms post stimulus presentation, and the N2 latency was extracted as the time when the amplitude reached 50% of its peak.

Procedure

Individuals who expressed interest in learning about the study procedures were sent an information sheet detailing the procedure. Next, they were contacted for a 15-min eligibility phone interview. Those who met criteria were sent a consent form indicating their rights as participants. After informed consent, an appointment was booked for the first EEG session and participants were sent a battery of questionnaires to complete via an online platform (i.e., Qualtrics, Provo, UT). Before entering the laboratory for the first EEG session, participants were instructed to withhold from food, caloric drinks, and nicotine for 2 h, as well as caffeinated drinks and alcohol for 24 h. During the laboratory session, participants were briefed about what the session will involve. They were then asked to sign a hard copy of the consent form, and their weight and head circumference were measured. After the appropriate EEG cap size was selected, the researcher put the cap on and applied electro-gel into the electrodes.

Before completing computerized tasks during EEG recording, participants were instructed to rest with their eyes open for 3 min and to rest with their eyes closed for 3 min. The researcher then explained the task rules and participants completed a practice trial of the go/no-go task, which included only 36 of the 216 trials of the full-length version. The average duration of the session was 2 h and 30 min. After 30 ± 2 days (i.e., post-intervention), the same procedure was followed for the second EEG session.

All procedures were revised and approved by the London Westminster Research Ethics Committee and the Health Research Authority (IRAS Project ID: 209609).

Study Design

The study followed a mixed models design, with intervention (food-specific vs. general) as the between subject variable and time (baseline vs. post-intervention) as the between subject variables.

Interventions

Inhibitory Control Training (Go/No-Go)

The inhibitory control training used was developed at the University of Exeter (Lawrence et al., 2015). Participants were encouraged to try to complete a computer-based go/no-go training task daily for 4 weeks. Participants allocated to the food-specific intervention group were asked to complete a food-specific go/no-task that is identical to the one described in section Implementation Intentions (If-Then Planning). Participants allocated to the general intervention group were asked to complete a general go/no-go task that had the same set of rules, but did not include food stimuli. While "go" and "no-go" trials were still present, the 18 food pictures were replaced with pictures of tools and stationery (see Lawrence et al., 2015 for details).

Implementation Intentions (If-Then Planning)

Implementation intentions involved encouraging participants to identify an unhelpful habit, reflect on situations and motivations that are likely to precede the unhelpful behavior, and then design an alternative behavior that could replace the unhelpful behavior. Participants allocated to the food-specific intervention group were asked to select an unhelpful behavior that was related to food/eating, while those allocated to the general intervention group were asked to select an unhelpful behavior that was unrelated to food/eating (e.g., social trouble). One example would be: "If I am home alone (situation) and feeling anxious (motivation), then I normally buy binge food (unhelpful eating-related habit)," would be replaced with "If I am home alone and feeling anxious, then I will meditate for 10 min (alternative behavior)." Each participant was assigned a trained mentor who followed up with him/her weekly via email for 4 weeks.

Statistical Analysis

Statistical analyses were conducted using SPSS 24 (IBM Corp, 2016) for Mac. Primarily, descriptive and frequency statistics were used to report the mean and standard deviation of intervention engagement, while splitting for intervention group. An independent samples *t*-test was conducted to explore between-group differences in training task completion, and a chi-squared test was conduced to explore between group differences in implementation intention (i.e., goal planning) engagement. Next, independent samples *t*-tests were conducted to ensure that the two interventional groups did not significantly differ on demographic and clinical characteristics.

For behavioral data analysis, a repeated measures ANOVA was conducted to measure reaction time to "go" cues at two time points, across two types of stimuli, and between two intervention groups. The same ANOVA structure was used to analyze commission and omission errors, separately. ANOVAs followed the structure: 2 (time: pre- vs. post- intervention) × 2 (type of stimulus: low/high energy-dense food vs. non-food) × 2 (intervention group: food-specific vs. general intervention). "No-go" analyses included high energy-dense foods and non-foods, while "go" analyses included low energy-dense foods and non-foods.

To ensure that ERP amplitudes reflected the expected task demands, two paired samples *t*-tests were used to compare N2 and P3 amplitudes to "no-go" and "go" non-food cues.

For the main analysis, two repeated measures ANOVAs (for P3 and N2 separately) were conducted to measure amplitudes to "no-go" cues at two time points, across two types of stimuli, and between two intervention groups. They followed the format: 2 (time: pre- vs. post- intervention) × 2 (type of stimulus: high energy-dense food vs. non-food) × 2 (intervention group: food-specific vs. general intervention). This was repeated for "go" cues, with the following format: 2 (time: pre- vs. post- intervention) × 2 (type of stimulus: low energy-dense food vs. non-food) × 2

TABLE 1 | Baseline demographic and clinical characteristics of the sample.

	Food-specific intervention	**General intervention**	***p*-value***
	(*N* = 25) **M (*SD*) or *N* (%)**	**(*N* = 23)** **M (*SD*) or *N* (%)**	
Demographic characteristics			
Age	38.36 (12.03)	34.78 (13.32)	0.33
Weight (kg)	83.28 (23.49)	74.29 (24.66)	0.21
BMI	29.77 (6.87)	26.36 (8.33)	0.13
Duration of illness (Years)	19.10 (14.41)	16.74 (11.11)	0.57
Gender	Female = 21 (87.5%)	Female = 21 (91.3%)	0.67
	Male = 3 (12.5%)	Male = 2 (8.7%)	
Ethnicity	White = 19 (79.2%)	White = 17 (73.9%)	0.11
	Black = 1 (4.2%)	Black = 1 (4.3%)	
	Middle eastern = 3 (12.5%)	Mixed (White/Black) = 2 (8.7%)	
	Latin American = 1 (4.2%)	Asian = 3 (13%)	
Clinical characteristics			
Diagnosis	Binge eating disorder = 13 (52%)	Binge eating disorder = 11 (47.8%)	0.77
	Bulimia nervosa = 12 (48%)	Bulimia nervosa = 12 (52.2%)	
Comorbid mood and/or anxiety disorder	Yes = 20 (80%)	Yes = 19 (82.6%)	0.82
	No = 5 (20%)	No = 4 (17.4%)	
Use of psychiatric medication	Medication = 8 (33.3%)	Medication = 9 (39.1%)	0.68
	No medication = 16 (66.7%)	No medication = 14 (60.9%)	

**P-values for Age, Weight, BMI, and Duration of Illness were obtained using independent samples t-tests. P-values for Gender and Ethnicity using Fisher's Exact Test. P-values for Diagnosis, Use of psychiatric medication, and Comorbid mood and/or anxiety disorder were obtained using Pearson's Chi-Square.*

(intervention group: food-specific vs. general intervention). The main analyses were repeated for ERP latencies.

Finally, two-tailed Pearson's correlations were used to assess the correlation between changes in binge eating frequency and changes in ERP amplitudes to high energy-dense foods across time. The variables were created using the following formulas: (1) Baseline *minus* post-intervention no-go N2 amplitudes to high energy-dense food, (2) Baseline *minus* post-intervention no-go P3 amplitudes to high energy-dense food, and (3) Baseline *minus* post-intervention binge eating frequency. This analysis structure was repeated for ERP latencies.

RESULTS

Participant Characteristics

No significant differences in demographic and clinical characteristics were found between the two intervention groups (all $p > 0.05$; see **Table 1**). The average number of go/no-go training tasks completed was 13.50 (out of 28 total trainings; $SD = 6.79$). There was no significant difference in the number of trainings completed between participants in the food-specific intervention group ($M = 14.64$; $SD = 6.42$) and participants in the general intervention group [$M = 12.26$; $SD = 7.10$; $t(46) = 1.22$, $p = 0.229$]. With regards to if-then planning, 50% of participants were minimally engaged at implementing their plan. There were no significant differences in engagement between participants in the food-specific vs. general intervention group [$X^2(3, 48) = 5.247$, $p = 0.155$].

Behavioral Results

There was a significant main effect of time on reaction time [$F(1, 46) = 28.12$, $p < 0.001$, $\eta^2 = 0.379$] and a significant interaction between time x type of stimulus x intervention group [$F(1, 46) = 7.27$, $p = 0.01$, $\eta^2 = 0.136$], indicating that participants in the food-specific intervention, compared to the general intervention group, showed a significantly greater reduction (training effect) in reaction time to low energy-dense foods, compared to non-foods, by post-intervention (see **Table 2** below). However, there were no significant main effects or interaction effects in omission errors (all $p > 0.05$). Although there was a main effect of time on commission errors [$F(1, 46) = 12.78$, $p = 0.001$, $\eta^2 = 0.217$], the direction, indicating that participants made more errors by post-intervention, compared to baseline, was unexpected. No other significant main effects of interaction effects were significant (all $p > 0.05$) see **Table 2** below.

Manipulation Check: Inhibition Evoked by Go/No-Go Task

Within non-food trials, as predicted, N2 amplitudes were more negative to "no-go" ($M = -1.45$; $SD = 1.73$) compared to "go" cues [$M = -0.87$; $SD = 2.03$; $t(48) = -2.62$, $p = 0.01$; see **Figure 3**], suggesting greater inhibitory control in this condition. P3 amplitudes to non-foods were more positive to "go" cues ($M = 1.99$; $SD = 0.29$) compared to "no-go" cues [$M = 1.48$; $SD = 0.21$; $t(47) = -4.20$, $p < 0.001$; see **Figure 4**], suggesting that attention was enhanced during "go" trials and blunted during "no-go" trials.

TABLE 2 | Mean reaction times and omission errors to low energy-dense foods and non-foods at baseline and post-intervention, and mean commission errors to high energy-dense foods and non-foods at baseline and post-intervention, split by intervention group.

		Baseline M (*SD*)	Post-intervention M (*SD*)	Mean differences (95% CI)	Effect size (d_z)
RT low ED foods (ms)	Food-specific intervention	591.18 (91.32)	522.06 (84.50)	69.12 (38.01–100.24)	0.92
	General intervention	583.12 (121.52)	539.20 (114.98)	43.92 (8.19–79.65)	0.53
RT non-foods (ms)	Food-specific intervention	615.76 (99.37)	549.11 (92.04)	66.65 (32.94–100.36)	0.82
	General intervention	607.06 (126.27)	541.38 (103.64)	65.68 (28.17–103.18)	0.76
Omission error low ED foods	Food-specific intervention	1.64 (2.64)	1.56 (2.37)	0.07 (–1.32–1.46)	0.02
	General intervention	1.62 (4.23)	1.14 (2.08)	0.48 (–1.51–2.48)	0.10
Omission error non-foods	Food-specific intervention	2.23 (2.92)	1.05 (1.78)	1.19 (–0.24–2.62)	0.34
	General intervention	2.98 (5.08)	1.62 (2.47)	1.36 (–0.80–3.53)	0.27
Commission error high ED foods	Food-specific intervention	1.42 (3.09)	1.79 (2.90)	–0.37 (–1.78–1.04)	0.11
	General intervention	1.22 (1.75)	2.43 (2.76)	–1.20 (–2.40–0.004)	0.36
Commission error non-foods	Food-specific intervention	1.04 (1.70)	2.46 (2.66)	–1.42 (–2.48–0.35)	0.55
	General intervention	1.06 (1.57)	3.15 (3.13)	–2.09 (–3.60–0.58)	0.49

ED, energy dense; N food-specific intervention, 25; N general intervention, 23; d_z*, effect size calculated for within subject power analyses.*

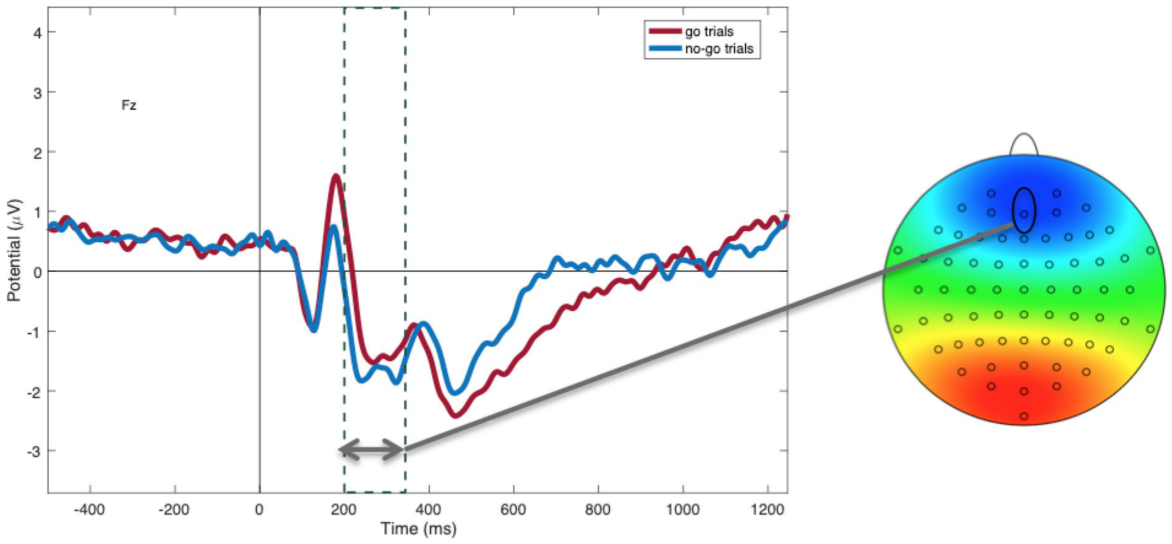

FIGURE 3 | Mean N2 amplitudes at electrode Fz between 200 and 350 ms, showing more negativity during "no-go" trials (blue) compared to "go" trials (red; $p = 0.01$).

EEG Results

"No-Go" Cues

There was no main effect of time on "no-go" N2 amplitudes [$F_{(1,46)} = 1.849$, $p = 0.181$, $\eta^2 = 0.039$]. Neither was there a time × type of stimulus × intervention group interaction effect [$F(1, 46) = 0.014$, $p = 0.906$, $\eta^2 = 0.001$]. There was no significant main effect of time [$F(1, 46) = 0.013$, $p = 0.911$, $\eta^2 = 0.001$] and no time x type of stimulus x intervention group interaction effect [$F(1, 46) = 0.863$, $p = 0.358$, $\eta^2 = 0.018$] on "no-go" N2 latency.

There was a marginal, but non-significant, main effect of time on "no-go" P3 amplitudes [$F(1, 46) = 3.801$, $p = 0.057$, $\eta^2 = 0.076$], but no significant time x type of stimulus x intervention group interaction [$F(1, 46) = 0.015$, $p = 0.904$, $\eta^2 = 001$]. There was a significant main effect of time on "no-go" P3 latency [$F(1, 46) = 12.47$, $p = 0.001$, $\eta^2 = 0.213$], indicating that "no-go" P3 latency decreased from baseline to post-intervention regardless of stimulus type. There was no time x type of stimulus x intervention group interaction effect [$F(1, 46) = 0.010$, $p = 0.922$, $\eta^2 = 0.001$] on "no-go" P3 latency.

See **Table 3** below for within group effect size calculations of no-go cues split by intervention group.

"Go" Cues

There was no main effect of time on "go" N2 amplitudes [$F(1, 46) = 1.849$, $p = 0.104$, $\eta^2 = 0.056$]. Moreover, the expected 3-way interaction was not significant [$F(1, 46) = 1.536$, $p = 0.222$, $\eta^2 = 0.032$]. There was no significant main effect of time [$F(1, 46) = 0.704$, $p = 0.406$, $\eta^2 = 0.015$] and no time × type of stimulus × intervention group interaction effect [$F(1, 46) = 0.255$, $p = 0.616$, $\eta^2 = 0.006$] on "go" N2 latency.

There was no main effect of time on "go" P3 amplitudes [$F(1, 46) = 0.678$, $p = 0.415$, $\eta^2 = 0.015$],

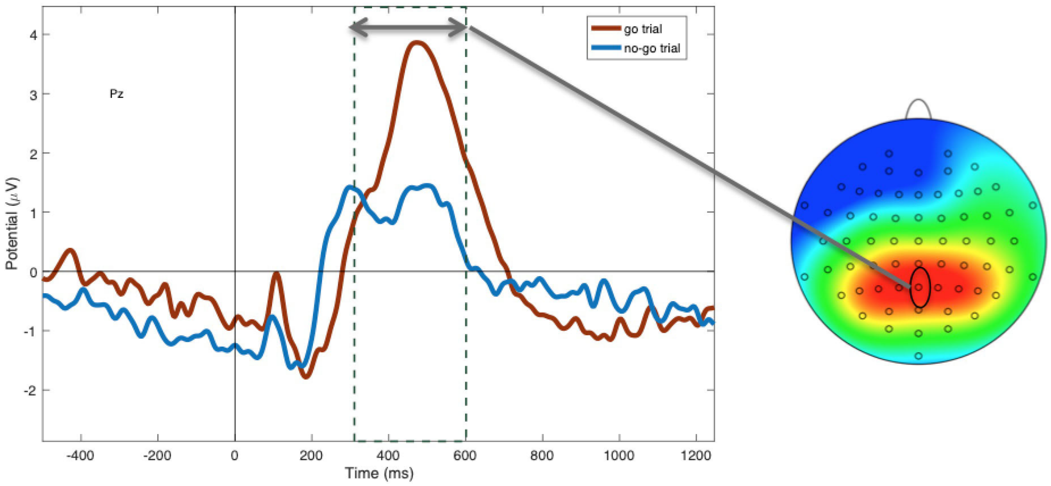

FIGURE 4 | Mean P3 amplitudes at electrode Pz between 300 and 600 ms, showing more positivity during "go" (red) compared to "no-go" trials (blue; $p < 0.001$).

TABLE 3 | N2 and P3 amplitudes and latencies to "No-Go" cues.

			Baseline M (*SD*)	Post-intervention M (*SD*)	Mean differences (95% CI)	Effect size (d_z)
N2 high ED foods	Amplitude (μV)	Food-specific intervention	−1.75 (2.17)	−1.92 (1.51)	0.17 (−1.03–1.37)	0.06
		General intervention	−1.91 (2.27)	−2.24 (2.14)	0.34 (−0.93–1.61)	0.11
	Latency (ms)	Food-specific intervention	268 (37)	268 (31)	0.63 (−19.66–20.91)	0.01
		General intervention	285 (28)	288 (29)	−3.23 (−20.61–14.15)	0.10
N2 non-foods	Amplitude (μV)	Food-specific intervention	−1.29 (1.70)	−1.93 (2.41)	0.64 (−0.72–2.00)	0.19
		General intervention	−1.64 (1.78)	−2.54 (2.30)	0.90 (−0.29–2.10)	0.33
	Latency (ms)	Food-specific intervention	269 (24)	272 (31)	−3.13 (−15.42–9.18)	0.08
		General intervention	283 (26)	275 (33)	7.81 (−12.69–28.32)	0.16
P3 high ED foods	Amplitude (μV)	Food-specific intervention	1.68 (1.33)	1.74 (0.80)	−0.06 (−0.62–0.50)	0.04
		General intervention	2.20 (1.57)	1.75 (1.58)	0.45 (−0.10–1.01)	0.35
	Latency (ms)	Food-specific intervention	444 (41)	419 (49)	25.47 (−2.63–53.57)	0.37
		General intervention	448 (39)	425 (61)	22.08 (0.73–43.43)	0.45
P3 Non-foods	Amplitude (μV)	Food-specific intervention	1.22 (1.15)	1.16 (1.10)	0.06 (−0.53–0.65)	0.04
		General intervention	1.59 (1.78)	0.96 (1.53)	0.64 (0.09–1.19)	0.50
	Latency (ms)	Food-specific intervention	431 (52)	401 (62)	29.84 (0.69–59.00)	0.42
		General intervention	445 (34)	416 (69)	28.54 (1.43–55.63)	0.46

ED, energy dense; μV, microvolts; N food-specific intervention, 25; N general intervention, 23; d_z, effect size calculated for within group power analyses.

and the expected 3-way interaction was not significant [$F(1, 46) = 0.730$, $p = 0.397$, $\eta^2 = 0.016$]. There was a significant main effect of time on "go" P3 latency [$F(1, 46) = 13.421$, $p = 0.001$, $\eta^2 = 0.226$], indicating that "no-go" P3 latency decreased from baseline to post-intervention regardless of stimulus type. There was no time x type of stimulus x intervention group interaction effect [$F(1, 46) = 0.439$, $p = 0.511$, $\eta^2 = 0.009$] on "go" P3 latency.

See **Table 4** below for within group effect size calculations of go-cues split by intervention group.

Correlations With Changes in Binge Eating Frequency

Across all participants, the mean reduction in binge eating frequency was 3.95 (*SD* = 10.28).

There was no significant correlation between changes in binge eating frequency and changes in no-go N2 amplitude to high energy-dense foods ($r = -0.139$, $p = 0.368$) or N2 latency to high energy-dense food ($r = -0.151$, $p = 0.326$). Moreover, there was no significant correlation between changes in binge eating frequency and changes in no-go P3 amplitude to high-energy dense food ($r = -0.284$, $p = 0.062$) or P3 latency to high energy-dense food ($r = -0.178$, $p = 247$).

DISCUSSION

This study examined behavioral (i.e., reaction times, omission errors, and commission errors) and event-related potential (i.e., N2 and P3) changes at baseline and at the end of an intervention

TABLE 4 | N2 and P3 amplitudes and latencies to "Go" cues.

			Baseline M (*SD*)	**Post-intervention M (*SD*)**	**Mean differences (95% CI)**	**Effect size (d_z)**
N2 low ED foods	Amplitude (μV)	Food-specific intervention	−1.18 (1.94)	−1.96 (2.20)	0.77 (−0.43–1.98)	0.26
		General intervention	−1.38 (2.31)	−1.64 (2.52)	0.26 (−1.13–1.65)	0.08
	Latency (ms)	Food-specific intervention	264 (39)	269 (35)	−5.16 (−24.72–14.31)	0.11
		General intervention	292 (30)	283 (41)	9.34 (−13.06–31.74)	0.18
N2 non-foods	Amplitude (μV)	Food-specific intervention	−0.96 (1.89)	−1.64 (2.53)	0.68 (−0.75–2.11)	0.20
		General intervention	−0.77 (2.22)	−1.81 (2.40)	1.05 (−0.19–2.28)	0.37
	Latency (ms)	Food-specific intervention	266 (36)	253 (29)	3.75 (−12.83–20.33)	0.09
		General intervention	274 (36)	264 (36)	9.68 (−10.88–30.24)	0.20
P3 low ED foods	Amplitude (μV)	Food-specific intervention	2.41 (1.78)	2.62 (1.30)	−0.20 (−0.77–0.36)	0.15
		General intervention	3.37 (2.45)	2.75 (2.10)	0.62 (−0.07–1.31)	0.39
	Latency (ms)	Food-specific intervention	446 (52)	425 (54)	20.47 (−2.42–43.36)	0.37
		General intervention	457 (43)	435 (45)	21.91 (0.69–43.13)	0.45
P3 non-foods	Amplitude (μV)	Food-specific intervention	1.90 (1.64)	2.07 (1.32)	−0.16 (−0.62–0.29)	0.15
		General intervention	2.46 (2.32)	2.09 (1.64)	0.37 (−0.34–1.08)	0.23
	Latency (ms)	Food-specific intervention	461 (56)	423 (41)	37.19 (7.15–67.22)	0.51
		General intervention	451 (48)	425 (48)	25.48 (−0.80–51.75)	0.42

ED, energy dense; μV, microvolts; N food-specific intervention, 25; N general intervention, 23; d_z, effect size calculated for within subject power analyses.

designed to modify inhibitory control for bulimia nervosa and BED. The research aimed to explore whether changes would be present, whether they would be specific to food, and whether they would differ between the two intervention groups.

In line with our hypothesis, individuals allocated to the food-specific intervention group, compared to the general intervention group, showed significantly greater reductions in reaction time to low-energy dense foods, compared to non-foods, from baseline to post-intervention. These indicate that successful stimulus-response learning to "go" cues had taken place, which may have induced a beneficial attentional bias toward these foods. Participants in both intervention groups showed significant reductions in P3 latency over time, indicating a speeding of task-related information processing (Kieffaber and Hetrick, 2005; Schaefer and Nooner, 2018). Contrary to our hypothesis, no significant changes in the number of omission errors were found. Furthermore, the number of commission errors increased from baseline to post-intervention, which was unexpected. This increase in commission errors may represent a speed-accuracy trade-off, where speeded reaction time is parallel to an increase in errors. It may also result from boredom or fatigue, as participants who complete the same training task, with no variation to interval durations, may have become more distractible.

At baseline, "no-go" cues elicited larger N2 amplitudes and smaller P3 amplitudes compared to "go" cues, suggesting that there was greater inhibition and less attention/salience toward "no-go" cues, lending evidence to the fundamental validity of the task and training.

Despite this, no significant increases in "no-go" N2 amplitudes were found from baseline to post-intervention, and no significant differences were found between the two intervention groups. This was in line with findings from previous research, which reported no increase in N2 amplitude as a result of inhibitory control training (Blackburne et al., 2016). Such findings, in addition to the non-significant correlation between changes in binge eating frequency and changes in "no-go" N2 to high energy-dense food may confirm that the N2 component might be more closely related to conflict monitoring (Dimoska et al., 2006), a process not targeted by the present interventions (i.e., inhibitory control training and implementation intentions). Previous research using a go/no-go task suggest that a greater number of "go," as opposed to "no-go," trials (i.e., where the stopping/no-go process needs to be evoked against a dominant, frequent response) are needed to evoke enhanced N2 amplitudes (Donkers and Van Boxtel, 2004).

Albeit marginally and non-significantly, P3 amplitudes to "no-go" cues descriptively decreased from baseline to post-intervention. Nonetheless, there was no significant interaction between time x type of stimulus x intervention group, and no significant correlation between changes in binge eating frequency and no-go P3 amplitudes to high energy-dense foods. These indicate that the marginal decrease in P3 to "no-go" cues may reflect a general depreciation that comes with repeated task completion. Given that the P3 amplitude is sensitive to the amount of attentional resources engaged (Polich, 2007), it is likely to reduce after the task is learnt over repeated trainings.

Our hypotheses regarding changes in N2 to "go" cues were not supported and no significant 3-way interaction was found. In addition, while we expected less negativity over time (suggestive of reduced inhibition), there was a non-significant trend in the opposite direction. These findings might have been influenced by the inclusion of a binary "left-right" decision to the "go" instruction (participants were required to press "C" or "M" depending on the location of the stimulus on the screen during "go" trials). This additional attentiontal control may have slowed down the "go" process and engaged inhibitory processes.

In addition, no significant changes in P3 amplitudes to "go" cues were found from baseline to post-intervention, and no significant 3-way interaction was found. While previous research using similar methodology had found enhanced P3 amplitudes in frontal electrodes over the course of training (Blackburne et al., 2016), the go/no-go task used in the present research failed to provoke a P3 response in frontal electrodes. Given that P3 amplitudes in the present study were more enhanced within parietal electrodes, which are thought to represent motivational relevance and salience (Herrmann and Knight, 2001; Heinze et al., 2007), attentional, as opposed to inhibitory, processes may have been involved.

In light of these findings, we were unable to identify changes in neural components that correlate with changes in eating behavior over time. Therefore, while changes in binge eating frequency were found on a behavioral level (Chami et al., in submission), it remains unclear what change processes had occurred on a neural level. A consideration of limitations is essential. For instance, the negligible error rates during task completion may suggest that the task was not challenging and hence, did not recruit inhibitory circuits. This is consistent with the absence of a P3 in fronto-central electrodes (Polich, 2007). To increase the differentiation between "go" and "no-go" trials, it may have been more informative to use a simple food go/no-go task, as opposed to a two-choice go/no-go task. Additionally, a random inter-trial interval may have increased our ability to ensure participants" attentiveness to the task. Another limitation of this study is that it combined inhibitory control training and if-then planning, making it challenging to assess the individual impact of each intervention. Moreover, while we used the go/no-go training task as a measure of change to allow for an understanding of what occurs during training completion, it has inevitably been designed as a training tool (Lawrence et al., 2015). Therefore, given that low energy-dense foods were always paired with "go" cues and high energy-dense foods were always paired with "no-go" cues, our ability to compare changes in ERP responses to high and low-energy dense foods over time was limited. These comparisons may be particularly relevant in individuals with eating disorders (see Carbine et al., 2018).

CONCLUSION

The present research shows that, while participants in the intervention showed reductions in binge eating frequency (Chami et al., in submission), the neural processes supporting this clinical effect could not be entirely uncovered. It remains unclear whether the null findings reflect an absence of change in neural activity over time, or an inability of the measures to detect change. It is advisable for future research to explore different task parameters, by potentially differing the ratio of "go" to "no-go" trials and increasing the speed-accuracy trade-off.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The London Westminster Research Ethics Committee and the Health Research Authority reviewed and approved all the procedures involved in this study (IRAS Project ID: 209609). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

RC has recruited participants and collected the data. GM has offered use of EEG equipment. RC and ML-M have pre-processed the data. KE has contributed to epoching the EEG data. JB has assisted in the creation of figures. RC has written the manuscript, with suggestions and corrections from JT, VC, ML-M, KE, GM, and JB.

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Age-Related Changes in the Neural Processes of Reward-Directed Action and Inhibition of Action

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Aging is associated with structural and functional brain changes which may impact the regulation of motivated behaviors, including both action and inhibition of action. As behavioral regulation is often exercised in response to reward, it remains unclear how aging may influence reward-directed action and inhibition of action differently. Here we addressed this issue with the functional magnetic resonance imaging data of 72 participants (aged 21–74) performing a reward go/no-go (GNG) task with approximately 2/3 go and 1/3 no-go trials. The go and no-go success trials were rewarded with a dollar or a nickel, and the incorrect responses were penalized. An additional block of the GNG task without reward/punishment served as the control to account for age-related slowing in processing speed. The results showed a prolonged response time (RT) in rewarded (vs. control) go trials with increasing age. Whole-brain multiple regressions of rewarded (vs. control) go trials against age and RT both revealed an age-related reduced activity of the anterior insula, middle frontal gyrus, and rostral anterior cingulate cortex. Furthermore, activity from these regions mediated the relationship between age and go performance. During rewarded (vs. control) no-go trials, age was associated with increased accuracy rate but decreased activation in the medial superior frontal and postcentral gyri. As these regions also exhibited age-related activity reduction during rewarded go, the finding suggests aging effects on common brain substrates that regulate both action and action inhibition. Taken together, age shows a broad negative modulation on neural activations but differential effects on performance during rewarded action and inhibition of action.

Keywords: aging, action, inhibition of action, reward, fMRI

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INTRODUCTION

Aging is associated with changes in brain structures and functions including those underlying goal-directed behaviors (Marschner et al., 2005). Previous imaging evidence suggests a negative relationship between age and neural activities during tasks involving action and inhibition of action. For instance, older individuals showed a diminished primary motor cortical activation to forceful hand grips (Ward et al., 2008) and sequential movements (Sharma and Baron, 2014). In inhibition of action, age was associated with an attenuated activity in the left orbitofrontal and dorsolateral prefrontal cortex during successful vs. unsuccessful stopping in the stop-signal task (Hu et al., 2012). Voxel-based morphometry further demonstrated gray matter volume reductions in the right dorsolateral prefrontal cortex, caudate head, and bilateral insula with age (Hu et al., 2018). These age-related neural alterations likely have behavioral implications. Indeed the latter study reported a relationship between age-related changes in the regional gray matter volume in these regions and prolonged stop-signal reaction time, an index of behavioral inhibition. Other studies showed that older, as compared to young, adults were slower in initiating actions in a two-choice decision (Eppinger et al., 2012), Stroop (Verhaeghen and De Meersman, 1998; Zysset et al., 2007), and stop-signal (Rush et al., 2006; Hu et al., 2019) tasks. Past evidence together suggests decreasing brain activities and weaker task performance during action and inhibition of action with advancing age.

Goal-directed behaviors are frequently driven by reward. As aging may alter reward responses, it is critical to understand how age influences reward processing during action regulation. Aging appears to broadly diminish both behavioral and brain responses to reward. During the reinforcement learning task, a study using an electroencephalogram reported that feedback-related negativity, an event-related potential in response to negative feedback, for monetary gains showed a monotonic reduction from childhood to old age (Hämmerer et al., 2011), suggesting age-related diminution in reward-related saliency response. In the monetary incentive delay task, age was negatively correlated with neural activations to anticipated large vs. small rewards in regions implicated in reward processing, including the orbitofrontal cortex and ventral striatum (Dhingra et al., 2019). These findings support previous reports of reduced dopaminergic signaling and reward sensitivity in aging (Kish et al., 1995; Volkow et al., 1996; Kumakura et al., 2010). In behavioral investigations, older adults exhibited decreased sensitivity to reward (SR) probability in a signal-detection task (Tripp and Alsop, 1999), greater risk aversion in economic decision tasks (Grubb et al., 2016; Mata et al., 2016; Rutledge et al., 2016), and less delay discounting (Green et al., 1994) as compared to young adults. Although older adults showed reduced sensitivity to winning a large vs. small reward, they were more sensitive to the loss of a small vs. large reward as compared to younger adults (Dhingra et al., 2019). These age-related changes in reward and risk/loss sensitivity likely influence motivated action and inhibition of action, respectively. One possibility is that diminished SR negatively impacts reward-directed action, manifesting in age-related decreases in brain responses. In contrast, higher sensitivity to loss or risk may be associated with increases in activations to inhibition of action in older relative to younger adults.

As motor slowing is commonly observed in aging (Salthouse, 2000), it is important to consider age-related changes in processing speed when examining changes in goal-directed behaviors. Previous work has associated age with motor slowing in the stop-signal task (Rush et al., 2006) as well as in both congruent and incongruent conditions in a Stroop task (Verhaeghen and De Meersman, 1998), indicating a general slowing in behavioral responses. Age-related decreases in processing speed also negatively affected response time (RT) in tasks that engaged memory, verbal, and spatial processing during cognitive control (Finkel et al., 2007). As such, general motor slowing may account for some of the changes in goal-directed behaviors in older adults. Nevertheless, no study, to our knowledge, has controlled for this motor component when examining how age may alter the neural substrates that support rewarded action and inhibition of action.

To investigate how age influences motivated action and inhibition of action, we employed a go/no-go (GNG) task in which both correct action and inhibition of action were rewarded and both incorrect trials were penalized. As reward/punishment sensitivity changes with age, we used two different monetary values, dollar and nickel, to explore potential differences related to win/loss magnitude in behavioral and neural responses. We included a no reward/punishment condition as a baseline to control for age-related decline in processing speed. Individual differences in reward and punishment sensitivity were further controlled to better identify age-specific effects. We tested the hypothesis that rewarded go performance as well as neural activations to go responses would diminish with age and that rewarded no-go performance and neural activations to no-go responses would both be enhanced with age. Finally, we used mediation models to investigate the inter-relationships between age, behavioral performance, and brain activations while controlling for processing speed and trait sensitivities.

MATERIALS AND METHODS

Participants and Assessments

Seventy-two healthy adults (36 females; age range = 21–74; mean ± SD, 36.4 ± 13.9 years) participated in the study. All the subjects were screened to ensure absence of major medical, including neurological, illness and lifetime Axis I psychiatric disorders. No participant was currently on psychotropic medications and all tested negative for illicit substances on the study day. The subjects provided written informed consent after the details of the study were explained, in accordance to institute guidelines approved by the Yale Human Investigation Committee.

All the participants completed the Sensitivity to Punishment and Sensitivity to Reward Questionnaire (Torrubia et al., 2001), which contains 48 yes–no items, with 24 items measuring behavioral impulsivity/responsiveness to reward and the other 24 measuring behavioral avoidance in response to potentially adverse consequences. The scores were obtained by totaling the number of yes answers in each scale, with higher subscores indicating greater SR and sensitivity to punishment (SP), respectively. The participants reported averages in SR score of 9.79 ± 4.73 and SP score of 8.58 ± 5.33.

Behavioral Task

The participants performed a GNG task, completing two reward runs, followed by one control and two additional reward runs (**Figure 1**). In the reward runs, a dollar image and a nickel

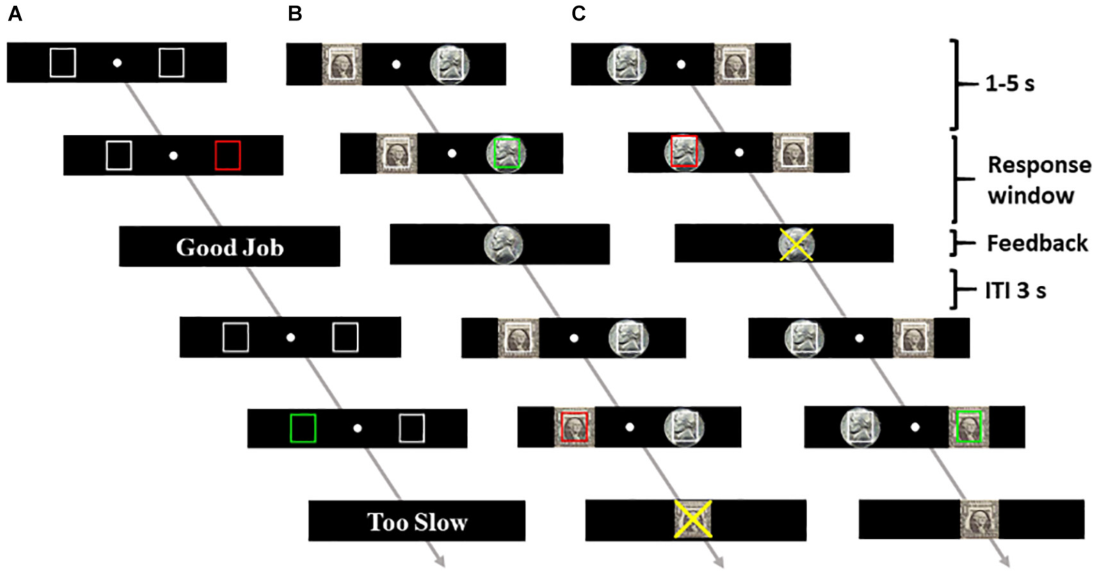

FIGURE 1 | Task schematic. The participants performed a go/no-go task for one control session (session 3) with no reward **(A)** and four sessions with the dollar reward on the left **(B)** and on the right **(C)**, counter-balanced in order across subjects. A successful go trial and a failed no-go trial are illustrated in both **(B)** and **(C)**.

image were presented to the left/right of the fixation in two runs and were reversed in direction for the other two, with the order counter-balanced across subjects. Go (∼66.6%) and no-go (∼33.3%) trials were randomly intermixed in presentation, with an inter-trial interval of 3 s.

At the beginning of each trial, two black squares (control run) or two images, one of dollar and one of nickel (reward runs), appeared to the left and right of the fixation. The squares and the images were outlined in white. After a randomized interval between 1 and 5 s, one of the outlines (i.e., either left or right square/image) turned green/red, indicating a GNG signal. The subjects were instructed to press the spatially corresponding left/right button as quickly as possible in response to the go signal and to withhold the button press to the no-go signal. Feedback was provided at button press or once the response window had elapsed. In the control run, the feedback displayed the text "Good Job" for correct responses or "Too Slow" and "Don't" for incorrect go and no-go responses, respectively. For the reward runs, the participants won a dollar or a nickel in each correct trial. An image of a dollar or nickel was shown as feedback to indicate the amount. In incorrect trials, the participants lost either a dollar or a nickel. A symbol "X" overlaid on the dollar or the nickel image informed of the amount of money loss. Premature button presses prior to the color change were treated as errors, resulting in the feedback "Don't" for control trials or symbol X overlaid on the dollar/nickel for reward trials. The participants performed approximately 50 go and 25 no-go trials in the control run and 100 go and 50 no-go each of the dollar-and-nickel trials in the reward runs. The participants won an average of \$123 ± 38 (mean ± SD).

Prior to imaging, the subjects completed a control session outside the scanner. A normal distribution function was fitted on the RT, and 10^7 data points were generated based on the fitted function. The response window for go success was set as the closest integer greater than 85% of the generated data points for the fMRI experiment.

Behavioral Analysis

The trial types were separated for the go and the no-go responses as well as the dollar and the nickel rewards: GS dollar, GS nickel, GE dollar, GE nickel, NGS dollar, NGS nickel, NGE dollar, and NGE nickel (GS: go success; GE: go error; NGS: no-go success; and NGE: no-go error). The number of trials for each condition and each block is detailed in **Supplementary Table S1**. For the response rate, a two-way (GS vs. NGS × dollar vs. nickel vs. control) analysis of variance (ANOVA) was conducted. *Post hoc* comparisons were performed to further investigate the potentially differential effects of reward on action and inhibition of action. Similarly, we used a two-way (GS vs. NGE × dollar vs. nickel vs. control) ANOVA to examine the RT. Subjects without NGE trials were omitted from the analysis. To examine the relationship between age and task performance, we performed partial correlations using sex, SR, and SP as covariates. We controlled for task performance in the control session to account for general age-related changes in processing speed. For instance, the RT of the go control trials was subtracted from the go dollar trials (e.g., GS dollar RT - GS control RT) in the analyses involving go dollar RT.

Imaging Protocol and Data Preprocessing

Conventional T1-weighted spin echo sagittal anatomical images were acquired for slice localization using a 3T scanner (Siemens Trio, Erlangen, Germany). Anatomical 3D MPRAGE images were obtained with spin echo imaging in the axial plane parallel to the anterior commissure–posterior commissure (AC–PC) line with repetition time (TR) = 1,900 ms, echo time (TE) = 2.52 ms, bandwidth = 170 Hz/pixel, field of view (FOV) = 250 mm × 250 mm, matrix = 256 × 256, 176 slices with slice thickness = 1 mm, and no gap. Functional blood oxygenation level-dependent (BOLD) signals were acquired using multiband imaging (multiband acceleration factor = 3) with a single-shot gradient echo-planar imaging sequence. Fifty-one axial slices, parallel to the AC–PC line covering the whole brain, were acquired with TR = 1,000 ms, TE = 30 ms, bandwidth = 2290 Hz/pixel, flip angle = 62°, FOV = 210 mm × 210 mm, matrix = 84 × 84, voxel size = 2.5 mm isotropic, and no gap.

The imaging data were preprocessed using SPM12 (Wellcome Trust Centre for Neuroimaging). Images from the first five TRs at the beginning of each run were discarded to ensure that only BOLD signals at steady-state equilibrium between radio frequency pulsing and relaxation were included in the analyses. The images of individual subjects were first realigned (motion-corrected) and corrected for slice timing. A mean functional image volume was constructed for each subject per run from the realigned image volumes. These mean images were co-registered with the high-resolution structural image and then segmented for normalization with affine registration followed by nonlinear transformation. The normalization parameters determined for the structure volume were then applied to the corresponding functional image volumes. The voxel size after normalization was 2.5 mm isotropic. Finally, the images were smoothed with a Gaussian kernel of 4-mm full width at half-maximum.

Imaging Data Modeling

A statistical analytical design was constructed for individual subjects using the general linear model (GLM), with the onsets of go or no-go signals convolved with a canonical hemodynamic response function (HRF) and with the temporal derivative of the canonical HRF and entered as regressors in the model (Friston et al., 1995). As go and no-go error trials were associated with an RT, a column of RT was entered as a parametric modulator each for GS, GE, and NGE trials in the model. Realignment parameters in all six dimensions were also entered in the model. The data were high-pass-filtered (128-s cutoff) to remove low-frequency signal drifts. Serial autocorrelation caused by aliased cardiovascular and respiratory effects was corrected by a FAST model. The GLM estimated the component of variance that could be explained by each of the regressors.

In the first-level analysis, we constructed for the statistical contrasts required for second-level analyses. To examine how brain activities associated with action and inhibition of action varied across subjects in relation to age and behavioral performance, we conducted whole-brain multiple regressions against age with sex and the SR and SP scores as the covariates. Specifically, we examined the contrasts (GS dollar > GS control) and (NGS dollar > NGS control) in correlation with age. We used the GS/NGS control as the baseline to account for age-related changes in processing speed which could confound any potential alterations in approach and avoidance. Similarly, sex and the SR and SP scores were used as covariates to rule out the effects of individual differences in gender and trait sensitivities. We further investigated the neural correlates of go performance by conducting a whole-brain multiple regression for the (GS dollar > GS control) contrast against (GS dollar RT - GS control RT), again using sex and trait sensitivities as the covariates. For no-go trials, as no RT was available, we used (NGS dollar accuracy rate - NGS control accuracy rate) and (NGS dollar > NGS control) contrast. Another set of analysis was conducted for the nickel condition. Cohen f^2 values were calculated to measure the effect size of multiple linear regressions with small (0.02), medium (0.15), and large (0.35) effects consistent with interpretation guidelines (Cohen, 1992). All regression results were examined with voxel $p < 0.001$ in combination with cluster $p < 0.05$, corrected for family-wise error, according to current reporting standards (Woo et al., 2014; Eklund et al., 2016). All activations were reported in Montreal Neurological Institute coordinates.

Mediation Analysis

To examine the inter-relationships of age, neural activity, and task performance, we conducted mediation analyses using a single-mediator model (MacKinnon et al., 2007). The methods were detailed in our previous work (Le et al., 2019a,b). Briefly, in a mediation analysis, the relationship between the independent variable X and dependent variable Y (i.e., $X \rightarrow Y$) is tested to determine whether it is significantly mediated by a variable M. The mediation test is performed using the following three regression equations:

$$Y = i1 + cX + e1$$

$$Y = i2 + c'X + bM + e2$$

$$M = i3 + aX + e3$$

where a represents $X \rightarrow M$, b represents $M \rightarrow Y$ (controlling for X), c' represents $X \rightarrow Y$ (controlling for M), and c represents $X \rightarrow Y$. a, b, c, and c' are path coefficients. Variable M is said to serve as a mediator of connection $X \rightarrow Y$ if $(c - c')$ is significantly different from zero (MacKinnon et al., 2007). If $(c - c')$ is different from zero and the paths a and b are significant, then $X \rightarrow Y$ is mediated by M. Additionally, if path c' is not significant, there is no direct connection from X to Y, in which case $X \rightarrow Y$ is completely mediated by M. The analysis was performed with package Lavaan (Rosseel, 2012) in R. To test the significance of the mediation effect, we used the bootstrapping method (Preacher and Hayes, 2004) as it is generally considered advantageous to the Sobel test (MacKinnon et al., 2007).

Specifically, we evaluated the inter-relationships between age, task performance, and neural activity of GS dollar > GS control (see section "Results"). For neural activity, we extracted the parameter estimates (effect size) from the overlapping voxels of the two multiple regressions of (GS dollar > GS control) against age and (GS dollar RT > GS control RT). We considered three models (**Figure 4**). In model 1, age served as the independent variable (*X*), RT as the dependent variable (*Y*), and neural activity as the mediator (*M*). Thus, age contributed to neural activity, which in turn modulated task performance: age → neural activity → RT. In model 2, age contributed to neural activity and this relationship was mediated by task performance: age → RT→ neural activity. In model 3, neural activity contributed to task performance and this relationship was mediated by age: neural activity → age → RT. We did not consider the remaining three models in which age or neural activity served as the dependent variable as these models lacked conceptual import. We used Bonferroni ($p = 0.017$) to correct for multiple-model testing.

RESULTS

The Effects of Age on Behavioral Performance

Figures 2A,B show the accuracy rate and the RT across conditions. For the accuracy rate, a two-way (GS vs. NGS × dollar vs. nickel vs. control) ANOVA showed a significant main effect of response [$F(1, 426) = 246.01$, $p < 0.001$, partial $\eta^2 = 0.37$], reward value [$F(2, 426) = 12.10$, $p < 0.001$, partial $\eta^2 = 0.05$], and response × reward value interaction [$F(2,426) = 23.71$, $p < 0.001$, partial $\eta^2 = 0.10$]. In *post hoc* analyses, the accuracy rate was significantly higher in the GS dollar than in the GS nickel and the GS control trials (*p*'s < 0.001) and higher in the GS control than in the GS nickel trials ($p < 0.001$). In contrast, the accuracy rate for NGS dollar trials was significantly lower than for the NGS nickel trials ($p < 0.001$). The NGS control rate was significantly lower than the NGS nickel rate ($p < 0.001$) but did not significantly differ from the NGS dollar rate ($p = 0.93$).

For RT, 28 subjects did not commit any error in one of the trial conditions and thus were not included in the analysis. A two-way (GS vs. NGE × dollar vs. nickel vs. control) ANOVA showed a significant main effect of response [$F(1, 258) = 8.52$, $p = 0.004$, partial $\eta^2 = 0.03$] and reward value [$F(2, 258) = 8.31$, $p < 0.001$, partial $\eta^2 = 0.06$] but not the response × reward value interaction [$F(1, 246) = 1.13$, $p = 0.32$, partial $\eta^2 = 0.008$]. RT was significantly faster in the GS dollar compared to the GS nickel and the GS control trials (*p*'s < 0.001) (**Figure 2B**). Response time for the GS nickel trials was slower than for the GS control trials ($p < 0.001$). The RT for NGE dollar trials was significantly faster than that for NGE nickel trials ($p < 0.001$) but did not differ significantly from the NGE control trials ($p = 0.28$), and the latter two were not significantly different after controlling for multiple corrections (uncorrected $p = 0.05$).

Next, we examined the relationship between age and behavioral measures of action and inhibition of action after accounting for processing speed, trait sensitivities, and sex. The results were evaluated at a corrected *p* value of 0.05/8 = 0.006. Age was significantly and positively correlated with (GS dollar RT - GS control RT), controlling for sex and the SR and SP scores ($r = 0.48$, $p < 0.001$, **Figure 2C**), but not with (GS nickel RT - GS control RT) ($p = 0.27$, **Figure 2D**). Age did not show significant correlations with the accuracy rate of (GS dollar - GS control) or (GS nickel - GS control) (*p*'s > 0.62). There was a significant correlation between age and the accuracy rate of (NGS dollar - NGS control) ($r = 0.26$, uncorrected $p = 0.03$, not significant after correction for multiple comparisons, **Figure 2E**) as well as (NGS nickel - NGS control) ($r = 0.42$, $p < 0.001$, **Figure 2F**). Taken together, we found partial evidence for age-related impediment of action and enhancement of inhibition of action, with the former primarily in the dollar condition and the latter in the nickel condition.

The Effects of Age on Regional Responses to Reward-Directed Action

As there was a significant relationship between age and (GS dollar RT - GS control RT), we focused on the GS dollar > GS control contrast. The whole-brain multiple regression against age showed a significant negative correlation with activations in the bilateral anterior insula, bilateral middle frontal gyri (MFG), superior frontal gyrus (SFG), postcentral gyrus (PoCG), bilateral superior temporal sulci, and dorsal/rostral anterior cingulate cortex (dACC/rACC) (**Figure 3A** and **Table 1**). No clusters showed an activity in significant positive correlation with age. The multiple regression for GS nickel trial showed a similar, albeit weaker, pattern of activation (**Supplementary Figure S1**).

Regional Responses to Reward-Directed Action in Correlation With RT Performance

Next, we examined the neural correlates of task performance during rewarded action. There was a negative correlation between (GS dollar RT - GS control RT) and activations to the contrast (GS dollar > GS control) in the bilateral anterior insula, mOFC, right MFG, rACC, dACC, mid-cingulate cortex, cerebellum, pre/PoCG, and a cluster containing the right posterior insula and putamen (**Figure 3B** and **Table 2**). No clusters showed an activity in positive correlation with RT.

Age- and Performance-Shared Correlates During Reward-Directed Action

The multiple regressions of (GS dollar > GS control) against age and against (GS dollar RT - GS control RT) revealed that voxels overlapped in the bilateral anterior insula, right MFG, rACC, and dACC (**Figure 4A**). Thus, we examined the inter-relationships between the activity of these overlapping voxels, age, and task performance during rewarded action. The averaged parameter estimates across these voxels were extracted for contrast (GS dollar > GS control), and, as expected, were significantly correlated with age ($r = 0.48$, $p < 0.001$, effect size = 0.30, **Figure 4B**) and (GS dollar RT - GS control RT) ($r = 0.53$, $p < 0.001$, effect size = 0.39, **Figure 4C**). As shown earlier, age and (GS dollar RT - GS control RT) showed a positive relationship ($r = 0.48$, $p < 0.001$, **Figure 4D**).

We conducted a mediation analysis (**Table 3**). Model 1 (age → neural activity → task performance) showed a significant mediation effect [$c - c' = 0.24$, $p = 0.013$, 95% confidence

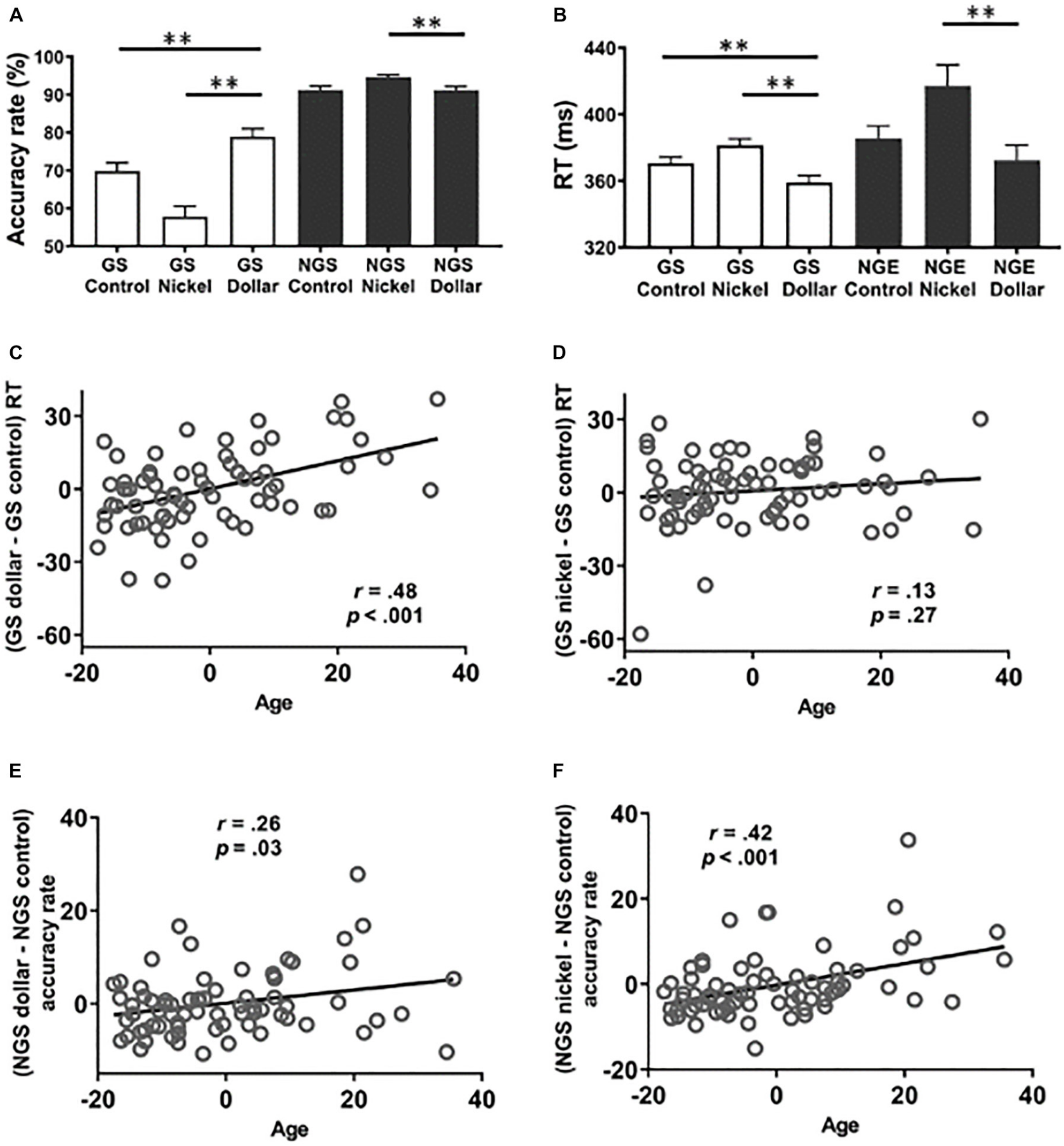

FIGURE 2 | Behavioral results. Behavioral results (mean ± SE) showed the accuracy rate **(A)** and the reaction time **(B)** across trial types. Age was positively correlated with response time of the go responses in the dollar **(C)** but not nickel **(D)** vs. the control trials. Age was also positively correlated with the accuracy rate of no-go dollar **(E)** and nickel **(F)** vs. the control trials. GS, go success; NGS, no-go success; NGE, no-go error. $^{**}p \leq 0.001$. NB: all scatterplots show partial correlations of residuals after the effects of trait sensitivities and sex were removed.

interval = (0.08, 0.45); highlighted, left]. Specifically, the path coefficient *c* (i.e., age → task performance before accounting for the mediating effect of neural activity) was significant ($p < 0.001$) and the path coefficient *c'* (i.e., after accounting for the mediating effect) was substantially weakened ($p = 0.05$). Thus, older age led to slower RT during rewarded action and the neural activity mediated this relationship. Model 2 (age → task performance → neural activity) also showed a significant mediation effect but did not survive correction for multiple-model testing (uncorrected $p = 0.022$). No significant mediation effect was found for model 3 (neural activity → age → task performance) (uncorrected $p = 0.084$).

The Effects of Age on Regional Responses to Reward-Directed Inhibition of Action

The multiple regression of (NGS dollar > NGS control) against age showed a significant negative correlation with activations in the bilateral SFG and right PoCG (**Figure 5**, dark

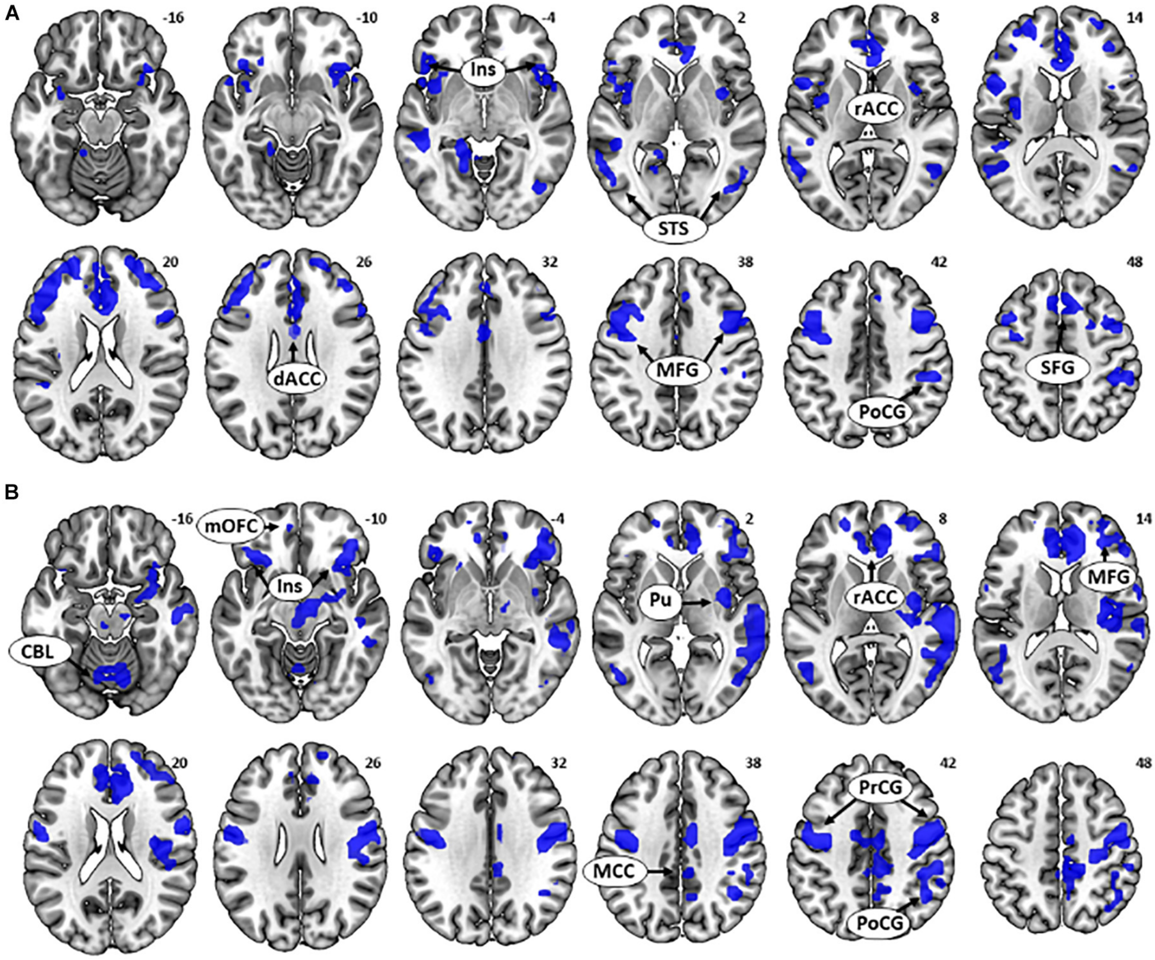

FIGURE 3 | (A) Multiple regression for the contrast [go success (GS) dollar > GS control] showed a negative correlation between age and activations in the bilateral anterior insula, middle frontal gyri (MFG), postcentral gyrus, superior temporal sulci, rostral anterior cingulate cortex (rACC), and dorsal anterior cingulate cortex. **(B)** Multiple regression for contrast (GS dollar > GS control) showed a negative correlation between [GS dollar response time (RT) - GS control RT] and activations in the bilateral insula, medial orbitofrontal cortex, right MFG, rACC, mid-cingulate cortex, precentral gyrus/postcentral gyrus, a cluster containing the right posterior insula and putamen, and cerebellum.

blue and **Table 1**). No clusters showed a significant positive correlation with age.

It is notable that the SFG, particularly the media part, and the right PoCG showed an age-related decrease in activations to both (GS dollar > GS control) (i.e., **Figure 2**; shown as green in **Figure 5**) and (NGS dollar > NGS control) (**Figure 5**, light blue). This indicates aging effects on common brain substrates that may regulate both rewarded action and inhibition of action.

No clusters showed a significant correlation in the multiple regression of (NGS dollar > NGS control) against the accuracy rate of (NGS dollar - NGS control) in either direction.

The multiple regression of (NGS nickel > NGS control) against age or against the accuracy rate of (NGS nickel - NGS control) did not show clusters in significant correlation in either direction.

DISCUSSION

Employing a GNG task, we examined the effects of age on behavioral performance and neural processes during rewarded action and inhibition of action, controlling for individual differences in gender and reward and punishment sensitivities. Age was associated with prolonged RT and a reduction of activity in the anterior insula, MFG, rACC, and dACC during rewarded action. These regions also showed activation in negative correlation with RT, indicating a potential inter-relationship between age, neural activity, and task performance. The mediation models confirmed that increasing age diminished brain activations to goal-directed action, which in turn slowed down behavioral responses. In contrast, age was positively correlated with the accuracy rate during rewarded inhibition of action, suggesting opposing effects of age on initiating and restraining an action. There was a negative relationship

TABLE 1 | Age modulation of activation to action and inhibition of action.

	Region	Montreal Neurological Institute coordinates (mm)			Voxel	Cluster
		x	*y*	*Z*	*T*	*k*
Go success (GS) dollar > GS control	SFG/dACC	9	17	55	5.52	2,276
	rACC	6	23	22	5.28	
	Insula	−33	−1	10	3.65	
		36	23	−14	4.52	137
		33	14	−14	3.79	
	MFG	27	59	22	4.60	168
		39	41	22	4.03	
	STS	51	−70	4	4.00	98
		−57	−58	10	3.96	127
		−48	−31	−8	4.33	119
		−48	−37	−2	4.31	
	PHG	−18	−55	−2	4.03	170
	PoCG	48	−34	46	4.20	100
		57	−37	49	3.87	
No−go success (NGS) dollar > NGS control	SFG	12	20	61	4.26	111
		12	11	67	3.91	
		6	26	55	3.75	
	PoCG	48	−43	46	3.98	106
		57	−49	46	3.70	

dACC, dorsal anterior cingulate cortex; MFG, middle frontal gyrus; PHG, parahippocampal gyrus; PoCG, postcentral gyrus; rACC, rostral anterior cingulate cortex; SFG, superior frontal gyrus; STS, superior temporal sulcus.

TABLE 2 | Neural correlates of response time during rewarded action.

Region	Montreal Neurological Institute coordinates (mm)			Voxel	Cluster
	x	*Y*	*z*	*T*	*k*
PrCG	51	−4	43	5.38	2,022
	−15	−28	55	5.63	
	−39	−13	40	5.25	277
	−54	−7	25	4.82	
	−54	−4	43	4.68	
rACC	12	32	19	5.16	1,258
	12	44	10	4.93	
Cerebellum	−9	−82	−35	4.96	533
	−15	−70	−38	4.84	
	−15	−61	−38	4.65	
PoCG	42	−37	40	4.59	205
	45	−55	40	4.55	
	54	−34	43	4.13	
Insula	−36	29	−11	4.49	102
	−45	29	−2	4.44	
	−27	26	−14	4.31	
STS	−54	−67	10	4.26	110
	−51	−70	1	4.19	

dACC, dorsal anterior cingulate cortex; PoCG, postcentral gyrus; PrCG, precentral gyrus; rACC, rostral anterior cingulate cortex; STS, superior temporal sulcus.

between age and activations to inhibition of action in the SFG and the PoCG. Both regions also showed age-related decreases in activations during rewarded action, thus pointing to a common age correlate for the execution and the inhibition of an action.

Age Effects on Behavioral Performance of Rewarded Action and Inhibition of Action

Age was associated with a prolonged RT of the rewarded go response, revealing a negative impact of age on motivated action, in agreement with previous investigations of the GNG task (Sebastian et al., 2013; Votruba and Langenecker, 2013). We controlled for processing speed with a neutral session to account for age-related motor slowing. Unlike most previous work using similar tasks, we incentivized responses to examine the relationship of age and reward-directed behavior. It is plausible that older adults experience a decline in motivation to act in pursuit of reward. Consistent with this interpretation, other studies have reported age-related decreases in impulsivity, sensation-seeking (Zuckerman et al., 1978; Willems et al., 2003), risky decision-making (Di Rosa et al., 2017), and reward sensitivity (Eppinger et al., 2012). As individuals become older, they may be less motivated by monetary reward and thus less vigorous in initiating reward-seeking actions. However, our findings do not imply a general age-related decline in motivation for rewards as there is evidence of enhanced sensitivity to social rewards in older, as compared to younger, adults (Rademacher et al., 2013).

Accuracy in rewarded no-go trials was found to improve with age, indicating opposite behavioral effects of age on inhibiting as compared to executing an action. Similar findings

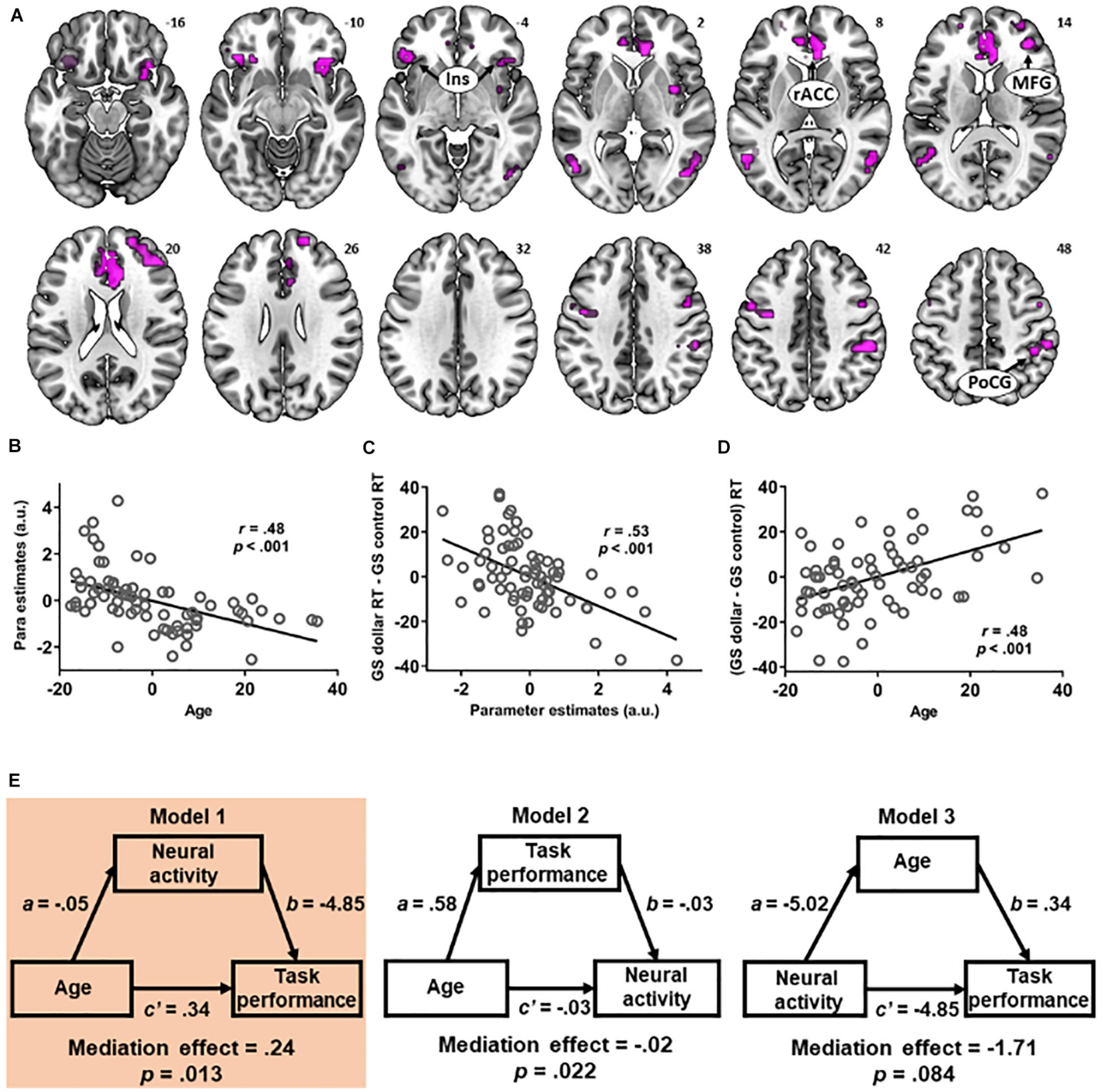

FIGURE 4 | (A) The multiple regressions of [go success (GS) dollar > GS control] contrast against age and against [GS dollar response time (RT) - GS control RT] showed an overlap in the bilateral insula, right middle frontal gyrus, rostral anterior cingulate cortex, and dorsal anterior cingulate cortex. The activity in the overlapping voxels during (GS dollar > GS control) showed a negative correlation with **(B)** age and **(C)** (GS dollar RT - GS control RT). **(D)** The latter two showed a positive relationship, as also shown in **Figure 2C**. **(E)** Mediation analysis revealed a significant mediation effect in model 1 in which age was associated with prolonged RT (GS dollar RT - GS control RT), and this relationship was mediated by a diminished activity during rewarded (vs. control) action.

have been reported with other tasks. For instance, age was associated with increased inhibition as indexed by the reduced tendency to draw from the disadvantageous decks during the Iowa gambling task (Cauffman et al., 2010). Older adults also showed better avoidance learning in a probabilistic selection task (Frank and Kong, 2008), Digit–Symbol Substitution test, and Spot-a-Word test (Eppinger and Kray, 2011) compared to the younger counterparts. However, previous studies employing the GNG task in a neutral context (i.e., without reward) did not report age-related effects on inhibition of action (Schulz et al., 2007; Kubo-Kawai and Kawai, 2010). The current findings, therefore, may be specific to behavioral contexts with a reward contingency. Taken together, our work offers behavioral evidence for contrasting modulations of age on motivated action and inhibition of action.

Age-Related Alterations in Neural Processes Underlying Rewarded Action

Consistent with the behavioral results, we found age-related attenuation in activity during rewarded action in regions involved in motivation and behavioral regulation,

TABLE 3 | Mediation of age, [go success (GS) dollar response time (RT) - GS control RT], and activity during rewarded action.

	Path *a* ($X \rightarrow M$)	Path b ($M \rightarrow Y$)	Path *c* ($X \rightarrow Y$)	Path *c'* ($X \rightarrow Y$)	Mediation path ($c - c'$)
Model 1: *X* (age) → *Y* (RT) mediated by *M* (neural activity)					
β	−0.05	−4.85	0.58	0.34	0.24
p-values	0.000	0.002	0.000	0.05	0.013
Model 2: *X* (age) → *Y* (neural activity) mediated by *M* (RT)					
β	0.58	−0.03	−0.05	−0.03	−0.02
p-values	0.000	0.003	0.000	0.001	0.022
Model 3: *X* (neural activity) → *Y* (RT) mediated by *M* (age)					
β	−5.02	0.34	−6.56	−4.85	−1.71
p-values	0.000	0.048	0.000	0.002	0.084

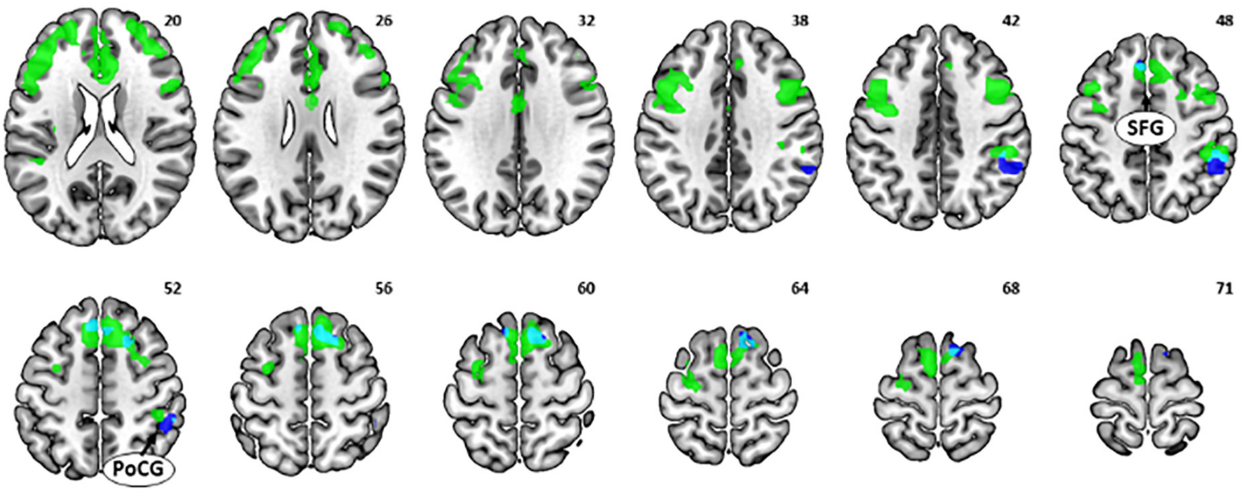

FIGURE 5 | Multiple regression of [no-go success (NGS) dollar > NGS control] against age showed a negative correlation with activations in the superior frontal gyrus and postcentral gyrus (dark blue). These neural correlates showed overlap (light blue) with the multiple regression of [go success (GS) dollar > GS control] against age (green).

including the insula, MFG, rACC, and dACC. The rACC has been implicated in the flexible regulation of goal-directed behaviors (Kolling et al., 2016), particularly those involving reward-based cognitive control (Shenhav et al., 2013). The rACC responds to decision-making and problem-solving during reward-related contingencies (Hampton and O'Doherty, 2007; Amiez et al., 2012; Payzan-LeNestour et al., 2013). Using similar behavioral tasks, other imaging studies also found increased rACC responses to motor actions and action preparation (Watanabe et al., 2002; Schulz et al., 2011). Single-unit recordings of the human ACC further showed that ACC neuronal activity not only reflected changes in reward outcomes but also predicted motor movements during a sequential two-choice selection task (Williams et al., 2004), again in support of the role of the rACC in motivating actions.

Age also negatively modulated the activity of the anterior insula, MFG, and dACC. Work in both non-human primates and humans has implicated these regions in goal-directed behaviors. Executing an effortful action to obtain rewards in various behavioral tasks, including the GNG, has been associated with increases in the activity of the insula (Asahi et al., 2006; Dixon and Christoff, 2012), MFG (Bjork and Hommer, 2007; Rademacher et al., 2010), and dACC (Williams et al., 2004; Hayden and Platt, 2010). As these regions are also involved in reward processing, the decreased activations during rewarded action may reflect reduced reward sensitivity with age. As the rACC and dACC have been proposed to be involved in the reward response and decision-making during motor processing, respectively (Bush et al., 2002; Marsh et al., 2007), they likely interact to guide motivated behaviors (Rogers et al., 2004).

The diminished activity of the ACC, MFG, and insula may be related to the loss of structural integrity in these regions during aging. Indeed aging was found to significantly reduce the gray matter volume (Vaidya et al., 2007) and the metabolic activity, as measured by glucose uptake (Pardo et al., 2007) and blood flow (Meltzer et al., 2000), of the rACC. Aging is further associated with altered molecular profiles, as reflected by the loss of dopamine D1 (MacDonald et al., 2012), and D2/D3 (Kaasinen et al., 2000) receptors in the ACC. As dopamine plays a central role in the reward mechanisms (Schultz, 2007), reduced dopaminergic signaling may exert a negative effect on the initiation of reward-directed actions. Gray matter volume loss (Kalpouzos et al., 2009; Peelle et al., 2012) and metabolic reduction (Petit-Taboue et al., 1996) were similarly found in the MFG and the insula in older adults. The relationship between a decline in structural integrity, attenuated brain activity, and behavioral outcomes poses an interesting avenue for further research.

Age-Related Alterations in Neural Processes Underlying Rewarded Inhibition of Action

Contrary to our hypothesis, we found age-related decreases in activation to rewarded inhibition of action in the medial SFG and the PoCG, both of which also exhibited age-related attenuation in activity during rewarded action. This finding indicates shared neural substrates between motivated action and inhibition of action in relation to aging. Accordingly the SFG has been implicated in the regulation of goal-directed behaviors and cognitive control (Konishi et al., 2003; Floden and Stuss, 2006; Hu et al., 2016), suggesting an important role in both action execution and inhibition. As part of the somatomotor cortex, the PoCG is involved in motor functioning in both humans (Raposo et al., 2009) and non-human primates (Iwamura and Tanaka, 1996). The age-related decrease in activation in this region may be associated with the slowing in motor processing as observed in the go performance in the current work.

Aging has been shown to negatively impact the structural integrity, including both the gray and the white matter, of the SFG (Raz et al., 1997; Oh et al., 2014) and PoCG (Raz et al., 1997; Minkova et al., 2017). Loss of gray matter may diminish their roles in action regulation, potentially leading to reduced activations to no-go responses as currently observed. This interpretation is in line with previous evidence of impaired cognitive control in older individuals (Braver and Barch, 2002; Andrés et al., 2008; Paxton et al., 2008). Nevertheless, it is important to note that we did not find a significant relationship between task performance during no-go trials and brain activity. Furthermore, the age effects on inhibition of action were most prominent for the nickel trials, yet the age-related diminution in activity during inhibition of action was observed for the dollar trials but not for the nickel trials. These findings suggest the complex influence of age on behavioral inhibition. Additionally, as no-go trials were less frequent than go trials, the biased incentivization may have rendered the no-go trials less salient than the go trials.

We found negative age effects in modulating the activities of shared regions, including the medial SFG and the right PoCG, during action and inhibition of action. Age was associated with poorer go performance but superior no-go performance. As such, the attenuation of these regional activity, particularly in the PoCG, may have opposite impacts on go and no-go trials. The PoCG has been associated with motor processing (Hyvärinen and Poranen, 1978; Woods et al., 2014). Thus, it is plausible that the lack of motor-related activation leads to a slower response initiation, making it less challenging to inhibit such response in older individuals. Indeed in regions associated with cognitive motor control, including the medial SFG (Rushworth et al., 2004; Sumner et al., 2007), diminishing activity with age may reflect less conflict between opposing actions (e.g., go vs. no-go). It is worth noting that the medial SFG has been shown to be functionally connected with motor regions (Zhang et al., 2012), putatively to modulate goal-directed movements. As the go response becomes weaker during aging, the amount of resources needed to inhibit a pre-potentiated action likely decreases, leading to the reduced need for motor control and recruitment of motor activities.

LIMITATIONS AND CONCLUSION

Findings from the current study should be examined with consideration of its limitations. Specifically, the high accuracy rate of the no-go trials indicates a relatively less challenging task condition. As the response window was titrated to the go response, no direct manipulation of the no-go trials was possible. Nevertheless, we examined the neural activations to action inhibition (i.e., contrast NGS dollar > NGS control) and found typical regions implicated in inhibitory control, including the MFG and the ACC (**Supplementary Figure S2**), indicating that the task was successful in eliciting the neural processes of inhibition. Additionally, given the insufficient number of no-go error trials in the nickel condition, we were unable to assess the brain substrates underlying reward loss sensitivity during inhibition in relation to age.

In sum, we found that brain activities underlying rewarded action and inhibition diminish with increasing age, potentially reflecting a broad attenuation in the neural processes involved in the integration of motivation and behavioral regulation. The regions previously implicated in cognitive control and reward processing, such as the MFG, ACC, and insula, all showed an age-related reduction in activity. The reduced brain activity mediated the effects of age on prolonged reaction time during rewarded vs. control go trials, suggesting more conservative responses in reward-seeking action beyond age-related motor slowing. These findings add to the neuroscience literature of motivated behaviors in healthy aging.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Yale Human Investigation Committee. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

C-SL, IL, and HC designed the study. TL collected and analyzed the data. All authors wrote the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2020.01121/full#supplementary-material

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Objective Versus Subjective Effort in Schizophrenia

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Background and Objectives: Performance on cognitive tasks is often impaired in individuals with schizophrenia (SCZ), possibly resulting from either cognitive deficits (e.g., limited working memory capacity) or diminished mental effort or both. Investment of mental effort itself can be affected by cognitive resources, task load, and motivational factors and has thus proven difficult to measure. Pupil dilation during task performance has been proposed as an objective measure, but it remains unclear to what extent this converges with self-reports of perceived task demands, motivation, and invested effort. The current study tried to elucidate this question.

Methods: A visual version of the digit span task was administered in a sample of 29 individuals with a diagnosis from the SCZ spectrum and 30 individuals without any psychiatric disorder. Pupil size was recorded during the task, whereas self-reported invested effort and task demand were measured afterward.

Results: No group difference was found for working memory capacity, but individuals with SCZ showed diminished trial-by-trial recall accuracy, showed reduced pupil dilation across all task load conditions, and reported higher perceived task demands.

Conclusion: Results indicate reduced effort investment in patients with SCZ, but it remains unclear to what extent this alone could explain the lower recall performance. The lack of a direct link between objective and subjective measures of effort further suggests that both may assess different facets of effort. This has important implications for clinical and research settings that rely on the reliability of neuropsychological test results when assessing cognitive capacity in this patient group.

Keywords: digit span, mental effort, task load, motivation, schizophrenia, pupillometry

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INTRODUCTION

Working memory deficits are commonly reported in persons with schizophrenia (SCZ; e.g., Horan et al., 2008; Ventura et al., 2009; Freeman et al., 2014) and have been explained by a lack of processing resources (Nuechterlein and Dawson, 1984; Granholm et al., 1997). However, persons with SCZ, particularly when negative symptoms are prevalent, seem to be less willing to engage with physically (Gold et al., 2013; Barch et al., 2014; Bergé et al., 2018) or cognitively effortful tasks (Wolf et al., 2014; Gold et al., 2015; Culbreth et al., 2016; Reddy et al., 2018; Chang et al., 2019) and, when engaged, tend to exert less effort during task performance (Gorissen et al., 2005; Granholm et al., 2006, 2016). Accordingly, diminished performance on cognitive tests of persons with SCZ might be explained not only by real cognitive impairments or limited resources but also by reduced invested effort (Gorissen et al., 2005). This has important implications for neuropsychological test situations in both clinical and research applications and led some authors to call for a combined assessment of neuropsychological performance and mental effort in persons with SCZ (Gorissen et al., 2005).

Mental effort has been described as the mediating processes between the theoretically achievable level of performance determined by task demands and cognitive capacity, and the actual level of performance achieved (Shenhav et al., 2017). These processes are affected by both cognitive and motivational factors, including personal goals, incentives, personality, and metacognitive knowledge (Fisher and Ford, 1998; Paas et al., 2005). Effort is inherently aversive and costly, as it requires the mobilization of energy (Gaillard, 1993; Fairclough and Houston, 2004; Shenhav et al., 2017). Hence, reduced effort exertion in persons with SCZ may be related to an overestimation of those (internal) costs (Gold et al., 2015; Shenhav et al., 2017) and could be related to a decreased tolerance of strain (van den Bosch and Rombouts, 1997). Measuring mental effort accurately has proven difficult. Studies investigating the willingness to exert effort often quantify this as choosing hard (high task demand) over easy tasks (low task demand) in favor of a larger monetary reward. Results may thus be confounded by subjective evaluation of monetary reward (see, e.g., Culbreth et al., 2016; Chang et al., 2019). In contrast, during standard neuropsychological assessments, no explicit external rewards are available, and patients usually cannot choose between hard and easy tasks. Measuring actual effort exertion in these contexts must therefore rely on different and more task-independent measures, for example, post-assessment self-reports (Moritz et al., 2017a). A more objective marker of mental effort exertion is pupil dilation during task performance (Granholm et al., 2016; van der Wel and van Steenbergen, 2018). The assumption that pupil dilation reflects effort allocation rests on the observation of positive correlations between pupil dilation and performance (Van Der Meer et al., 2010; Rondeel et al., 2015). Accordingly, smaller task-related pupil responses in persons with SCZ have been interpreted as an indication of reduced mental effort in SCZ and were found to be related to the severity of negative symptoms and defeatist attitudes (Granholm et al., 2006, 2016). Surprisingly, only a few studies investigated to what extent this objective measure of mental effort converges with self-reports of invested effort and motivation in these samples. Moreover, the role of subjectively perceived task demands and experienced strain remains unexplored, despite its likely detrimental role in effort investment (van den Bosch and Rombouts, 1997; Gold et al., 2015).

The current study aimed to investigate the relationship between working memory capacity, recall accuracy, pupil dilation, and subjective measurements of perceived task demands and motivated effort in a sample of participants with SCZ as compared to a sample without any psychiatric diagnosis. Participants with SCZ were expected to show smaller working memory capacity, recall accuracy, and pupil dilation as compared to participants without any psychiatric disorder across conditions of differing task demands. Further, patients were hypothesized to report higher strain caused by the task demands overall in combination with lower motivated effort. The self-report measures of strain and motivated effort were expected to correlate with the severity of negative symptoms.

MATERIALS AND METHODS

Inpatients and outpatients with a diagnosis from the SCZ spectrum were contacted directly and through the distribution of leaflets at the Department of Psychiatry and Psychotherapy of the University Medical Center Hamburg-Eppendorf (UKE), Germany. Healthy control participants were recruited through leaflets and posts on social media and student job websites. Participants had to meet the following inclusion criteria: (1) 18–65 years of age, (2) very good command of the German language, (3) IQ above 80, (4) capacity to give informed consent, (5) no substance dependence, (6) no recreational drug consumption within 1 week prior to the assessment (excluding alcohol, nicotine, and caffeine), (7) no history of neurological disorders, (8) normal or corrected-to-normal eyesight, and (9) a primary diagnosis of SCZ or schizoaffective disorder (SCZ group; DSM-V, American Psychiatric Association, 2013) or no psychiatric diagnosis at all (HC group). For all participants, written informed consent was obtained prior to the study. The study was approved by the local ethics committee of psychologists at the UKE.

This study was part of a larger project, and the total sample contained 61 participants. Only 59 of those completed the version of the digit span task and the corresponding motivation questionnaire as described here. Analyses of overall performance and questionnaires therefore rely on the data of 59 participants. For trial-wise analyses of pupil dilation and performance, another three participants were excluded due to large amounts of missing pupil data and technical difficulties during pupil recording.

Measures

Visual Digit Span Task

A visual, computerized version of the digit span task was administered. All stimuli were white on gray background. A trial started with the presentation of a fixation cross (4 s). A number of digits between one and nine were then shown one after another (1 s each), with a 1-s interstimulus interval. At the end of each trial, participants had to recall the digits in the order they were presented in and manually type in their responses on a standard keyboard. To keep the task as similar as possible to the standard forward digit span subtest of the Wechsler adult intelligence scale (WAIS-IV; Wechsler, 2008), the amount of digits presented in one trial increased over time: starting off with two digits, an additional digit was added after every second trial until the maximum amount of nine digits. Thus, for each load condition between two and nine, two trials were completed. During digit presentation, pupil size was recorded at a rate of 500 Hz with a desktop-mounted infrared video-based eye tracker (Eyelink 1000, SR Research).

Post-assessment Questionnaire

Self-reported motivation, invested effort, and subjective task demand were assessed after completion of the digit span task. The scales were newly compiled from items of the NASA Task Load Index (N-TLX; Hart and Staveland, 1988) and an authorized adaptation of items from the Momentary Influences, Attitudes and Motivation Impact on Cognitive Performance Scale (MIAMI; Moritz et al., 2017b) to cover topics such as motivation, invested effort, perceived task difficulty, and strain. In total, 17 items were posed on a Likert scale from 1 (completely disagree) to 4 (completely agree) (example items: "The task was very easy."; "I was very motivated.").

Clinical Assessments

Clinical diagnoses (SCZ group) or the absence thereof (HC group) was confirmed with the Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 1998). Positive and negative symptoms were assessed with the Positive and Negative Symptoms Scale (PANSS; Kay et al., 1987) within the SCZ group. Since the validity of the original PANSS dimensions has been criticized, particularly with regard to the negative symptoms scale (van der Gaag et al., 2006; Khan et al., 2013), negative symptom scores were calculated both according to the original publication (subsequently PANSS-N) and according to the scoring suggestions by van der Gaag et al. (2006; subsequently PANSS-N_{vdGaag}). As a proxy for premorbid intelligence, the German multiple choice vocabulary test (Lehrl et al., 1995) was administered.

Analysis

For overall analyses of working memory capacity, questionnaire responses, and clinical assessments, Spearman correlations and Mann–Whitney U-tests were used due to violated normality assumptions. Non-parametric effect sizes are reported as Cliff's delta d_C. For trial-wise analyses of recall accuracy, load condition, group membership, and pupil dilation, linear mixed regression models were built hierarchically and compared with the likelihood-ratio chi-squared test. For detailed model comparison and model parameters at each step, see **Supplementary Tables S1–S3**. All confirmatory testing was conducted with a significance level of 0.05, using the R programming language (R version 3.5.1, R Core Team, 2018).

Pupil Dilation Preprocessing

Eye blinks and artifacts were detected with a custom-built filter based on the pupil signal's velocity and removed through cubic-spline interpolation (Mathôt et al., 2018). The signal was then smoothed with a 3-Hz low-pass Butterworth filter, and periods of missing and aberrant data spanning more than 1000 consecutive milliseconds were treated as NA. Baseline pupil size for every trial was calculated as the mean pupil size of the 200 ms prior to the first digit. Percentage change in pupil size from baseline was then calculated for each sample of the trial. Baseline-corrected pupil dilation at each digit was then calculated by averaging the signal across the 1-s period after digit onset. Consistent with Granholm et al. (2016), the average pupillary response to the last digit presented in each trial was the main variable of interest. Only trials with less than 25% of missing data and where less than 50% of the signal used to calculate this main variable had been interpolated were submitted to subsequent analyses.

RESULTS

There were no significant group differences in any of the demographic variables or premorbid intelligence (see **Table 1**).

The SCZ group consisted of five inpatients and 24 outpatients. Thereof, 24 participants reported taking antipsychotic medications (83%; first generation: 1; second generation: 19; both first and second generations: 4). The mean percentage of the clinically recommended maximum dosage (Kane et al., 2003) was 60.94 (SD = 78.84). One participant took additional anticholinergic and 11 (38%) took other psychotropic drugs.

An exploratory factor analysis with varimax rotation revealed two subscales of the post-assessment questionnaire. The first one reflected perceived task demands and to what extent participants felt challenged and stressed (including items such as "In my opinion, the task was very difficult." and "I felt very stressed."). This scale included seven items and was labeled "ease" due to its reverse coding (i.e., lower values reflect higher experienced task demands). The possible score range was 7–28, and Cronbach's alpha was 0.82. The second scale reflected self-reported motivation and invested effort (including items such as "I was very motivated." and "I put in a lot of effort and gave it my best shot."). This scale encompassed eight items and was labeled "motivated effort" to distinguish it from effort driven by task demands (for full scales, see **Supplementary Material**). The possible score range was 8 to 32, and Cronbach's alpha was 0.81.

Overall Analyses: Maximum Digit Span and Correlation With Questionnaire Scales

General working memory capacity was assessed as the maximum number of correctly recalled digits in a row in the task overall, independent of load condition. The SCZ and the HC group only differed at a statistical trend ($Md_{SCZ} = 6$, $Md_{HC} = 7$; $W = 551.1$, $p = 0.07$, $d_C = 0.27$). Both groups reported similar motivated effort ($Md_{SCZ} = 25$, $Md_{HC} = 28$; $W = 541.5$, $p = 0.11$, $d_C = 0.24$). However, participants with SCZ reported smaller values for ease, i.e., they felt more challenged and strained by the task ($Md_{SCZ} = 16$, $Md_{HC} = 19$; $W = 617.5$, $p = 0.01$, $d_C = 0.42$).

There was a positive relationship between reported ease and maximum digit span across the whole sample ($\rho = 0.26$, $p = 0.04$) but no relationship between motivated effort and maximum digit span ($\rho = 0.21$, $p = 0.12$). Within the SCZ group, negative symptoms correlated neither with maximum digit span (PANSS-N: $\rho = 0.03$, $p = 0.90$; PANSS-N_{vdGaag}: $\rho = 0.30$, $p = 0.13$), ease (PANSS-N: $\rho = 0.11$, $p = 0.57$; PANSS-N_{vdGaag}: $\rho = -0.03$, $p = 0.87$), nor motivated effort (PANSS-N: $\rho = 0.03$, $p = 0.89$; PANSS-N_{vdGaag}: $\rho = 0.05$, $p = 0.80$). Ease and motivated effort were moderately correlated ($\rho = 0.34$, $p < 0.01$).

As anticholinergic agents can have detrimental effects on cognitive functions like working memory (Spohn and Strauss,

TABLE 1 | Sample demographics per group (total sample size = 59).

	SCZ (*n* = 29)			HC (*n* = 30)			*P*
	n	***M* (*SD*)**	***Md* (*IQR*)**	***n***	***M* (*SD*)**	**Md (*IQR*)**	
Gender (m/f)	14/15			13/17			0.90
Education ("1"/"2"/"3")	1/2/26			1/5/24			0.51
Age		47.55 (11.66)	51 (15)		45.80 (11.64)	47 (16.75)	0.57
WST		33.52 (3.54)	34 (4)		32.37 (4.55)	34 (6.25)	0.28
PANSS							
Positive Scale		12.07 (4.17)	11 (6)				
Negative Scale		10.41 (3.12)	10 (4)				
Negative Scale$_{vdGaag}$		12.59 (4.21)	12 (4)				
Total score		49.79 (14.24)	45 (15)				
Time since onset		19.38 (12.14)	18 (14)				
Inpatients/outpatients	5/24						

Sample sizes (n), counts, means (M; with standard deviations SD), and medians (Md; with inter-quartile ranges IQR) are displayed. Education was recorded in German school system categories corresponding to completion of 1 = secondary school I (up to age 15), 2 = secondary school II (up to age 16), 3 = sixth form college (up to age 19). WST, German vocabulary test. Negative Scale$_{vdGaag}$, negative symptom scoring according to van der Gaag et al. (2006). P-values for group comparisons are provided for the demographical variables gender and education (chi-squared tests) as well as age and the WST scores (T-test).

1989; Minzenberg et al., 2004) and affect pupil size (Naicker et al., 2016), benztropine mesylate equivalents, where available, were used to assess the anticholinergic load induced by each participant's daily dosage of the prescribed antipsychotics (Minzenberg et al., 2004). There was no difference in maximum digit span ($W = 103$, $p = 0.98$) or pupil dilation at the four-digit load condition, i.e., the load condition equivalent to the minimum digit span achieved in this sample ($W = 69$, $p = 0.69$), between participants who received an antipsychotic with a known anticholinergic effect ($Md_{digitspan} = 6$, $Md_{pupil} = 2.54$, $n = 16$) and those who did not ($Md_{digitspan} = 6$, $Md_{pupil} = 1.89$, $n = 13$). Anticholinergic load was correlated neither with maximum digit span ($\rho = 0.26$, $p = 0.27$, $n = 20$) nor with average pupil dilation at the four-digit load condition ($\rho = 0.15$, $p = 0.59$, $n = 16$). Similarly, the percentage of maximum dosage of all antipsychotics was not related to the maximum digit span ($\rho = 0.11$, $p = 0.63$, $n = 23$) or average pupil dilation at the four-digit load condition ($\rho = -0.10$, $p = 0.67$, $n = 19$).

Trial-Wise Analyses: Recall Accuracy

Trial-wise recall accuracy was measured as the percentage of digits recalled in the correct order on a given trial until the first error was made. To illustrate, within a load condition of eight digits, recall accuracy would be 50% if the first four digits were remembered correctly, but digits from the fifth digit onward were reported in an incorrect order. As seen in **Table 2**, average recall accuracy per load condition expectedly decreased with increasing load. This was confirmed by linear mixed regressions, which revealed main effects of load, $\chi^2(1) = 313.32$, $p < 0.001$, and group, $\chi^2(1) = 4.94$, $p = 0.03$, on recall accuracy, while the interaction between load and group was not significant, $\chi^2(1) = 2.23$, $p = 0.14$. In the winning model with only the two main effects, recall decreased as load increased, $b = -9.89$, $t = -22.11$, $p < 0.001$, and was lower in the SCZ group as compared to the HC group, $b = -6.56$, $t = -2.26$, $p = 0.03$.

TABLE 2 | Average percentage of items recalled in correct order per load condition for each group (*N* = 56).

Load	**SCZ (*n* = 27)**		**HC (*n* = 29)**	
	***M* (*SD*)**	***Md* (*IQR*)**	***M* (*SD*)**	**Md (*IQR*)**
2	100 (0)	100 (0)	100 (0)	100 (0)
3	97.9 (14.6)	100 (0)	100 (0)	100 (0)
4	94.3 (22.1)	100 (0)	98.7 (10.0)	100 (0)
5	90.9 (23.0)	100 (0)	91.6 (22.7)	100 (0)
6	67.1 (36.6)	83.3 (66.7)	81.2 (29.0)	100 (33.3)
7	49.3 (38.0)	35.7 (85.7)	62.5 (37.6)	71.4 (85.7)
8	42.3 (35.0)	25 (62.5)	47.5 (35.2)	37.5 (50)
9	35.1 (36.1)	22.2 (55.6)	43.5 (35.1)	38.9 (58.3)

Means (M; with standard deviations SD) and medians (Md; with inter-quartile ranges IQR) are displayed. Trials with NA entries for pupil dilation excluded per subject for comparability with regression models.

Trial-Wise Analyses: Pupil Dilation

As seen in **Figure 1**, in the HC group, trial-wise pupil dilation to the last digit increased with increasing processing load before it reached asymptote and decreased in higher load conditions. In contrast, this inverse U-shaped relationship was less prevalent in the SCZ group, and pupil dilation was smaller across almost all load conditions. These observations were confirmed by linear mixed regressions. Given the observed inverse U-shaped relationship between load and pupil dilation, both linear and quadratic load terms were tested as predictors. There was no significant effect for the linear load term, $\chi^2(1) = 0.95$, $p = 0.33$; the reverse was true for the quadratic one, $\chi^2(1) = 18.50$, $p < 0.001$. There was a significant main effect of group, $\chi^2(1) = 4.07$, $p = 0.04$. The interaction between load and group was not significant, $\chi^2(1) = 1.05$, $p = 0.31$, but the interaction between quadratic load and group indicated a trend, $\chi^2(1) = 2.89$, $p = 0.09$. In the winning model, which included the main effects only, both the linear and quadratic load terms were significantly

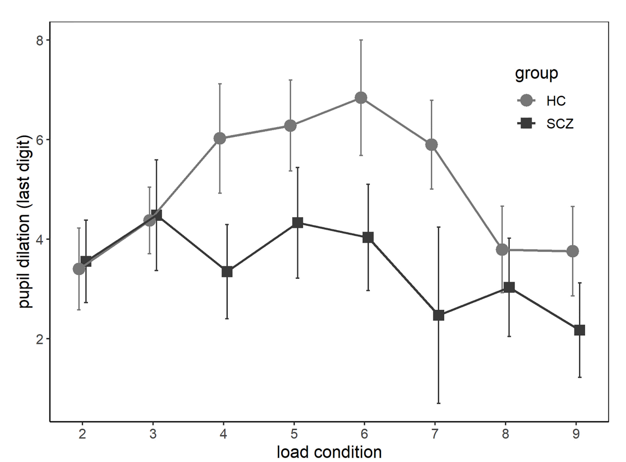

FIGURE 1 | Average baseline-corrected pupil dilation at the last digit of each load condition (2–9) for participants with diagnosis from the schizophrenia spectrum (SCZ group) and without (HC group). Error bars reflect standard errors of the mean.

related to pupil dilation, linear: $b = 2.08$, $t = 4.06$, $p = < 0.001$; quadratic: $b = -0.20$, $t = -4.31$, $p = < 0.001$. Further, participants with SCZ showed generally smaller pupil dilation across load conditions, $b = -1.77$, $t = -2.04$, $p = 0.046$. Notably, there was no group difference in baseline pupil size across all trials, $\chi^2(1) = 2.37$, $p = 0.12$.

Trial-Wise Analysis: Can Pupil Dilation at Last Digit Predict Recall Accuracy?

In another linear mixed regression analysis, the final model from Section "Trial-Wise Analyses: Recall Accuracy" was extended to establish if pupil dilation could predict variance in performance above and beyond the amount explained by load condition and group membership. Adding pupil dilation to the model indeed improved it significantly, $\chi^2(1) = 4.58$, $p = 0.03$. In this model, coefficients for load and group were consistent with the results of Section "Trial-Wise Analyses: Recall Accuracy," with performance decreasing as load increased, $b = -9.86$, $t = -22.22$, $p < 0.001$, and being lower in the SCZ as opposed to the HC group, $b = -6.00$, $t = -2.04$, $p = 0.046$. In line with an interpretation of pupil size as a measure of invested mental effort, larger pupil dilation predicted better performance, $b = 0.32$, $t = 2.15$, $p = 0.03$.

To test if this relationship was similar for all load and group conditions, interaction effects were added. The interaction term of load and group was not significant, $\chi^2(1) = 1.63$, $p = 0.20$, and therefore excluded from further models. However, the interactions between load and pupil dilation, $\chi^2(1) = 5.14$, $p = 0.02$, and between group and pupil dilation, $\chi^2(1) = 4.59$, $p = 0.03$, improved the model significantly. The final model therefore included load, group, pupil dilation, and the interactions between load and pupil, as well as group and pupil. Here, recall accuracy decreased with increasing load, $b = -10.34$, $t = -20.62$, $p < 0.001$, but in the presence of the interaction terms, there was no significant main effect for group, $b = -3.05$, $t = -0.99$, $p = 0.33$, or pupil dilation, $b = -0.05$, $t = -0.11$, $p = 0.91$. There was a meaningful trend for the interaction between load and pupil dilation, $b = 0.12$, $t = 1.86$, $p = 0.06$, indicating that the detrimental effect of load on performance was smaller on trials with larger pupil responses. Further, the interaction between group and pupil dilation was significant, $b = -0.65$, $t = -2.16$, $p = 0.03$, suggesting that pupil dilation was less predictive of performance in the SCZ as compared to the HC group.

Overall Analysis: Pupil Dilation and Subjective Effort in Max Span Condition

Linear mixed regression analyses for pupil dilation in the four-digit trials were conducted to explore the relationship between pupil dilation and the self-report questionnaire. This load condition was chosen because four was the minimum working memory capacity within the whole sample. Thus, a negative relationship between pupil dilation and maximum digit span within this condition would be expected as participants with more available cognitive resources would need to invest less effort (relative to their cognitive capacity) than persons with fewer resources. Adding self-reported motivated effort and perceived ease to the model while controlling for capacity and group would then give an indication to what extent pupil dilation is affected by motivational factors in addition. Since motivated effort and ease were correlated, two separate models were built. In the motivated effort model, only the group effect that had already being observed across all load conditions achieved marginal significance ($b = -3.02$, $t = -1.97$, $p = 0.05$, $n = 54$), but no effect of maximum digit span ($b = -0.48$, $t = -0.90$, $p = 0.37$, $n = 54$) or motivated effort ($b = 0.04$, $t = 0.20$, $p = 0.84$, $n = 54$) was found. Results from the ease model were similar, with no effects for maximum digit span ($b = -0.36$, $t = -0.68$, $p = 0.50$, $n = 54$) or ease ($b = -0.26$, $t = -1.19$, $p = 0.24$, $n = 54$), but smaller pupil dilation in the SCZ group ($b = -3.49$, $t = -2.26$, $p = 0.03$, $n = 54$). Within the SCZ group, the average pupil dilation in the four-digit trials was not related to negative symptoms (PANSS-N: $\rho = 0.01$, $p = 0.95$, $n = 25$; PANSS-N$_{vdGaag}$: $\rho = -0.09$, $p = 0.68$).

DISCUSSION

This study investigated the relationship between performance in a working memory task, self-reported motivated effort and ease, and objective effort allocation as indexed by pupil dilation in individuals with a clinical diagnosis from the SCZ spectrum (SCZ group) and individuals with no psychiatric disorder (HC group).

While there was no significant group difference in working memory capacity measured as maximum digit span, the SCZ group showed decreased recall accuracy on a trial-by-trial basis. The absence of a significant difference in maximum digit span may seem surprising, as working memory deficits in SCZ are well established. However, not all studies using the digit span task have replicated this finding (Park and Holzman, 1992; Franke et al., 1993). In the current study, participants had multiple opportunities to demonstrate their general working memory capacity, as performance in all trials were considered when assessing maximum digit span. In contrast, trial-by-trial assessment of recall accuracy may have been more sensitive to momentary fluctuations in attention, which in turn might be affected by motivation (Engelmann et al., 2009). Given similar general capacity in both groups, at first glance, the differences in trial-wise performance seem more likely to have been caused by reduced effort rather than by a general lack of cognitive resources. In line with this, pupil dilation was reduced in the SCZ group across all load conditions, suggesting that participants with SCZ indeed invested less effort while doing the task. The inverse U-shaped relationship between load and pupil dilation was present across groups, though more prominent in the HC group, and can be interpreted as a detachment from the task at hand as task demands exceed available cognitive resources and thus decreasing expectations of success (Granholm et al., 2016). While some studies found group differences in pupil dilation only for high task demands (Granholm et al., 1997, 2006), others have reported differences across all demands, similar to the findings of this study (Granholm et al., 2016). Such discrepancies are likely the result of methodological differences and categorization of high and low demands. While the interaction effect between load and group on pupil dilation did not reach significance, the descriptive results suggest that pupil dilation was actually similar in trials where task load was below four digits (see **Figure 1**).

The interpretation of trial-wise pupil dilation as a measure of effort was supported by its positive relationship with trial-wise recall accuracy in a basic linear mixed regression model. In the regression model with interaction terms, recall accuracy of participants with larger pupil responses declined less as task load increased. Thus, increased task load can be compensated with an increase in invested effort. Nevertheless, the significant interaction between pupil dilation and group suggested that the positive relationship between pupil dilation and performance was smaller, if not absent, in the SCZ group. This makes it difficult to conclude if decreased trial-by-trial performance in this group can truly be attributed to less effort and proposes the role of additional explanatory factors. Interestingly, participants with SCZ reported feeling more challenged and stressed by the task, and this feeling of strain was correlated with maximum digit span and with motivated effort across the entire sample. On the one hand, it is likely that limited cognitive capacity leads to higher perceived task demands and strain. On the other hand, the cognitive resources available might not be exploited fully in situations where the task environment induces stress, which in turn may lead to an increase in perceived strain (Fairclough and Houston, 2004). Momentary sensitivity to stress has, in fact, been found to negatively affect cognitive functioning in SCZ (Morrens et al., 2007). Similarly, a generally reduced tolerance of strain in persons with SCZ could potentially explain the pattern of findings including heightened self-reported strain, smaller pupil dilation, and impaired recall accuracy across all load conditions (van den Bosch and Rombouts, 1997). This interpretation fits also well with the idea that persons with SCZ may invest less effort as a consequence of an overestimation of the costs associated with it (Gold et al., 2015; Shenhav et al., 2017). However, self-reported ease (i.e., reversed strain) did not predict pupil dilation in the four-digit trials and neither did self-reported motivated effort. Further, self-reported effort did not differ between groups, conflicting with the finding of smaller pupil dilation in SCZ across the task. This indicates little convergence between subjective and objective measures of effort, which may be linked in part to the way both constructs were measured (trial wise vs. after task completion) and to the fact that self-reports can be biased by lack of retrospective insight as well as social desirability.

None of our variables of interest correlated with negative symptom severity. This may seem unexpected, as previous studies have demonstrated a negative relationship between negative symptom severity and effort investment (e.g., Gorissen et al., 2005; Wolf et al., 2014) or that effort investment was predominantly impaired in subgroups scoring high on negative symptoms (Granholm et al., 2006; Bergé et al., 2018). However, other findings indicate that the relationship between effort investment and negative symptoms may, in fact, be non-linear and moderated by other factors, such as defeatist attitudes (Granholm et al., 2016; Reddy et al., 2018). Given the small sample size and the rather low average negative symptom score of the patient sample, no subgroups of high- and low-scoring patients were compared in the current study. The low scores were likely related to the large percentage of outpatients who tend to express fewer negative and other symptoms (e.g., Kasckow et al., 2001). Note that inconsistencies in findings regarding negative symptoms can further be related to the fact that measurement instruments differ across studies. The PANSS, which was chosen here, has received criticism for not reflecting the latest research results on negative symptoms (Kumari et al., 2017), which poses a limitation on the interpretability of the findings.

Further limitations of the study include the rather small sample sizes (particularly for the analyses including medication variables), the fact that medication was self-reported, the heterogeneity of the sample in terms of mixing in- and outpatients and including participants with schizoaffective disorders, as well as the possibility that matching groups by level of education may have contributed to the selection of an atypical, high-achieving group of persons with SCZ (Resnick, 1992). All of these factors may explain why some results from previous studies could not be replicated. The sample may have also been biased by the large proportion of chronically ill patients who, in turn, have been exposed to antipsychotic medication for long periods of their lives.

One potential limitation of the design is the fact that task load conditions were not randomized to ensure comparability with the standard version of the digit span subtest from the WAIS-IV (Wechsler, 2008). However, depletion or fatigue effects (Hagger et al., 2010) cannot account for the consistently smaller pupil dilation in SCZ across all load conditions. Another limitation is that subjective effort was only assessed after task completion with scales that have not been externally validated, although they were derived from well-validated measures.

Taken together, the findings of this study demonstrate once again the complex relationships between performance, effort, cognitive resources, and task demands. The results involving pupil dilation suggest that, in cognitive tasks, participants with SCZ might indeed exert less mental effort. However, it remains unclear to what degree this accounts for impaired momentary performance in this sample and to what extent this is linked to the higher perceived strain imposed by task demands. To accurately judge the outcome of clinical or research-related neuropsychological assessments, these and other motivational factors have to be taken into account. Importantly, the lack of convergence between subjective and objective measures of effort might indicate that both objective and subjective measures can complement each other in unique ways and should thus be both considered for applications in this context.

DATA AVAILABILITY STATEMENT

All datasets generated for this study are included in the article/**Supplementary Material**. Data as well as task and questionnaire material are available in an Open Science Framework repository: DOI 10.17605/OSF.IO/GCH97.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the ethics committee of psychologists at the University Medical Center Hamburg-Eppendorf, Hamburg, Germany. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

All authors contributed to the article and approved the submitted version. IK, SM, and GP designed the study and edited the manuscript. IK collected and analyzed the data and wrote the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2020.01469/full#supplementary-material

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Losing Money and Motivation: Effects of Loss Incentives on Motivation and Metacognition in Younger and Older Adults

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Incentives are usually expected to increase motivation and cognitive control and to thereby improve performance. A small but growing number of studies have begun to investigate whether the effects of incentive on cognitive performance differ for younger vs. older adults. Most have used attention and cognitive control paradigms, trial-wise implementation of incentive condition, and gain incentives (reward), with only a very few investigating the effects of loss incentives. The present study takes a complementary approach: We tested younger and older adults in a working memory paradigm with loss incentives implemented session-wide (between subjects). We also included self-report measures to ask how loss incentive affected participants' perceptions of the mental demand of the task, as well as their perceived effort, frustration, motivation, distraction, and metacognitive judgments of how well they had performed. This allowed us to test the disparate predictions of different theoretical views: the intuitive hypothesis that incentive should increase motivation and performance, the motivational shift proposal that older adults are especially motivated to avoid losses (Freund and Ebner, 2005), a heuristic "positivity effect" perspective that older adults ignore losses (Brassen et al., 2012; Williams et al., 2017), and a more nuanced view that suggests that when negative information is unavoidable and increases perceived costs, older adults may instead disengage from the situation (Charles, 2010; Hess, 2014). The results seemed most consistent with the more nuanced view of the positivity effect. While neither group showed incentive-related performance differences, both younger and older adults reported greater perceived demand and frustration under loss incentive, especially in the most challenging conditions. Loss incentive increased the accuracy of immediate metacognitive judgments, but reduced the accuracy of later, more global judgments of competency for older adults. Self-report measures suggested that the loss incentive manipulation was distracting to young adults and demotivating for older adults. The results suggest a need for caution in generalizing from existing studies to everyday life, and that additional studies parameterizing critical aspects of task design and incentive manipulation are needed to fully understand how incentives affect cognition and motivation in younger and older adults.

Keywords: loss incentives, working memory, motivation, metacognition, cognitive aging

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INTRODUCTION

The enthusiasm for this Research Topic in Frontiers reflects the rising interest in the last 10 years on the effects of monetary incentives on cognition. That interest was sparked in part by the integration of cognitive and computational perspectives on reinforcement learning and has spread to the effects of incentive on other aspects of cognition. The general assumption is that incentives increase motivation and that motivation in turn increases the engagement of attention and cognitive control (Botvinick and Braver, 2015; Yee and Braver, 2018). As the papers in this issue, as well as several recent reviews, indicate, a great deal of progress has been made on this topic in a relatively short period of time. However, several important gaps in the literature remain.

First, most studies have built on the reinforcement learning literature and implemented incentives on a within-subjects, trial-wise basis (i.e., comparing performance on rewarded vs. unrewarded trials). A common finding in that literature is that older adults show reduced neural responsivity to anticipated losses but similar results to young adults for anticipated gains, experienced gains, and experienced losses (reviewed by Samanez-Larkin and Knutson, 2015). Trial-wise incentive manipulations likely translate well to real-world reinforcement learning and value-based decision-making (e.g., after repeated exposures, one learns that Restaurant A is more likely to produce a rewarding experience than Restaurant B). However, in these cases, as well as in studies examining the prioritization of high- vs. low-value items in episodic memory (Castel et al., 2002; Cohen et al., 2016), incentive valence and magnitude attach to specific items, actions, or decision options.

It is not clear that conclusions from these more specific, trial-wise incentive manipulations apply to most "real world" (e.g., school, work, or sports) situations with incentivized performance. For example, a junior accountant performing an audit would likely receive bonus pay for completing all the steps needed thoroughly and efficiently (or have their pay docked for underperforming), rather than having one step be associated with bonus pay for correct completion and another step associated with lost pay for failure (e.g., Libby and Lipe, 1992). The same is likely true in many cognitively challenging situations in everyday life: following directions to reach a desired location, debugging a computer program, or organizing a weekly work schedule for oneself or a group of employees.

Second, many of these real-world situations rely heavily on working memory, and age differences in working memory are both large and a topic of central interest in both theoretical work and empirical studies of cognition and performance (see Park and Festini, 2017 for a recent review). However, most performance-incentive studies have focused on measures related to attention and cognitive control (Di Rosa et al., 2015; Schmitt et al., 2015, 2017; Williams et al., 2017, 2018; Yee et al., 2019), and only a handful have compared young and older adults. As noted above, there have also been a number of reinforcement learning and episodic memory studies focusing more on the ability to learn reward/loss associations or prioritize high vs. low reward items (e.g., Castel et al., 2002; Cohen et al., 2016), as well as studies on incentivized episodic memory encoding (e.g., Spaniol et al., 2014; Geddes et al., 2018).

To our knowledge, only one study has examined the effects of incentive on working memory in both younger and older adults (Thurm et al., 2018). The lack of studies on how incentives might affect working memory performance in younger and older adults stands in contrast to the training and neurostimulation literatures, where working memory is a frequent target because of its large age differences and importance in everyday life (Basak et al., 2008; Buschkuehl et al., 2008; Li et al., 2008; Stephens and Berryhill, 2016; Rhodes and Katz, 2017; Di Rosa et al., 2019). From a scientific perspective, another reason to examine working memory is that the range of set sizes used in many working memory tasks also provides a relatively straightforward way of examining whether age differences in the response to incentive vary as a function of task load.

Third, many studies have focused on reward ("gain") incentives (e.g., Castel et al., 2002; Spaniol et al., 2014; Cohen et al., 2016; Thurm et al., 2018; Di Rosa et al., 2019; Yee et al., 2019; Bowen et al., 2020). However, loss is thought to play an increasingly important part in older adults' experience, and real-world attempts to motivate their behavior often focus on the opportunity to avoid such losses (e.g., of health, of employment or financial stability, of driving privileges). Finally, the assumption that incentive will increase motivation (and then increase attention and control) is rarely tested directly. This is despite an earlier literature – interestingly, often in more ecologically valid settings – indicating that extrinsic motivators such as monetary incentive can often have paradoxical effects (see meta-analytic reviews by Deci et al., 1999; Cerasoli et al., 2014).

The present study begins to address some of these gaps. We examined the effects of loss incentive, implemented across the entire session, on both younger and older adults. We examined both working memory performance and subjective reports of related constructs including perceived demand, frustration, motivation, distraction, and metacognition. We focused on losses both because they have been understudied and because different theoretical perspectives make competing hypotheses about the effects of loss incentives on older adults, whereas predictions are the same (and thus the incentive manipulation less incisive) for reward ("gain") effects. The subjective measures were used to provide potentially converging or disconfirming evidence for each of these views.

Before describing the rationale for our study, we review different theoretical perspectives that make disparate predictions for the effects of loss on older adults' cognitive performance and subjective response. See Analyses for a summary of the major predictions of each view, and how they will be assessed in the current study.

First, *the intuitive prediction* is that incentive increases motivation, which increases performance. This might also be expected to reduce perceived demand and increase metacognitive accuracy, as participants pay closer attention to their performance in order to improve it. Building off of lifespan development theory and the idea that losses become more prominent in later life, the *motivational shift* hypothesis is that older adults are particularly motivated to avoid losses:

"With advancing age, however, personal goals are expected to shift toward an increasingly stronger focus on maintenance and prevention of loss" (Freund and Ebner, 2005). If one follows the logical chain, described above – that greater motivation should increase the application of cognitive control and thus increase performance – this hypothesis would seem to suggest that older adults would show even larger performance and motivation increases in the loss condition than do young adults.

However, the motivational shift theory appears to primarily apply to older adults' goal setting and preferences in decision-making scenarios, and in particular whether one gravitates toward opportunities for growth and improvement in cognitive or physical performance vs. maintenance or compensation for loss on those fronts (e.g., Freund and Ebner, 2005; Best and Freund, 2018). It may also be of relevance in avoidance-learning paradigms, where older adults have sometimes shown faster learning in response to loss (Frank and Kong, 2008; Eppinger and Kray, 2011; Hämmerer et al., 2011). It does not seem to straightforwardly apply to the motivation-cognitive performance questions of interest here. Indeed, those studies that have examined the effects of loss incentive on older adults' response to cognitive demands are relatively consistent in showing that older adults have either an equivalent or reduced response to loss incentive compared to young adults and/or to positive incentive (e.g., Bagurdes et al., 2008; Di Rosa et al., 2015; Schmitt et al., 2015, 2017; Pachur et al., 2017; Williams et al., 2017, 2018). Thus, while we note that the motivational shift hypothesis might superficially appear to predict larger performance improvements, greater motivation, and increased metacognitive accuracy for older adults in the loss condition, we do not consider it likely to apply to the current study.

Most of the studies finding apparently reduced sensitivity to loss incentives in older adults have interpreted it as an example of the *positivity effect* – the finding that older adults tend to prioritize positive, and deprioritize negative, information for attention and memory (Bagurdes et al., 2008; Di Rosa et al., 2015; Pachur et al., 2017; Williams et al., 2017, 2018). This interpretation of the positivity effect would seem to predict that, compared to young adults, older adults should show less effects of loss incentive (results more similar to the control condition) on both our performance and subjective measures.

However, some caution is needed in making that leap. As noted above, in some situations, older adults are in fact even more responsive to loss than are young adults (Frank and Kong, 2008; Eppinger and Kray, 2011; Hämmerer et al., 2011). The apparent reduction in sensitivity to loss in some other studies may be at least partially an artifact of how incentive cues were implemented in those experiments. In most cases, the reduced loss sensitivity of older adults primarily concerns neural or electrophysiological responses to the incentive cue. Overall performance quality often shows similar incentive effects for the two age groups, although there may be some differences in speed–accuracy tradeoffs (e.g., Schmitt et al., 2015; Williams et al., 2017, 2018). This suggests that older adults may be less responsive to loss-incentive cues, but equally (and in some cases, even more so) responsive to the actual delivery of loss incentive. That interpretation would fit with findings from the reinforcement learning literature that older adults have reduced neural and arousal responses to loss cues but equivalent or greater responses to loss delivery [reviewed by Samanez-Larkin et al. (2007)].

Similar results indicating potentially greater responses by older adults to loss delivery have been reported in the Monetary Incentive Delay task (Kircanski et al., 2018). In addition, using an analysis approach that emphasizes spatiotemporal covariance patterns, Spaniol et al. (2015) found that at cue presentation, young and older adults showed similar reward-network recruitment, but older adults showed increased recruitment of frontal–parietal control networks and decreased deactivation of the default network; these effects did not differ by valence. At the point of feedback/incentive delivery, young and older adults again showed similar patterns related to general feedback/reward processing, but older adults recruited two additional networks in response to error feedback and to loss (Bowen et al., 2019).

A neuroimaging study by Geddes et al. (2018) generally replicated the pattern of a specific reduction in older adult's activation of reward networks in response to loss cues for the Monetary Incentive Delay task but a different pattern for incentivized encoding trials for an upcoming (24 h delay) recognition memory test. Behaviorally, young adults showed incentive (reward or punishment) advantages on recollection but not familiarity; older adults had low recollection performance and no effects of incentive (see Spaniol et al., 2014 for slightly different results as well as the Geddes et al. discussion of the similarities and differences between these studies). Interestingly, the neuroimaging data showed similar activations of memory- and reward-related region in both young and older adults during the incentive cue, regardless of incentive valance, but reduced engagement of these regions by older adults during the encoding period. The authors suggest that differences between their memory task vs. the Monetary Incentive Delay task as well as value-directed memory tasks in terms of the immediacy of feedback/incentive manipulation – and thus the ability to modulate processing in response – might partially explain the differences in results.

In short, whether older adults show the same, less, or more responsivity to loss than do young adults seems to vary widely across different paradigms. A more nuanced view of the positivity effect, integrated with the concepts of proactive vs. reactive control, may provide a more comprehensive explanation for the patterns seen across different tasks. Both theoretical and empirical work indicate that the age-related positivity effect is primarily seen in low-constraint situations that allow or require older adults to direct their attention toward or away from emotional information (see Reed and Carstensen, 2012; Carstensen and DeLiema, 2018 for reviews). It does not usually occur when negative information is highly salient or otherwise processed relatively automatically. Likewise, the Dual Mechanisms of Control theory's perspective on aging is that older adults are less likely than young adults to engage self-initiated proactive control to prepare for upcoming cognitive demands but often show even greater (perhaps compensatory) reactive control when the critical stimulus is presented (Braver, 2012; see earlier work by Craik and Byrd, 1982, for similar ideas on age differences in self-initiated processing). Thus, in many previous studies using trial-by-trial incentive cues, older adults may have failed to engage with the loss cues at presentation. This could explain the failure to show the same neural or physiological responses to those cues as did young adults. Notably, one study using block-wise presentation of incentive cues found if anything increased sensitivity to loss cues in older adults, suggesting that experienced (rather than merely anticipated) losses carried over to subsequent trials (Schmitt et al., 2017).

It has been suggested that when negative information is unavoidable, older adults may instead disengage or distance themselves from the situation and, in addition, may later reframe the situation to take a more positive view (Charles, 2010). For example, Charles and Carstensen (2008) found that after participants listened to conversations ostensibly consisting of disparaging remarks about them, young adults wanted to learn more about the cause of the complaints and made more appraisals about the speakers, whereas older adults distanced themselves from the situation with remarks such as "you can't please all the people all the time." Compared to incentive cues, the actual delivery of loss feedback – especially performance-based incentives in a domain (memory) that is important to older adults (Reese et al., 1999; Dark-Freudeman et al., 2006) – may be more personally relevant and thus difficult to ignore and paradoxically lead older adults to disengage from the situation rather than increase their motivation to improve (but see Barber and Mather, 2013; Barber et al., 2015, for evidence suggesting a non-linear relationship).

A related proposal from Selective Engagement Theory (SET; Hess, 2014) is that a person's motivation to engage depends on their calculation of benefits vs. costs of that engagement, and that those costs – and thus the likelihood of disengagement – may occur at earlier levels of objective task difficulty for older adults. Although to our knowledge Hess and colleagues have not directly addressed the question of monetary incentives, if losses after error incentives magnify the perceived costs of performance, they would be predicted to increase the likelihood of disengagement. Consistent with this idea, previous studies in our lab using an attention task found that loss incentives reduced focused-attention performance and increased self-reported mind wandering in older adults (Lin, 2018; Lin et al., 2019).

An alternative, more "competitive" pathway to disengagement has been suggested by Ferdinand and Czernochowski (2018): Processing incentive information may itself create a cognitive load that draws cognitive processing away from the task. Thus, incentive could paradoxically reduce performance, with effects presumably most evident at the highest working memory loads. Alternatively, as suggested in some of their papers, the cognitive load of the task may cause older adults to ignore or less completely process incentive information (Schmitt et al., 2015, 2017). Thus, the predictions that this view would make for many of the measures in the current study are not entirely clear. As a first step toward testing this possibility, we asked participants about the degree to which they found the feedback (control or incentive) provided to them to be distracting.

MATERIALS AND METHODS

Rationale and Overview of Methods for the Present Study

As noted earlier, although the number is small, there have been several studies examining age differences in the response to loss incentives on cognitive control tasks using the trial-based incentive cue method borrowed from reinforcement learning paradigms. These have generally indicated a reduced responsivity to loss cues in older adults, although that reduced responsivity is typically most evident on neural or physiological measures, rather than performance. Although these studies are interesting and important, it was not our goal to add another variation.

Instead, our aim was to take a first step toward closely related questions that have been thus far largely unaddressed. We used a session-wide incentive manipulation rather than trial-wise changes, since as noted above, session-wide incentives are more likely to reflect real-world situations. We examined working memory, which thus far has been the focus of only one age × incentive study despite the importance of working memory to cognitive performance in many domains and its well-known decline in aging. We focused on losses, rather than gains, since this again has been a neglected area despite the putatively increased importance of loss in later adult life, and because most of the theoretical perspectives above have the same predictions for rewards/gains but differ in their predictions for losses, making the latter more incisive.

Based in part on other data from our lab suggesting that loss incentive reduced focused attention in older adults and increased mind wandering (Lin et al., 2019), we were especially interested in the possibility that loss incentive might lead older adults to disengage from the task. Our task and procedures thus closely followed those previously used by Hess et al. (2016) to examine age differences in a physiological measure of task engagement as a function of working memory load. We used largely the same working memory task and questionnaires to assess self-reported mental demand, effort, and related constructs such as frustration, and added the loss-incentive manipulation. This also allowed our control sample to provide a basic replication test of the behavioral age differences reported by Hess et al., 2016. Finally, we added an exploratory set of subjective measures of motivation, distraction, and metacognition as a first step toward examining the effects of loss incentives on these constructs in young and older adults.

Participants

Eighty-five young adults and 84 older adults were included in the analysis (**Table 1**; see **Supplementary Material S8** for exclusion information). Young adults (61 female, mean age = 19.99 years, range = 18–29) were students recruited from the University of Michigan. Older adults (52 female, mean age = 71.67, range = 60–88) were recruited from the Ann Arbor community. Participants were screened to ensure physical and psychological health with no history of anxiety, depression, attention deficit hyperactivity disorder (ADHD), or head injury, and no use of medications that could affect cognition. As in other studies in our lab, the Extended Range Vocabulary Test Version 3 (ERVT;

TABLE 1 | Demographics and self-reported Poor Attentional Control (PAC).

	Young control (n = 43, 31 f)	Young loss (n = 42, 30 f)	Old control (n = 41, 24 f)	Old loss (n = 43, 28 f)
Age				
Mean	20.19	19.79	71.37	71.95
SD	1.93	2.06	6.83	6.39
Years of education				
Mean	14.40	14.04	17.45	17.21
SD	1.53	1.42	2.11	2.30
ERVT				
Mean	19.65	17.95	29.51	30.33
SD	5.88	4.73	9.04	8.41
PAC mind wandering				
Mean	14.58	15.86	12.15	12.47
SD	4.29	3.06	3.06	3.06
PAC boredom				
Mean	13.72	14.81	10.51	10.79
SD	3.51	3.37	2.66	2.72
PAC distractibility				
Mean	15.42	15.67	12.39	13.79
SD	3.53	4.18	3.12	3.94
MMSE				
Mean	n/a	n/a	28.83	28.95
SD	n/a	n/a	1.18	1.11

f, female; ERVT, The Extended Range Vocabulary Test; PAC, the Poor Attentional Control scale.

Ekstrom, 1976) was used to screen for participants who might not understand the instructions or were generally unmotivated or not willing/able to complete the experimental session; a minimum score of 9 out of a possible 48 was required. For older adults, a Mini-Mental State Examination score (MMSE; Folstein et al., 1983) of 27 or greater was required. Young and older adults received \$10 and \$12 per hour, respectively, for their participation (older adults received a slightly higher amount to compensate for their driving to the testing site). Written informed consent was obtained from all participants. The study was approved by the Institutional Review Board (IRB) of the University of Michigan.

Design

Age group (young, old) and incentive condition (control, loss) were the group-level, between-subjects variables; set size was a within-subjects variable of secondary interest. Participants within each age group were randomly assigned to the control or loss condition. Our previous study using an attention task (Lin et al., 2019) found an effect size of $f = 0.217$ (equivalent $\eta_p^2 = 0.045$) for the age (young vs. old) by motivation (control vs. loss) interaction on task performance. Power analysis using $G^{*}Power$ (Faul et al., 2007) suggested a total sample size of 169 to detect the age by motivation interaction with an effect size f of 0.217; α error probability of 0.05; power (1 - β probability) of 0.80; numerator degrees of freedom of 1; four groups in a two-way ANOVA. For the exploratory correlation analyses within each group, a sensitivity analysis indicated that r of 0.304 was the minimum to be detected at 0.80 power.

Working Memory Task

The Letter Number Sequencing (LNS) task from the Wechsler Adult Intelligence Scale-III (Wechsler, 1997) was used to measure working memory. The task was programmed using PsychoPy version 3 (Peirce, 2007) and presented on a Dell PC computer. On each trial, participants received intermixed letters and numbers at a rate of one item per second. Participants were asked to report the numbers in numerical order, the letters in alphabetical order. Each run had six trials of the same set size (the number of items to be memorized). Set size increased in an ascending order across runs, from set size 2 (run 1) to set size 9 (run 8). There were eight runs in total. At the end of each run, participants were given performance feedback (percent correct/incorrect for a given run). For interactions with the within-subjects variable set size, sensitivity analyses indicated power of 0.80 for $f = 0.111$, which is equivalent to $\eta_p^2 = 0.012$ (4 groups, 8 measures, $r = 0.217$ between measures; non-sphericity correction set at 1).

Questionnaires

All questionnaires were self-administered after the instructions for it were provided by the experimenter and the participant given the chance to ask any questions.

Poor Attentional Control Scale

The Poor Attentional Control (PAC) scale serves as a trait measure of attentional function in everyday life. It was administered before the LNS task to avoid the possibility that participants' perceptions of their performance might influence their responses. The PAC subscale consists of 15 items identified by factor analysis (Huba et al., 1982) from the larger 36-item Imaginal Processes Inventory (Singer and Antrobus, 1970). As in previous studies in our lab (e.g., Berry et al., 2014a,b; Kim et al., 2017), participants completed all 36 items so that they were viewed in context, with analyses focused on the PAC scale items. For each item, the participant indicated how true the statement was for them (1 = *not all true of me*; 5 = *very true of me*).

NASA Task Load Index

The NASA Task Load Index (NASA-TLX) measures subjective workload experienced during the task (Hart and Staveland, 1988). It was administered after each LNS run, and it has six subscales that ask the following: (1) How mentally demanding was the task? (Mental Demand); (2) how physically demanding was the task? (Physical Demand); (3) how hurried or rushed was the pace of the task? (Temporal Demand); (4) How successful were you in accomplishing what you were asked to do? (Performance); (5) How hard did you have to work to accomplish your level of performance? (Effort); (6) How insecure, discouraged, irritated, stressed, and annoyed were you? (Frustration). The responses are rated on a 0 (very low) to 100 (very high) point scale, except for the Performance scale, which uses a "reversed" scale, 0 (successful) to 100 (failure). In the results and figures below, we present the results for the Performance scale using the more intuitive 0 (failure), 100 (success) format.

TABLE 2 | An overview of the predictions from each of the theoretical perspectives.

Perspective	Actual performance	NASA-TLX measures	SAMQ and IMI	Other
"Intuitive" view (greater motivation and cognitive control under incentive)	Better in incentive condition	**Performance:** More accurate metacognition in incentive condition **Demand:** Lower in incentive condition **Effort:** Higher in incentive condition **Frustration:** No strong predictions; loss may lead to greater frustration at higher set sizes	Greater motivation in incentive condition Weak prediction for greater pressure/tension in incentive condition	
Motivational shift (older adults especially motivated by losses)	Generally the same as the "intuitive" hypothesis but with larger effects for older adults			
Heuristic positivity effect (older adults ignore negative information including losses)	Generally, the opposite of the "motivational shift" hypothesis; older adults *less* responsive to the loss incentive. Potentially less accurate metacognition (NASA-TLX Performance and IMI Perceived Competence) for older adults in the loss condition, if they are ignoring loss-related feedback.			
Nuanced positivity effect (older adults have reduced proactive, increased reactive responses to negative information; potentially followed by reframing)	Reduced performance for older adults in loss condition	**Demand:** Higher in loss condition **Effort:** No differences or reduced for older adults in loss condition **Frustration:** Increased by loss	Reduced motivation for older adults in the loss condition Reframing may inflate IMI Competence scores	Reframing may reduce long-term metacognitive accuracy for older adults in the loss condition
Incentive as cognitive load	Reduced performance under loss incentive, especially for older adults and at higher set sizes	**Performance:** If performance monitoring competes with the task itself for cognitive processing, ratings may be less accurate under loss incentive, especially at higher set sizes. **Demand:** Higher in loss condition, especially for older adults and at higher set sizes	Increased self-reported distraction in loss condition	

NASA-TLX, NASA Task Load Index; SAMQ, State Attention and Motivation Questionnaire; IMI, Intrinsic Motivation Inventory.

State Attention and Motivation Questionnaire

The State Attention and Motivation Questionnaire (SAMQ) was administered after finishing the LNS task and the final NASA-TLX form. It was created by our lab to ask "state" questions related to boredom, difficulty focusing attention, distraction, and motivation using the same wording as the "trait" level PAC scale. It has been shown in several previous studies to correlate with both the PAC trait measures and with construct-related performance measures (e.g., Berry et al., 2014a,b; Kim et al., 2017). The version used in the present study modified the last two questions to specifically assess the distracting or motivating potential of monetary incentive: "I found the possibility of (*Control*: getting feedback; *Loss*: losing money) to be distracting;" "I found the possibility of (*Control*: getting feedback; *Loss*: losing money) to be motivating " (see **Supplementary Material S4** for full questionnaire).

Intrinsic Motivation Inventory

The Intrinsic Motivation Inventory (IMI) is a standard 22-item questionnaire assessing participants' subjective experience regarding a task in an experiment (Ryan, 1982). After completing the task and SAMQ, participants completed the IMI, indicating how true each statement was for them during the LNS task (1 = *not all true*; 7 = *very true of me*). This inventory has four subscales: Interest/Enjoyment, Perceived Choice, Perceived Competence, and Pressure/Tension. Due to a misunderstanding regarding different versions of the IMI, the additional "Effort" scale also used by Hess et al. (2016) was unfortunately omitted. Interest/Enjoyment is often used as a self-report measure of intrinsic motivation.

Procedure

Participants completed informed-consent procedures, a health and demographic survey, and the PAC questionnaire. Participants then received instructions for the LNS task and completed a practice run consisting of five trials of set sizes of 2–5. Participants had to get more than 80% correct on the practice trials to proceed to the main task. If not, they repeated the practice. Failure to reach criterion within three practice runs terminated the session (*n* = 5 older adults).

After the practice run, participants in the loss condition were endowed with $24. This money was put on the table in front of them. They were told that it was theirs to keep for good performance (in addition to the hourly compensation for study participation), but that 50 cents would be deducted for every incorrect trial. Both performance feedback (percent incorrect) and incentive feedback (the amount of money lost) were given after each run. After that, the experimenter immediately removed the amount lost and placed the new amount on the table. Control participants were given performance feedback only. Participants next completed the NASA-TLX with reference to the run they had just completed.

After the final LNS run and corresponding NASA-TLX questionnaire, participants completed the SAMQ and IMI to assess their evaluation of their attention, motivation, and performance during the task as a whole. They next completed the MMSE (Cockrell and Folstein, 2002; older adults only) and AD8 (Galvin et al., 2005; older adults only), and Extended Range Vocabulary Test (ERVT; Ekstrom, 1976), and were thanked, debriefed, and given the hourly compensation for their participation.

Analyses

Analyses were conducted using R version 3.6.1 (R Core Team, 2017). Our overall analysis strategy followed that of Hess et al. (2016) in examining effects of age group and set size, with the additional between-subjects variable of incentive condition (control, loss). As described below, we also used correlation analyses to assess the relative accuracy of participants' metacognitive reports.

See **Table 2** for an overview of the predictions from each of the theoretical perspectives described in the Introduction; critical hypotheses are discussed in more detail below. The primary questions were whether the loss incentive would affect the dependent measures of performance, motivation, and metacognition, and whether incentive effects on these variables would interact with age and/or set size. A secondary question was whether we would replicate the age group and set size effects reported by Hess et al. (2016), especially for participants in the control condition (see **Supplementary Material** for these analyses). In some cases, especially for unexpected findings, we conducted additional *post hoc* analyses to provide potentially converging or disconfirming evidence or to give insight into potential mechanisms.

LNS Task Performance and Subjective Task Load (NASA-TLX)

The LNS data were analyzed using a mixed ANOVA design, with incentive and age group as the between-subjects variables and set size as the within-subjects variable. Greenhouse–Geisser corrected *df*, *F*, and *p*-values are reported where the sphericity assumption was violated. For easier reading, *df* values are rounded to the nearest integer in the text.

As in Hess et al. (2016), the NASA-TLX data were analyzed using multilevel modeling (MLM), rather than ANOVA, because the questions were consistently presented in the same sequential order, making the scales non-independent[1]. Included predictors were age group (young adults = referent), incentive condition (control = referent), linear and quadratic trends of set sizes (centered at 5.5), and all interaction terms. To control for individual variability, we included the random intercept for each individual (Field et al., 2012).

Posttask Motivation

The SAMQ questions regarding distraction (Q5) and motivation (Q6) were of primary interest for the present study; the other questions were included to be consistent with other publications from our lab that have used the questionnaire (Berry et al., 2014a,b; Lin et al., 2019), allowing interested readers or eventual meta-analyses to compare across experiments and study populations. The IMI subscales were used as posttask, holistic measures of participants' metacognition and emotional–motivational response to the task, as compared to the run-specific questions presented by the NASA-TLX. Both the SAMQ and IMI subscales were analyzed using ANOVA with incentive condition and age group as between-subjects variables.

Correlations Between Questionnaires and Task Performance

The NASA-TLX "Performance" scale asked participants to rate their performance on a 0–100 scale immediately after completing the run and receiving feedback. It therefore provides a relatively specific, "in the moment" assessment of the participants' metacognitive judgment of their performance. The IMI "Competence" scale measures a similar construct, but posttask, and in a more general sense (sample questions: "I think I did pretty well at this task, compared to my peers;" "I am satisfied with my performance on this task"). We used correlation analyses to examine whether age or incentive changed the relationship between these measures (NASA-TLX Performance and IMI Competence) and actual performance. Correlations between these measures and actual performance provided an estimate of participant's *relative* metacognitive accuracy. That is, stronger positive correlations between these measures and actual performance would indicate that those individuals who gave themselves high ratings relative to others in their group did in fact tend to obtain higher scores than others in their group. Fisher's *z* tests were used to test our *a priori* question of potential differences in correlation strengths between the groups.

The NASA-TLX Performance scale, with a range from 0 to 100, also allows for the calculation of *absolute* metacognitive accuracy, or the distance between a person's actual performance, and their rating of their performance on the NASA-TLX scale (e.g., if four people all had an actual score of 75% correct, those rating themselves at either 77 or 73 would have better absolute accuracy than those rating themselves at 65 or 85). To measure this, we calculated a "metacognitive difference score" for each run by subtracting the participant's NASA-TLX Performance rating on that run from their actual performance. The metacognitive difference scores were analyzed using the same MLM design as used to analyze the NASA-TLX scales. We included this as a *post hoc* analysis to explore the unexpected finding that participants in the loss condition gave themselves higher ratings for performance. However, in hindsight, it provides an additional

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[1] One might question whether the LNS runs were truly independent given previous findings suggesting that ascending set-size presentation leads to both practice effects, differentially affecting young adults, and proactive interference, differentially affecting older adults (e.g., May et al., 1999; Lustig et al., 2001; Rowe et al., 2008). As a precaution we also used MLM to analyze the LNS results; conclusions did not differ between the two methods.

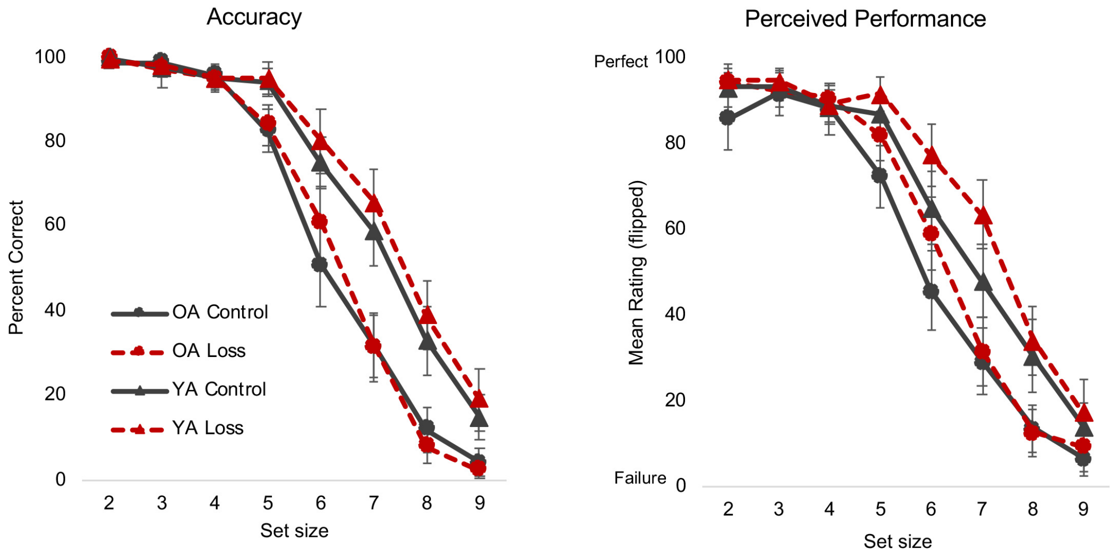

FIGURE 1 | Letter Number Sequencing (LNS) accuracy and NASA-TLX perceived performance ratings. Different colors/lines (control = black solid line, loss = red dashed line) and shapes [triangle = young adults (YA), circle = older adults (OA)] are used to highlight the different conditions. Error bars represent 95% confidence intervals. The loss incentive did not affect actual performance **(left panel)** but did increase participants' self-report ratings of their perceived performance **(right panel)**. See text and **Table 3** for statistical details for this and other figures. NASA-TLX, NASA Task Load Index.

test of the version of the "positivity effect" sometimes used to explain the results of previous studies: If older adults in the loss condition are ignoring the feedback information provided at the end of each run, they should be less accurate than the other groups.

RESULTS

Loss Incentives Increase Perceived Performance but Not Actual Performance in the Working Memory Task

Loss incentive did not affect LNS performance, $F(1, 159) = 1.27$, $p = 0.262$, $\eta_p^2 = 0.008$, nor did it interact with age, $F(1, 159) = 0.56$, $p = 0.455$, $\eta_p^2 = 0.003$, or set size, $F(4, 159) = 1.26$, $p = 0.281$, $\eta_p^2 = 0.008$ (**Figure 1**). We replicated commonly observed set size and age effects and interactions: Accuracy decreased as set size increased, $F(4, 159) = 879.29$, $p < 0.001$, $\eta_p^2 = 0.84$; older adults showed lower accuracy compared to young adults, $F(1, 159) = 67.80$, $p < 0.001$, $\eta_p^2 = 0.29$; and older adults' accuracy decreased at earlier set sizes than young adults', $F(4, 159) = 26.88$, $p < 0.001$, $\eta_p^2 = 0.14$.

As an exploratory analysis of potential incentive effects on metacognition, we examined participants' self-ratings on the Performance subscale of the NASA-TLX, administered after each run. The full MLM results for the Performance subscale and all NASA measures can be found in **Table 3**. To briefly summarize the critical results, in contrast to the lack of incentive effects on actual performance, participants in the loss condition perceived themselves to be more successful in accomplishing the task than did those in the control condition, $\beta = 8.28$, $t(165) = 2.66$, $p < 0.01$ (**Figure 1**).

The results so far indicate that loss incentives do not improve performance, contradicting the intuitive hypothesis. As we describe in *Discussion*, in hindsight, this may not be surprising given the task constraints (relatively fast presentation of stimuli, verbal response required on every trial) and that several other studies have failed to find incentive effects on performance; Hess et al. (2016) also did not find effects of an alternative motivation manipulation on this same task. More importantly, we did not find any evidence in either actual or perceived performance that older adults were any more (motivational shift hypothesis) or less (heuristic positivity effect hypothesis) sensitive to the loss incentive.

The higher Performance self-ratings in the loss condition were an unexpected finding, which we discuss in the context of the other metacognitive measures below. Before turning to those issues, we review the results for the other NASA-TLX subscales and posttask questionnaires.

Loss Incentives Increase the Perceived Demands and Frustration at Higher Task Loads but Not the Effort to Meet That Demand

The main measures of interest for the NASA-TLX were the Mental Demand, Effort, and Frustration subscales. Hess et al. (2016) noted that the Mental Demand and Effort scales were especially related to the construct of engagement, both in terms of face validity and in their ability to predict a physiological measure of engagement [systolic blood pressure (SBP) reactivity]. As noted in **Table 2**, an intuitive "incentive

TABLE 3 | NASA-TLX MLM results (β).

Effect	Mental demand	Physical demand	Temporal demand	Performance	Effort	Frustration
Intercept	45.69***	9.32***	32.36***	74.20***	44.67***	24.97***
Age	−0.49	5.95*	7.26	−14.12***	2.56	9.06*
$\text{SS}_{\text{linear}}$	10.08***	1.00***	7.30***	−12.07***	9.46***	5.40***
$\text{SS}_{\text{quadratic}}$	0.33	0.09	0.77***	−1.76***	0.34	0.35
Age × $\text{SS}_{\text{linear}}$	0.51	1.59***	2.77***	−1.64**	1.04*	3.93***
Age × $\text{SS}_{\text{quadratic}}$	0.32	0.08	−0.12	0.63*	0.47	0.02
Incentive	−2.49	−2.71	−1.09	8.28**	0.65	3.19
Age × Incentive	−0.37	−2.70	−0.66	−1.86	−4.24	−1.95
$\text{SS}_{\text{linear}}$ × Incentive	1.11*	0.55	−0.86	0.90	0.65	1.53**
$\text{SS}_{\text{quadratic}}$ × Incentive	0.24	0.20	−0.01	−0.54	0.03	−0.04
Age × $\text{SS}_{\text{linear}}$ × Incentive	−0.28	−1.59**	0.36	−1.43	−0.60	−0.92
Age × $\text{SS}_{\text{quadratic}}$ × Incentive	0.22	−0.09	0.25	0.24	0.05	0.31

****$p < 0.001$, **$p < 0.01$, *$p < 0.05$.NASA-TLX, NASA Task Load Index; MLM, multilevel model; SS, set size.*

increases motivation" perspective predicts that incentive should increase the effort people put in to maintain performance as actual demand (set size) increases and may also reduce perceived demand (i.e., people may perceive the task as less demanding if they are strongly motivated). In contrast, a "disengagement" perspective predicts a lack of willingness to increase effort in response to an increase in perceived demand (The "positivity effect" view does not make obvious predictions for these measures).

The results were more consistent with the disengagement perspective. For the Mental Demand measure, the incentive × set size interaction was significant (**Table 3**) with participants in the loss condition giving numerically lower ratings of demand until about set size 6 and giving numerically higher ratings from set size 8 (**Figure 2**; see also **Supplementary Material S2**, which shows the results more clearly by collapsing across age group). *Post hoc t* tests suggested that this interaction is due to a significant increase in ratings from set size 8 to set size 9 in the loss group [$t(168) = -2.35$, $p = 0.019$], but not in the control group [$t(166) = -1.71$, $p = 0.087$). In contrast, for the Effort measure, there was no effect of incentive (**Table 3**). In other words, despite perceiving greater demand, participants in the loss condition were not inclined to increase effort to meet that demand.

We were also interested in the Frustration subscale, as the "positivity effect" view would make different predictions than the other two perspectives. That is, if older adults ignore or downplay negative information in the service of regulating emotion, they might be expected to show less frustration than young adults (especially in the loss condition) at the higher set sizes, when errors and thus losses are more likely. The "disengagement" perspective predicts a different chain of events: The feedback and loss information immediately after the trial is relatively difficult to ignore or avoid, and a resulting increase in frustration would be predicted to lead to subsequent, downstream disengagement. The "incentive increases motivation" viewpoint might also predict increased frustration, if that motivation or desire to achieve/retain reward is literally frustrated by the increase in errors, and thus losses, at higher set sizes (Carver and Harmon-Jones, 2009; Angus and Harmon-Jones, 2019).

For the Frustration subscale, set size had significant interactions with both incentive and age group. The three-way interaction was not significant (**Table 3**). In both cases, the two groups (young vs. old; loss vs. control) were largely identical at the lower, easier, set sizes, with larger differences between the groups appearing at the higher, more difficult set sizes (**Figure 2**). Age group differences in particular closely paralleled the accuracy data in when they began to show a separation (i.e., older adults had low Frustration scores for set sizes 2–4 and began to show an increase around set size 5, whereas for young adults, the sharper increase occurred around set size 6). In short, these data support the idea that the loss incentive increases frustration specifically at higher set sizes when errors are more likely to occur, and there is no evidence that older adults are either immune to or especially sensitive to this effect.

The other subscales were not as incisive theoretically but are reported (**Table 3** and **Supplementary Materials S1, S3**) for completeness, including comparison with the prior study by Hess et al. (2016).

Loss Incentives Increase Distraction in Young Adults and Decrease Motivation in Older Adults

Figure 3 shows the results of directly asking participants about their focus of attention and the degree to which the feedback or incentive was distracting or motivating. Older adults gave lower ratings for difficulty focusing attention than did young adults, replicating counterintuitive but typical findings in the literature, $F(1, 160) = 8.47$, $p = 0.004$, $\eta_p^2 = 0.05$.

A significant age × incentive interaction for the distraction question indicated that young and older adults had different reactions to the loss incentive feedback, $F(1, 160) = 8.51$, $p = 0.004$, $\eta_p^2 = 0.049$. Young adults under loss incentive reported higher distraction than those in the control condition, $t(83) = -4.89$, $p < 0.001$, but this effect was not observed in older adults, $t(82) = -1.08$, $p = 0.285$. For the motivation question, we observed a significant incentive effect, $F(1, 160) = 8.25$,

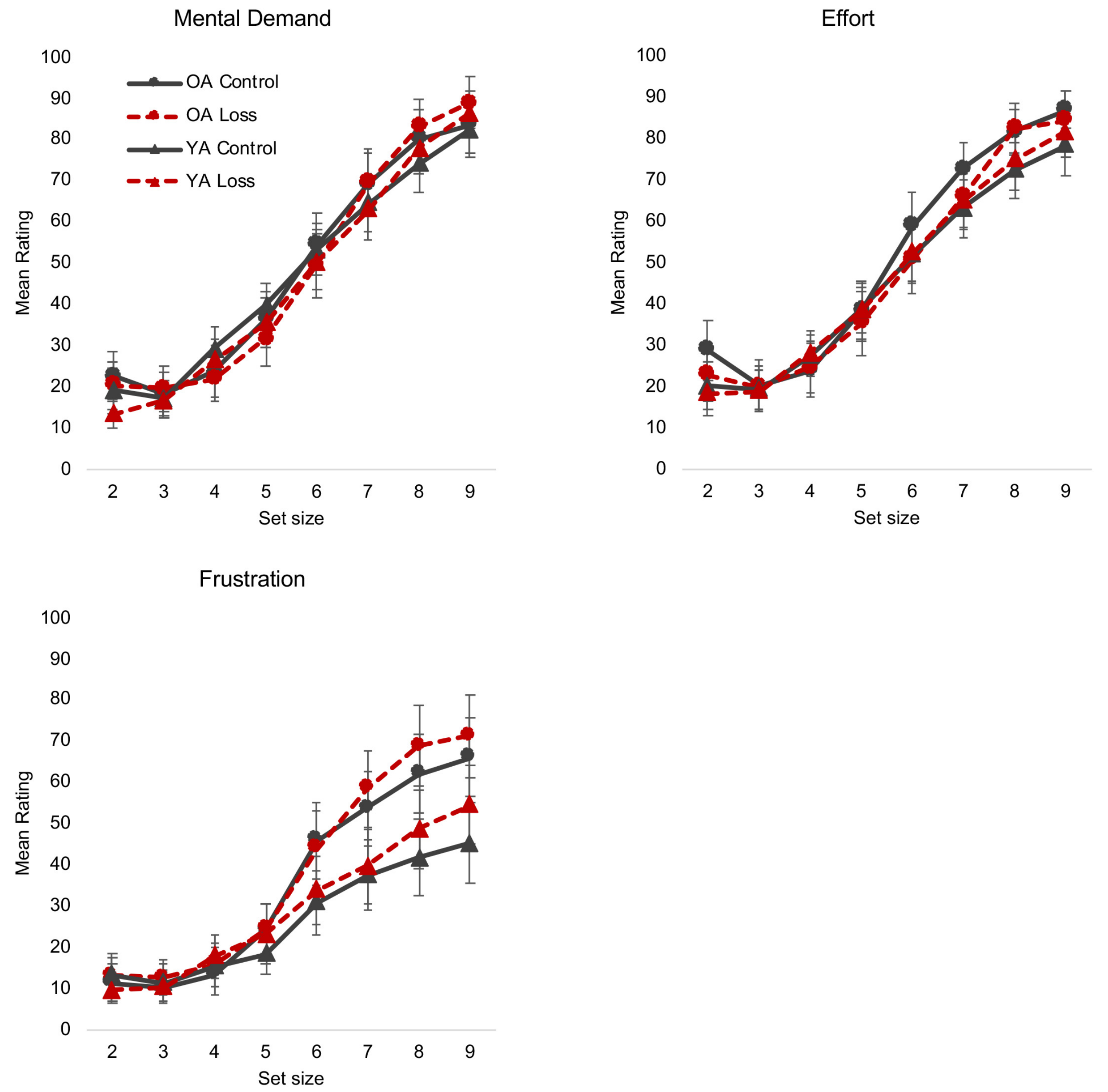

FIGURE 2 | NASA-TLX mental demand, and effort, and frustration. Different colors/lines (control = black solid line, loss = red dashed line) and shapes [triangle = young adults (YA), circle = older adults (OA)] are used to highlight the different conditions. Error bars represent 95% confidence intervals. The loss incentive increased participants' reports of mental demand and frustration but did not increase effort to meet those demands. NASA-TLX, NASA Task Load Index.

$p = 0.005$, $\eta_p^2 = 0.05$ where those under loss incentive show lower motivation. Although the age × incentive interaction was not significant, $F(1, 160) = 3.40$, $p = 0.067$, $\eta_p^2 = 0.02$, the incentive effect was largely driven by older adults, $t(82) = 3.08$, $p = 0.003$, and not significant for young adults, $t(83) = 0.80$, $p = 0.428$.

One caveat to these results is that they reflect participant's answers to the direct questions about their responses to the incentive and feedback. We did not see incentive effects on the more general measures provided by the IMI, including the Interest/Enjoyment scale (**Supplementary Material S5**). This may be due to the less targeted nature of the IMI questions and their focus on how fun, interesting, or enjoyable the task is rather than the participant's inner motivation or desire to do well.

Loss Incentives Improve the Accuracy of Immediate, Absolute Metacognitive Judgments, but May Distort Relative Judgments of Competence for Older Adults

We next conducted further exploratory analyses of how the loss incentive might affect participants' metacognitive judgments.

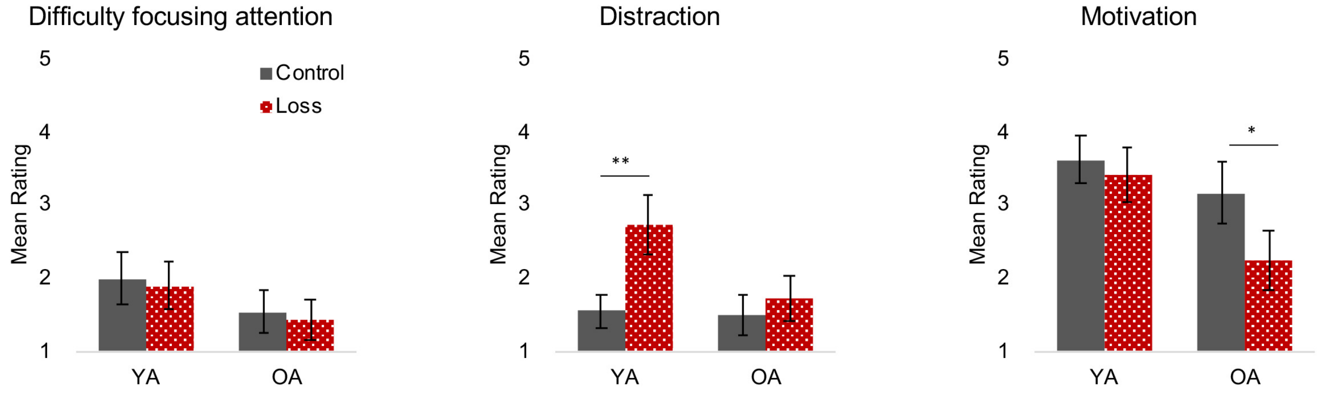

FIGURE 3 | State Attention and Motivation Questionnaire (SAMQ) (Q4–Q6). Different colors/patterns (control = black filled, loss = red dotted) are used to highlight the different conditions for young (YA) and older adults (OA). Error bars represent 95% confidence intervals. $^{**}p < 0.001$, $^{*}p < 0.01$. Loss incentive increased distraction for young adults and decreased motivation for older adults.

The hypothesis that older adults ignore negative information predicts that older adults in the loss condition would have a weaker relationship between their actual and perceived (self-rated) performance. This was not the case for the Performance subscale of the NASA-TLX: Correlations between perceived and actual performance were moderately strong for all four groups (all $r = 0.68$, $p < 0.001$; **Figure 4**, top panel).

Moreover, the metacognitive difference scores (actual performance - self-rated performance) were analyzed using the same MLM design as used to analyze the NASA-TLX scales (see **Supplementary Material S6** for the full results). The results showed that both younger and older adults in the loss condition in fact showed less discrepancy between their actual performance and perceived performance than did their counterparts in the control condition, $\beta = -4.84$, $t(165) = -2.43$, $p = 0.016$ (**Figure 5**). There was also a significant quadratic interaction between set size and incentive condition, $\beta = 0.45$, $t(1175) = 2.22$, $p = 0.026$. Both the control and loss groups tended to underestimate their performance in the lower set sizes and get close to accurate judgment or slight overestimation at the higher set sizes. The discrepancies between the groups appear to be greatest at the middle set sizes (4–7), where the loss incentive group's ratings underestimated their performance less than did those of the control group. Full MLM results for metacognitive difference scores are shown in **Supplementary Material S6**.

A different pattern emerged for the IMI Competence rating, which was given after the entire task (rather than immediately after run feedback) and focused on participants' overall satisfaction with their performance and whether they felt they had performed well in comparison with their peers. While the other three groups maintained moderate correlations between this measure and their actual performance, this correlation was only marginal for older adults in the loss condition, $r = 0.29$, $p = 0.061$ (**Figure 4**). This was significantly smaller than the correlation between their NASA-TLX Performance rating and actual performance (modified Fisher's z test, $z = 2.37$, $p = 0.009$; Steiger, 1980; calculation tool provided by Lee and Preacher, 2013). For the other groups, the correlations between IMI Competence and actual performance remained in the moderate range, all $r \geq 0.57$, $p < 0.001$. Comparing across groups, Fisher's z tests showed that the correlation for older adults in the loss condition was significantly weaker than that of the young adults in the loss condition ($p = 0.009$), marginally so compared to the other two groups (both $p = 0.06$).

DISCUSSION

We examined the effects of a loss-based incentive on young and older adults' working memory performance, motivation, and metacognition. Incentive did not impact performance, but instead increased participants' perceptions of mental demand and their frustration at the higher, more demanding set sizes. The loss incentive also increased the absolute accuracy of immediate metacognitive judgments, that is, participants' ratings of how well they did compared to their actual performance. These results are not consistent either with the "incentive increases motivation" or the heuristic "older adults ignore loss information" hypotheses. Older adults were at least as sensitive to loss information in the immediate postrun ratings as were young adults, and their immediate postrun metacognitive performance ratings were particularly accurate in the loss condition, suggesting close attention to the loss incentive feedback.

The results did not completely fit any of the predictions outlined in **Table 2**, but overall seemed most consistent with the idea that, especially at the highest set sizes when errors were most common, loss incentive increased the perceived "costs" (mental demand, frustration) of performance. Somewhat contrary to the suggestion that older adults may be more sensitive to unavoidable negative information and/or more sensitive to such costs (c.f., Charles, 2010; Hess, 2014), the effects appeared to be of similar size for younger and older adults. However, other aspects of the results suggest that these equivalent effects occurred for different reasons, with the loss incentive being more distracting to young adults, more demotivating to older adults. The change in

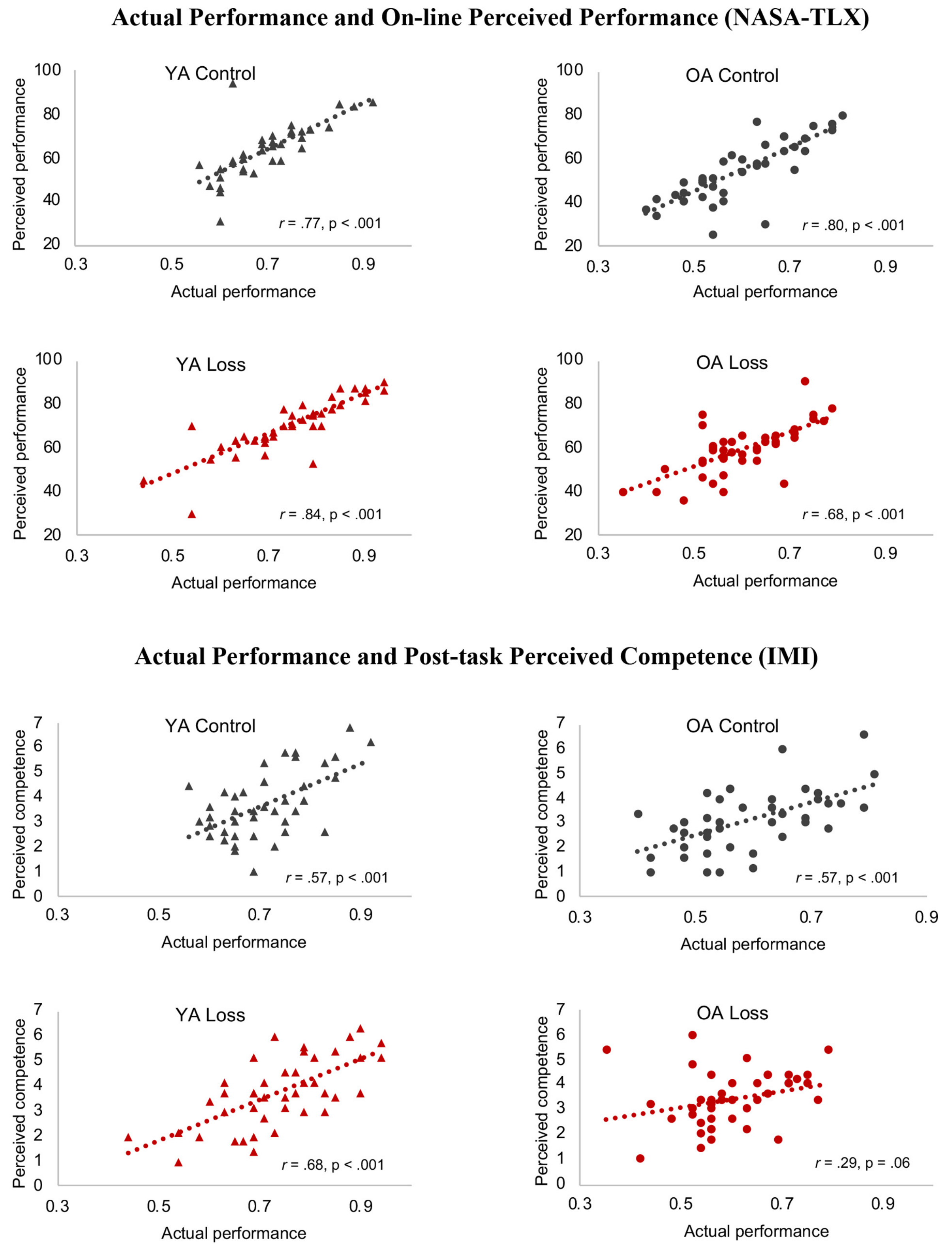

FIGURE 4 | *Relative* metacognitive accuracy. Different colors (control = black, red = loss) and shapes [triangle = young adults (YA), circle = older adults (OA)] are used to highlight the different conditions. Correlations between actual and perceived performance were moderately strong for all four groups. A different pattern emerged for correlations between actual performance and IMI Competence ratings: this correlation was only marginal for older adults in the loss condition, while the other groups maintained moderate correlations. NASA-TLX, NASA Task Load Index; IMI, Intrinsic Motivation Inventory.

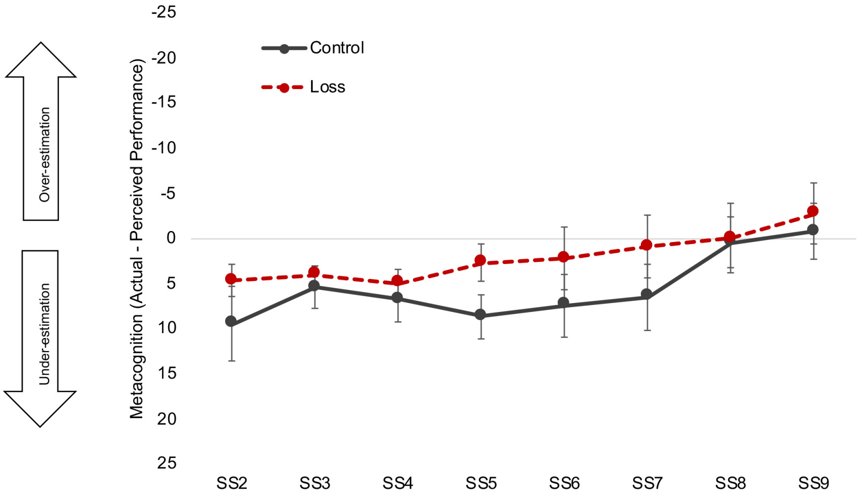

FIGURE 5 | *Absolute* metacognitive accuracy. Black solid line and red dashed line denote control and loss condition, respectively. Error bars represent 95% confidence intervals. Participants in the loss incentive condition had less discrepancy between their perceived and actual performance than did participants in the control condition, with group differences largest at the intermediate set sizes (see text and **Supplementary Table S6** for statistical details). Note: Scale on *y*-axis is reversed for ease of interpretation. Zero means accurate judgment. See **Supplementary Material S7** for the full age × incentive graph. SS, set size.

metacognitive accuracy by older adults in the loss condition from immediate, specific performance judgments vs. later judgments of competency in the task as a whole also seems consistent with the suggestion that, when negative information is unavoidable in the moment, older adults may instead cope by reframing later on (Charles, 2010).

Despite their increased perception of demand and frustration, as well as more accurate judgments of performance, participants in the loss condition did not increase their effort to meet that demand and improve their performance. To further explore the possibility that, for older adults, this failure to increase effort might be related to disengagement and decreased motivation, we conducted additional exploratory analyses examining correlations between changes on the NASA-TLX Effort scale from the lowest (2) to highest (9) set size and the posttask question about motivation [*p*-values corrected for multiple comparisons using the false discovery rate (FDR) approach because of the exploratory nature of the analyses]. The relationship between effort and motivation change went in the opposite direction for older adults in the control and loss conditions, Fisher's $z = 2.12$, $p = 0.034$. However, this result should be considered only suggestive and interpreted with caution given the exploratory nature of the analyses and that the individual correlations did not reach significance (control condition Kendall rank correlation coefficient $tau = 0.22$, $p_{\mathrm{FDR}} = 0.14$; loss condition $tau = -0.25$, $p_{\mathrm{FDR}} = 0.14$). The loss-reversal pattern appears to be specific to older adults and to the motivation measure: Correlations for young adults did not approach significance (all $p_{\mathrm{FDR}} > 0.40$), and in the older adults, the control and loss incentive groups showed similar correlations between distraction ratings and increases in effort (control $tau = -0.38$, $p_{\mathrm{FDR}} = 0.006$; loss $tau = -0.26$, $p_{\mathrm{FDR}} = 0.034$).

In addition, although it had not been part of our thought process in setting up the correlation matrix, we also observed that for the control groups, motivation and distraction tended to be negatively correlated ($tau = -0.35$, $p_{\mathrm{FDR}} = 0.021$ for young adults; $tau = -0.25$, $p_{\mathrm{FDR}} = 0.07$ for older adults) with the opposite pattern in the loss groups ($tau = 0.23$, $p_{\mathrm{FDR}} = 0.07$ for young adults; $tau = 0.55$, $p_{\mathrm{FDR}} < 0.001$ for older adults). This again seems inconsistent with the idea that older adults ignored the negative loss incentive information. Instead, for both age groups, the more motivated they were by the loss incentive information, the more distracting they found it.

Performance vs. Subjective Measures

Contrary to initial expectations, we did not see either beneficial or detrimental effects on performance by either group. **Figure 1** suggests a very small numerical advantage for the loss condition, but even at the set size with the largest difference, the effect is quite small ($d = 0.24$) and most likely noise. We originally chose this task because Hess et al. (2016) had found age and set size differences in a physiological measure of engagement during the task. An earlier set of studies in our lab found that loss incentive reduced older adults' performance on a measure of focused attention and increased their self-reported mind wandering (Lin, 2018; Lin et al., 2019), and so we had thought we might see similar effects here.

Of course, it is possible that our loss incentive manipulation was simply ineffective and inadequate. A reviewer raised the question of whether this might be the case because of the between-subjects design and whether a within-session contrast with reward or neutral trials might be necessary to make the loss salient produce an effect. Although that explanation cannot be ruled out, we think it is unlikely to be the case. First, there are the findings of effects on the subjective measures, suggesting that the loss incentive was indeed salient and that the lack of effects on working memory performance were due to a lack of sensitivity in the measure. Other studies suggest that between-subjects incentive manipulations can affect performance in older adults: Barber and Mather found crossover interactions for between-subjects manipulations of stereotype threat and gain/loss incentive on both working memory and clinical cognitive assessments (Barber and Mather, 2013; Barber et al., 2015). As we have already noted, other datasets from our lab show that older adults' performance can be impaired by similar between-subjects incentive manipulations, although these findings should be considered preliminary until they have undergone full peer review and publication (Lin, 2018; Lin et al., 2019; see also Jang et al., 2020).

Instead, although targeted experiments will be required to test it, our working hypothesis is that discrepancies across studies, whether they show performance differences as a result of incentive, especially loss incentive, may be heavily influenced by differences in the task constraints and proactive control requirements. Incentives appear to largely affect the engagement of proactive control (Chiew and Braver, 2016; Mäki-Marttunen et al., 2019; general reductions in response time may be an exception). The focused-attention task used in our earlier study made strong demands on self-initiated, proactive processing (rare targets and responses, low-salience targets distinguishable only by their duration). The LNS task uses a relatively fast presentation of to-be-remembered stimuli (one per second) and requires a verbal response on each trial – literally requiring the participant to "engage with" the experimenter. Thus, it may rely more on reactive control; the low ratings of mind wandering and difficulty focusing attention seem consistent with that interpretation. Future experiments that specifically isolate task constraints and top–down control requirements will be needed to determine the plausibility of this interpretation.

On the other hand, the lack of performance differences helps to alleviate concerns that the effects we see on the subjective measures are simply downstream artifacts of poor performance. That is, it is difficult to say that the higher mental demand ratings (for example) by participants in the loss condition are simply an attempt to "excuse" lower performance, since they did not in fact have lower performance.

We also examined whether the end-of-task measures might be especially influenced by the last few runs. This was the case for the IMI competence measure, as might be expected, given that the final runs are also the ones where performance is most difficult and competence becomes a question: For all groups except the older adult loss group, correlations between performance and the IMI Competence ratings were higher for the last three set sizes ($r = 0.36$–0.60) than for the first three set sizes ($r = -0.31$–0.31). For the older adult loss group, correlations were consistently low ($r = -0.06$–0.17 for the first three set sizes; $r = 0.07$–0.27 for the last set sizes), as would be expected from the results shown in **Figure 4**. There were no systematic changes in correlation with set size for the SAMQ Motivation or Distraction questions, or IMI Interest/Enjoyment measures, especially for the incentive groups. [The young adult control group showed hints of such a pattern for the IMI Interest/Enjoyment measure ($r = -0.06$–0.28 for the first three set sizes; $r = 0.13$–0.36 for the last three), but given fluctuations across the set sizes, this seems unlikely to be meaningful.] Thus, there is no evidence that the end-of-task measures of motivation and distraction were unduly influenced by the last few runs/highest set sizes.

The opposite critique may come to mind when considering age differences: Young adults had better performance than older adults. Of course, that is also the case in most previous studies of age × incentive interactions in cognitive control tasks. The present task has the advantage that the range of set sizes used here allows us to examine the issue, at least for the postrun NASA-TLX ratings. We did a follow-up analysis using only those set sizes where performance for young and older adults was equivalent (between 25 and 75% accuracy; set sizes 5–7 for older adults; set sizes 6–8 for young adults; rescaled as "low, medium and high" for each group). In that case, the Mental Demand and Effort ratings were generally higher for young adults, whereas Frustration remained somewhat higher for older adults. It did not introduce any new age × incentive interactions compared to the analyses reported above, although there was a trend for the Effort ratings of older adults in the loss condition to be especially low. In general, comparing the restricted-range results to the full dataset suggests that incentive effects overall were greatest at the highest set sizes, when load exceeded capacity, but there was no suggestion of interactions with age or that age differences in performance played a role.

Limitations and Comparisons (or the Lack Thereof) With Previous Studies

There are several limitations and differences from other studies that should be kept in mind when interpreting these results and their place in the literature, as well as strengths and weaknesses that are shared with other studies in this field. First, we focused on loss incentives because they are understudied; losses are thought to be increasingly important in later life (Baltes et al., 1999), the opportunity to avoid losses is often used to motivate older adults, and this is the condition that is most theoretically incisive: The general/intuitive "incentive increases motivation and thus attention and performance," heuristic positivity effect ("older adults ignore negative information"), and nuanced positivity effect/disengagement hypothesis all make similar predictions for reward conditions. The "incentive as cognitive load" makes similar predictions for reward and loss incentive. Prior studies that did examine both reward and loss effects on cognitive performance in young and older adults have already found patterns contradicting the "motivational shift" hypothesis, which appears to apply to more general orientations and choice behaviors, and possibly to avoidance learning.

It is the case that we cannot rule out that "gain" incentives would have had similar results in the present study; the complementary criticism applies to the majority of studies that have focused solely on gain incentives. Behavioral (O'Brien and Hess, 2019) and neural (e.g., Paschke et al., 2015; Cubillo et al., 2019) evidence suggests that gain and loss operate through partially independent processes. However, this issue needs further examination, and in general, studies in this field would benefit from including both conditions. What we can say is that we did not find any evidence that loss incentive generally improved performance and motivation and that older adults appeared to be at least as responsive to the loss incentive as were young adults.

Second, as stated earlier, it was explicitly *not* our intention to do another incremental variation on existing studies that, besides focusing on gain effects, have with rare exception used trial-wise manipulations on cognitive control tasks. We instead wanted to take the first step in addressing several important but understudied questions, not only of incentive type (loss, as noted above) but also of cognitive domain (working memory) and session-wide implementation of incentives. While the differences in our approach make it difficult to compare our results directly to existing laboratory studies, we believe that this last aspect is especially important, given how performance incentives are typically implemented in everyday life. Trial-wise implementations have an advantage in statistical power, but this may come at the cost of generalization to real-world situations (c.f., Deci et al., 1999; Cerasoli et al., 2014).

Another reason we have specifically avoided trial-by-trial incentives in our studies is that the changing incentive cues and delivery of reward/loss information on every or almost every trial are likely to drive attention and engagement in the "bottom–up" fashion described earlier. Several studies have already found different incentive effects for block- or run-wise implementation of incentives vs. trial-wise manipulations (Jimura et al., 2010; Paschke et al., 2015; Bruening et al., 2018); differences from session-wide effects may be even more pronounced (Lin, 2018). Although they examined downstream effects of correct/error and gain/loss feedback on incidental encoding during a previous task rather than incentivized performance, analysis by Mather and Schoeke (2011) suggest that trial-history effects could be an interesting compromise method to test whether, e.g., disengagement (or overarousal) builds up over multiple errors or losses (see also Schmitt et al., 2017). Regardless, it seems important to have both types of studies in the literature to see where effects converge or diverge and, in the latter case, to ultimately conduct targeted, parametric manipulations to understand why. We hope that the present findings will – to coin a phrase – provide some incentive to do so.

Third, our use of subjective response measures, especially examination of potential effects on metacognition, is relatively novel and provides further insights into the pathways by which incentives may have their effects. However, such measures come with their own limitations, including potential response bias, impression management, and so on. As noted above, although the lack of incentive effects on performance can be seen as a limitation in some respects, raising questions about whether the incentive manipulation was effective, on the other hand, has the advantage of alleviating the concerns that the loss groups' higher ratings of mental demand, frustration, and distraction (young adults) or reduced motivation (older adults) might be attempts to "blame" poor performance on those factors in retrospect. Besides their preserved actual performance, participants in the loss condition also gave themselves higher and more accurate immediate self-ratings of performance, especially at the higher set sizes. It seems hard to reconcile this greater confidence and accuracy with the idea that they were more likely to use increased mental demand, frustration, distraction, or loss of motivation to excuse performance declines. Again, what we have here is a complementary set of advantages and disadvantages compared to studies that have examined physiological or neural responses to incentive manipulations; what is ultimately needed is a combined approach.

Another critique that can be applied both to this study – and almost every other study of age × incentive effects, including many of the others in this Frontiers Research Topic – is "maybe older adults just don't care (as much) about the money." This seems a bit hard to reconcile with the equivalent effects of the incentive on young and older adults for many of our measures. However – although it should be considered exploratory – the different patterns shown by young and older adults for the posttask distraction vs. motivation questions suggests that there may be at least some truth to this. In a larger sense, we agree entirely that older adults, at least those who are likely to participate in studies in our lab and the labs of other university-based investigators, are unlikely to find the money *per se* of primary interest. We suspect that, instead, the loss incentive in particular has its power by drawing attention to errors. We are beginning studies to test this possibility more directly. Providing some indirect support, Dhingra et al. (2020) reported less behavioral and neural sensitivity to incentive magnitude (dollar vs. cent) in older vs. young adults. However, in the case of losses, this was due to a relatively higher response to even small losses in older adults. Another important question for this area of study more generally is how different incentive amounts and types may affect results, and potentially interact with participant demographics.

Finally, an aspect of the present study lacking in many others was our examination of subjective measures, both immediately and posttask. It is interesting that younger and older adults showed similar incentive effects for the ratings of mental demand, performance, and frustration taken during the task, with age differences emerging in the more holistic, posttask measures. This could be seen as consistent with claims that older adults may be just as affected as young adults by unavoidable negative information "in the moment," but more likely to respond to it with more passive strategies, and by later reframing or reappraising the situation to put it in a more positive light (e.g., Charles, 2010). Future studies using instruments designed to more systematically explore how metacognition and the emotional/motivational response to incentives is affected by the specificity (atomistic vs. holistic) and temporal (during/immediately after performance vs. somewhat later on) dimensions, as well as their interaction, will be important for more definitively identifying which factors exert a critical influence over these effects.

What Are the Roles of "Engagement" and Task Constraints in Studies of Incentive?

As noted in *Introduction*, incentives are often used (or assumed) to increase proactive control in an effort to improve performance (Botvinick and Braver, 2015); the "engagement" idea of Hess and colleagues (Ennis et al., 2014; Hess, 2014) is similar. This leads to the question of how to define "engagement." Although Hess's theoretical writings have not specifically addressed issues of top–down (proactive, goal-related) vs. bottom–up (reactive, task or stimulus related) factors, he has noted that he means the term to be synonymous with "effort" and also emphasizes the idea of the choice whether or not to engage, which seems more consistent with the top–down interpretation. However, the degree to which engagement of this type is required likely varies inversely with the degree to which the task itself is inherently "engaging" because of constraints or stimuli that drive attention in a more bottom–up or reactive fashion. Several functional MRI (fMRI) studies indicate that incentives may have their primary effects on proactive, self-initiated control (e.g., whether participants engage frontoparietal regions at the point of a cue which would allow them to prepare for the upcoming probe, vs. waiting for the probe), although this has primarily been demonstrated for reward incentives (e.g., Jimura et al., 2010; Etzel et al., 2015; see Cubillo et al., 2019 for effects of loss incentives suggesting a shift to reactive control).

Putting this together with the boundary conditions on the positivity effect noted by Carstensen and colleagues, when loss information is unavoidable but task constraints are high, older adults may react to the negative information at a subjective and motivational–emotional level without this drop in motivational "engagement" decreasing performance. One interesting prediction is that higher task constraints should lead to preserved performance at the cost of greater subjective demand and frustration, whereas relatively unconstrained tasks provide an opportunity to reduce engagement and negative subjective experience but at the cost of reduced performance. This hypothesis regarding the potential role of task constraints should be regarded as that – a hypothesis – rather than a definitive conclusion.

An alternative, less process-specific explanation for the differences between the studies might be that the present task was simply more difficult, especially at the higher set sizes. However, this alternative runs into some complications given that, on the one hand, more difficult tasks typically decrease mind wandering (e.g., Baird et al., 2012; Konishi et al., 2015; see Seli et al., 2018 for discussion of exceptions) but, on the other hand, are usually considered to be exactly the situations in which incentive and motivation are likely to be most important (e.g., Botvinick and Braver, 2015; Ferdinand and Czernochowski, 2018; Kostandyan et al., 2019).

To our knowledge, there has not been a systematic investigation of how either incentive effects or the positivity effect may be impacted by changing the degree to which engagement is driven by "bottom–up" vs. "top–down" within the same task. One way to differentiate these ideas while controlling for task difficulty might be, e.g., comparing rare-response vs. frequent-response versions of the same attention task (c.f., Staub et al., 2015), or varying retention intervals in a working-memory task. This kind of task analysis and testing of parameters and boundary conditions may be an important direction for future research, especially as many real-world tasks are relatively unconstrained (e.g., reading, writing, participating in a conversation, driving) and thus may rely more on the top–down, self-initiated aspects of attention (Hess et al., 2011, 2018).

CONCLUSION

The study of age differences in the response to incentives during cognitive challenging tasks is still at very early stages, although growing quickly. Thus far, most studies have used attention and cognitive control tasks, used reward incentives, and implemented incentive on a trial-wise basis. We took a complementary approach (working memory task, loss incentive, session-wide incentive implementation), with a complementary set of strengths and weaknesses in our methods, design, and the conclusions that can be drawn.

Our results suggest caution in generalizing the results of previous studies, especially to everyday life scenarios: They do not support the idea that incentive generally (i.e., regardless of valence) increases motivation and performance even for young adults, or that older adults ignore negative information provided by loss incentives. Another relatively novel aspect of our study was the inclusion of metacognitive and self-report measures of motivation, distraction, and related constructs. The loss incentive appeared to increase participants' attention to their own performance, their perceptions of mental demand at higher set sizes, and their frustration at not being able to maintain good performance at those higher set sizes. Interestingly, these perceived increases in demand and frustration at higher set sizes were not met with concomitant increases in effort. Instead, young adults reported finding the incentive distracting, whereas older adults found it demotivating.

These results come with the usual caveats accompanying self-report measures, although supposedly more objective physiological measures have a complementary problem of somewhat subjective interpretation by the investigator (as opposed to the participant). That is, they are often related to some aspect of sympathetic arousal, but is this arousal indexing "engagement" or some other construct such as frustration or anxiety? Ideally future studies will combine these approaches; self-report measures may provide richer and more precise interpretations of the neural and physiological results, especially if combined with fine-grained analysis of performance results [e.g., response time, vigor (speed or force), or variability] and careful experiment construction to get at different cognitive, emotional, or motivational constructs. The role of individual and cultural differences in attitudes toward different types and levels of incentives is also an understudied topic. Finally, task constraints vs. the demand for proactive, self-initiated top–down control may be an important but as yet somewhat understudied factor in determining when and how incentives may affect performance and/or subjective responses.

In short, our study may raise as many questions as it answers. One of the most important questions it raises concerns the degree to which the results of previous studies can be generalized, especially to real-world scenarios. However, we believe that, in the long run, a careful consideration of issues related to proactive, top–down control vs. reactive, bottom–up attention will provide an important organizing principle for understanding the literature and driving it forward. We look forward to reading the other papers in this issue that will inform our own understanding of these issues, as well as future studies to test those ideas.

DATA AVAILABILITY STATEMENT

The datasets generated for this study will not be made publicly available as unfortunately we were not able to obtain permission from our IRB to share the data to a public repository. Data may be shared with other investigators upon request with a data use agreement and approval from the IRBs at both institutions.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the University of Michigan IRB. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

HJ and CL contributed to study design, data collection, data analyses, and manuscript writing. ZL contributed to study design. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2020.01489/full#supplementary-material

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Losses Motivate Cognitive Effort More Than Gains in Effort-Based Decision Making and Performance

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Human behavior is more strongly driven by the motivation to avoid losses than to pursue gains (loss aversion). However, there is little research on how losses influence the motivation to exert effort. We compared the effects of loss and gain incentives on cognitive task performance and effort-based decision making. In three experiments, participants performed a cognitively effortful task under gain and loss conditions and made choices about effort expenditure in a decision-making task. Results consistently showed significant loss aversion in effort-based decision making. Participants were willing to invest more effort in the loss compared to the gain condition (i.e., perform a longer duration task: Experiments 1 and 2; or higher task load: Experiment 3). On the other hand, losses did not lead to improved performance (sustained attention), or higher physiological effort (pupil diameter) in Experiments 1 and 2. In Experiment 3, losses did enhance working memory performance, but only at the highest load level. Taken together, these results suggest that loss aversion motivates higher effort investment in effort-based decision-making, while the effect of loss aversion during a performance may depend on the task type or effort level.

Keywords: cognitive effort, effort discounting, loss aversion, framing effect, motivation, sustained attention, N-Back, pupillometry

INTRODUCTION

Motivation can be seen as the willingness to exert effort in the pursuit of a goal or outcome (Chong et al., 2016; Pessiglione et al., 2017). Exerting effort can aid performance by mobilizing cognitive or motor resources, leading to faster and/or more accurate responses (Manohar et al., 2015). It is thought, however, that such resource mobilization is costly (Kool et al., 2010), and optimal behavior relies on a constant weighing of effort-costs against the expected value of the outcomes (Kurzban et al., 2013; Westbrook and Braver, 2015). The higher the value of the outcomes, the more likely an individual is to expand the required effort.

How outcomes are valued depends on the way they are framed. A long literature on decision-making shows that people weigh avoiding losses more strongly than acquiring equivalent gains (loss aversion: Tversky and Kahneman, 1979). Accordingly, people are more willing to take risks

(De Martino et al., 2006; Tom et al., 2007), or wait for an outcome (Xu et al., 2009; Blackburn and El-Deredy, 2013), if the outcome is framed as a loss rather than as a gain.

Although loss aversion is highly pervasive in decision making, most research has focused on decision making under risk, or on intertemporal choice. Very little research has been done on how losses affect the willingness to exert effort. The few studies exploring loss aversion in effort-based decision making have yielded inconclusive findings (Nishiyama, 2016; Lockwood et al., 2017; Byrne and Ghaiumy Anaraky, 2019; O'Brien and Ahmed, 2019; Chen et al., 2020). Similarly, studies examining cognitive performance under gain and loss incentives have not consistently found evidence for loss aversion (i.e., better performance and/or higher effort in loss incentive conditions compared to gains; Yechiam and Hochman, 2013; Belayachi et al., 2015; Paschke et al., 2015; Carsten et al., 2019).

In this study, we examined the effects of loss aversion on cognitive effort allocation. We tested this both in the context of performance (and associated physiology), and effort-based decision-making. Moreover, we tested this across different cognitive domains (sustained attention: Experiments 1 and 2; working memory: Experiment 3). In short, we found robust evidence for loss aversion in effort-based decision-making across all experiments. In contrast, loss aversion in performance was dependent on the cognitive domain and effort level.

EXPERIMENT 1

Methods

Participants

Thirty healthy participants were recruited from the student population [mean age (stdev) = 23.13 (3.07), 14 females]. Participants signed informed consent upon arrival in the lab. All procedures were approved by the Institutional Review Board (IRB) of the National University of Singapore.

Motivated Vigilance Task

To assess sustained attention performance under gain and loss incentives, participants performed a Motivated Vigilance Task (see **Figure 1A**; Massar et al., 2016, 2019). Participants had to respond as quickly as possible a target (a running millisecond counter) by pressing a button. Target stimuli appeared at random intervals and were separated by a fixation dot. Upon response, the millisecond counter came to a stop, displaying the RT as performance feedback for 1 s. Each task run was 10 min, comprising approximately 80 targets.

Participants first performed an unincentivized baseline run, after which they performed two incentivized runs (gain and loss, order counterbalanced). In the gain run, they could earn 10¢ for each response that was faster than an individual reaction time (RT) criterion (their individual median RT in baseline; for full instruction see **Supplementary Materials**). Total earnings in this run could be up to approximately \$8. In the loss condition, participants first received \$8. They were then instructed instructed that they would lose 10¢ for every trial in which they responded slower than the criterion. The main performance outcome was response speed (1/RT). Furthermore, to obtain a physiological measure of cognitive effort, pupil diameter was during task performance using a Tobii X60 eye-tracker (Tobii AB, Danderyd, Sweden). Pupil diameter is reliably found to index effort during the cognitive performance (Kahneman, 1973), as it increases with task difficulty, motivation, and effort sensation). If losses would provoke higher effort exertion than gains, we would expect to see larger pupil diameter during the performance of the loss run. Following our earlier work (Massar et al., 2016), we extracted the average pupil size in a 1-second window before the target presentation as an index of sustained (tonic) effort (see **Supplementary Materials** for analysis details).

Effort Discounting Task

To examine the influence of gain vs. loss framing on effort-based decision making, participants performed an effort discounting task (Libedinsky et al., 2013). Participants were presented with a series of choice trials (see **Figure 1F**) in which they were given the option to earn a reward in return for further performance of the vigilance task for a specified duration. Each trial presented two choice options. One option offered a small reward in return for the performance of a short duration task (1 min). The other option offered a larger reward for a longer task duration (5, 10, 20, or 30 min). As sustained attention is perceived as more effortful with longer task duration, this can be thought of as a parametric increase in effort level. The discounting task was completed in two framing conditions, gain and loss (order counterbalanced).

In the gain condition, the larger reward for the longer duration task was fixed (\$10). The smaller reward, for the short duration task, was dynamically updated after each trial, to approach the individual's indifference point (i.e., the smaller reward at the lower effort that they found equally valuable as \$10 for the higher effort level). Participants performed two runs of five trials per effort level and resulting indifference points were averaged per level.

In the loss condition, participants were first instructed that they could receive \$10. They then completed the discounting task, in which they chose a shorter duration vigilance task and losing an amount of money, or longer duration task, and losing nothing. The amount to be lost was updated similarly as in the gain condition Initial amounts in the loss condition were pegged to those in the gain condition, such that the potential outcomes (the eventual reward, or what is left after subtracting the loss from the initial endowment) would be identical between both conditions. Two runs of five iterations per effort level were completed to obtain the average indifference points. After completion of the gain and loss runs, one trial was randomly drawn for execution (participants performed the vigilance task for the chosen duration and received the associated reward). To ensure participants did not make decisions based on their perceived (in)ability to perform, they were instructed that RT did not matter for this last run, but they should sustain effort throughout. To ensure decisions were not influenced by the temporal delay to reward, all participants were to stay in the lab for 30 min before receiving their rewards. During this time, they

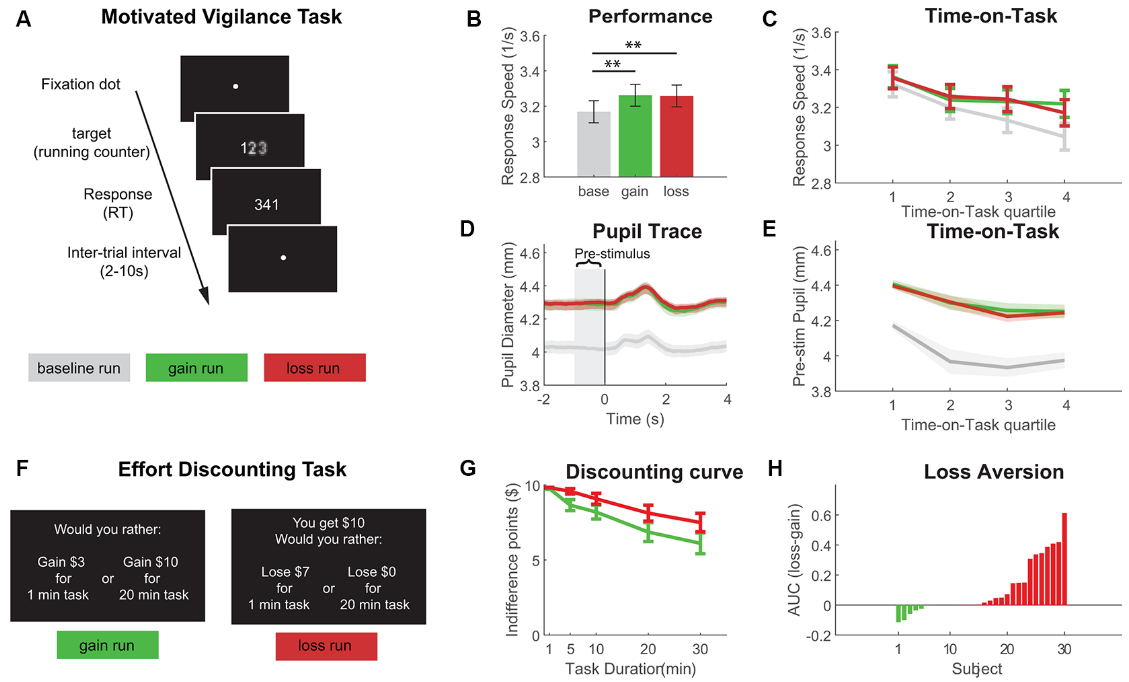

FIGURE 1 | Results from Experiment 1 with **(A)** schematic of the Motivated Vigilance Task, **(B)** response speed in the vigilance task for baseline, gain and loss conditions, **(C)** Time-on-Task decline of response speed (Time-on-Task quartiles for illustrative purposes, statistical analysis was based on linear slopes), **(D)** target-locked pupil trace in the vigilance task (time = 0 indicates target presentation), **(E)** Time-on-Task decline of pre-stimulus pupil diameter (Time-on-Task quartiles for illustrative purposes only, statistical analysis was based on linear slopes), **(F)** example trials of the effort-discounting task, **(G)** effort-discounting curve, and **(H)** loss-gain difference in the area under the discounting curve (AUC; positive difference scores denote less discounting for loss vs. gain choices). $^{**}p < 0.01$.

performed the vigilance task for the indicated duration and rested for the remaining time (see **Supplementary Materials** for full instructions).

Results

Motivated Vigilance Task

There was a significant difference in response speed between the incentive conditions (see **Figure 1B**; $F_{(2,58)} = 10.51$, $p < 0.001$). Response speed was faster in both gain and loss conditions compared to baseline (gain: $t_{(29)} = -3.68$, $p < 0.001$; loss: $t_{(29)} = -3.80$, $p < 0.001$), but was equivalent between the gain and loss conditions ($t_{(29)} = 0.197$, $p = 0.845$). On average, 59.88% (± 12.55%) of responses were faster than RT criterion in the gain condition vs. 60.05% (± 13.43%) in the loss condition, with no difference between conditions ($t_{(29)} = -0.093$, $p = 0.926$). For pupil diameter, one subject did not have sufficient quality data and was excluded from analysis. Pre-stimulus pupil diameter was taken as a measure of physiological effort (**Figure 1D**). Pupil diameter was significantly different between conditions ($F_{(2,56)} = 16.55$, $p < 0.001$), with larger diameter in both gain ($t_{(28)} = -3.96$, $p < 0.001$) and loss conditions ($t_{(28)} = -4.92$, $p < 0.001$), compared to the baseline condition, but no difference between the gain and loss conditions ($t_{(28)} = -0.193$, $p = 0.849$).

To analyze the development of performance and pupil diameter over the 10-min task duration (Time-on-Task), linear slope coefficients were calculated for each incentive condition. Both response speed and pupil diameter showed a gradual reduction over time-on-task (see **Figures 1C,E**). However this decline was not significantly different between conditions (performance: $F_{(2,59)} = 2.206$, $p = 0.119$; pupil: $F_{(2,56)} = 1.198$, $p = 0.309$).

Effort Discounting Task

Rewards were discounted with longer task duration (i.e., higher effort) in both the gain and loss conditions (see **Figure 1G**). The area under the discounting curve (AUC) was used as a summary metric for discounting (larger AUC denotes less discounting). Discounting AUC was smaller in the gain compared to the loss condition ($t_{(29)} = -3.139$, $p = 0.0039$), indicating that people discounted less in the loss condition (see **Figure 1H**).

Order Effects

As the different incentive conditions in both tasks were performed in separate runs (gain, loss, counter-balanced between-subjects), we tested for the potential effects of condition order. For PVT performance, a mixed ANOVA with Incentive (gain, loss) as within-subjects factor and Order (gain-loss, loss gain) as a between-subjects factor, yielded a significant Incentive × Order interaction ($F_{(1,59)} = 9.54$, $p = 0.0045$). Participants who performed the gain condition first, had better performance in the gain vs. the loss condition ($t_{(14)} = 2.638$, $p = 0.0195$), while participants who performed the loss condition first, performed slightly better (although non-significant) in the loss vs. the gain condition ($t_{(14)} = -1.841$, $p = 0.087$; see **Supplementary Figure S2**). Analysis of order effects in pupillometry did not yield a significant interaction ($F_{(1,57)} = 0.189$, $p = 0.667$).

Analysis of order effects in the Choice task yielded a significant Incentive × Order interaction ($F_{(1,59)} = 6.20$, $p = 0.019$), showing a strong loss aversion effect for participants who started with the gain condition ($t_{(14)} = -3.367$, $p = 0.0046$), but not for participants who performed the loss condition first ($t_{(14)} = -0.953$, $p = 0.357$; see **Supplementary Figure S2**).

Discussion

Results of Experiment 1 indicated that gain and loss incentives were associated with better performance and larger pupil size on the sustained attention task, compared to the unincentivized condition. However, there was no difference in performance nor pupil diameter between the gain and the loss conditions during vigilance performance. In the discounting task, on the other hand, there was a significant difference between the gain and loss conditions. Participants were more willing to invest effort if they stood to lose money, compared to when an equivalent outcome was framed as a gain. These findings suggest that loss aversion influences effort investment during effort-based decision making, but not during the actual exertion of cognitive effort.

An important limitation, however, was that gain and loss conditions were presented in separate runs (both in vigilance and discounting tasks). Analysis of order effects indicated that loss aversion effects were different for participants who started with the gain condition vs. participants who started with the loss condition. To account for this, we conducted a second experiment in which loss and gains trials were intermixed on a trial-by-trial level.

EXPERIMENT 2

Methods

Participants and Procedure

We recruited an independent sample of 30 participants [mean age (stdev) = 21.90 (2.54), 16 females]. Like Experiment 1, participants performed a Motivated Vigilance Task, followed by a Discounting task. In contrast to Experiment 1, gain and loss trials were intermixed. After completion of the Discounting task, one choice trial was randomly drawn for execution.

Motivated Vigilance Task

As in Experiment 1, the task started with an unincentivized baseline run, from which the median RT was extracted as a criterion for the subsequent runs. After this, participants performed two incentivized runs. Trials started with a reward cue indicating the incentive condition for that trial (**Figure 2A**). On gain trials, participants could win 10¢ if they responded faster than the criterion. On loss trials, they would lose 10¢ for responses slower than the criterion. On neutral trials, no incentives were given. Gain, loss, and neutral trials were pseudo-randomly intermixed, such that approximately equal numbers of trials from each condition were presented throughout the runs, and no more than three consecutive trials of the same incentive condition were presented. Participants completed two incentivized runs amounting to a total of approximately 60 trials per incentive condition.

Effort Discounting Task

The discounting task followed the same procedure as in Experiment 1, except that gain and loss trials were randomly intermixed (**Figure 2F**). While gain and loss trials were presented in intermixed fashion, adjusting staircase procedures updated the values for the gain and loss condition separately from trial to trial. Therefore, a separate set of indifference points was derived for gain and loss-framed decisions. The staircase procedure was repeated twice. Resulting indifference points were averaged for each effort level and incentive condition. As in Experiment 1, the discounting task was followed by the execution of one randomly drawn trial (see **Supplementary Materials** for full instructions).

Results

Motivated Vigilance Task

Comparing response speed for gain, loss and neutral trials showed that there was a significant incentive effect (see **Figure 2B**; $F_{(2,58)} = 14.23$, $p < 0.001$), with responses faster in gain and loss trials compared to neutral trials (gain: $t_{(29)} = -3.786$, $p < 0.001$; loss: $t_{(29)} = -3.781$, $p < 0.001$), but no difference between gain and loss trials ($t_{(29)} = -0.349$, $p = 0.729$). In the gain condition 56.96% (±12.21%) responses were faster than criterion vs. 58.33% (±12.71%) in the loss condition ($t_{(29)} = -0.739$, $p = 0.466$). Eight participants did not have sufficient pupillometry data and were excluded from analysis. The remaining 22 subjects all had at least 23 trials with valid pupillometry data per incentive condition (see **Figure 2D**). Comparing pre-stimulus pupil diameter between incentive conditions showed that, there was a significant effect for incentive on pre-stimulus pupil diameter ($F_{(2,42)} = 5.67$, $p = 0.007$), with larger pupil size for gain and loss trials, compared to neutral trials (gain: $t_{(21)} = -2.187$, $p = 0.044$; loss: $t_{(21)} = -2.928$, $p = 0.008$), but no difference between gain and loss trials ($t_{(29)} = -0.814$, $p = 0.425$).

Time-on-Task effects were analyzed by calculating linear slope coefficients for each incentive condition in each run. As in Experiment 1, response speed and pupil diameter reduced over time-on-task (see **Figures 2C,E**), but there were no significant difference between incentive conditions (Run1 performance: $F_{(2,58)} = 0.744$, $p = 0.480$; Run1 pupil: $F_{(2,42)} = 0.616$, $p = 0.545$; Run2 performance: $F_{(2,58)} = 0.038$, $p = 0.962$; Run2 pupil: $F_{(2,42)} = 1.21$, $p = 0.306$).

Effort Discounting Task

Rewards were discounted with longer task durations (higher effort; see **Figure 2G**). Replicating Experiment 1, AUC was higher for loss compared to gain choices, indicating that participants discounted less strongly for losses than gains ($t_{(29)} = -3.434$, $p = 0.0018$; see **Figure 2H**).

Discussion

Results from Experiment 2 fully replicated Experiment 1. During the performance of a vigilance task, both gain and loss

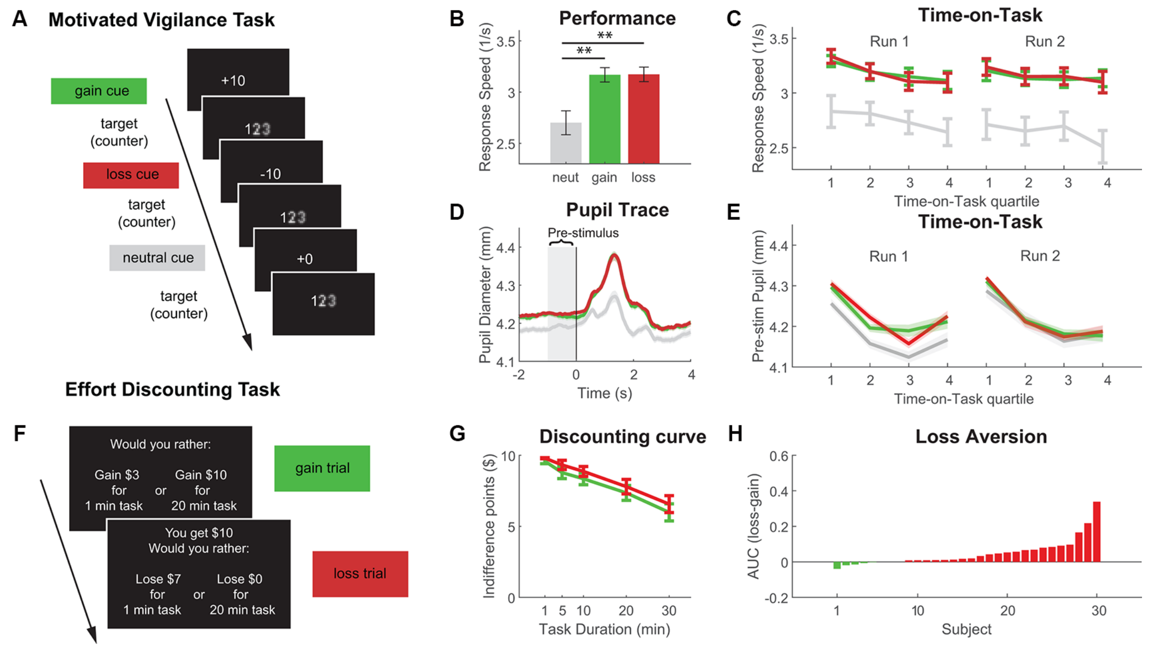

FIGURE 2 | Results from Experiment 2 with **(A)** schematic of the Motivated Vigilance Task, **(B)** response speed in the vigilance task for baseline, gain and loss conditions, **(C)** Time-on-Task decline of response speed (Time-on-Task quartiles for illustrative purposes, statistical analysis was based on linear slopes), **(D)** target-locked pupil trace in the vigilance task (time = 0 indicates target presentation), **(E)** Time-on-Task decline of pre-stimulus pupil diameter (Time-on-Task quartiles for illustrative purposes only, statistical analysis was based on linear slopes), **(F)** example trials of the effort-discounting task, **(G)** effort-discounting curve, and **(H)** loss-gain difference in the area under the discounting curve (AUC; positive difference scores denote less discounting for loss vs. gain choices). $^{**}p < 0.01$.

incentives motivated higher effort exertion (performance and pupil diameter) compared to neutral, unincentivized trials. There was no difference between gain and loss trials, however. In contrast, participants did show loss aversion in the discounting task, as they were more willing to engage in further task performance if choices were framed as losses compared to gains. Importantly, as gain and loss trials were intermixed, these results could not be due to the influence of order effects. This demonstrates the robustness of the effects within the context of sustained attention. To further extend our findings to a different cognitive domain (working memory), we conducted a third experiment.

EXPERIMENT 3

As cognitive tasks generally require mental effort, it is important to explore whether our findings about sustained attention extend to other domains. Working memory has been studied previously in the context of cognitive effort. A higher working memory load is experienced as more effortful (Bijleveld, 2018), and is associated with physiological and neural signs of increased effort (Kahneman and Beatty, 1966; Jansma et al., 2007; Richter et al., 2008), and effort-discounting (Westbrook et al., 2013, 2019). In this experiment, we examined whether effort allocation in the N-Back task would be differentially affected by gains and losses. Paralleling Experiments 1 and 2, we tested this both in the context of cognitive performance, and effort-based decision making. Since a larger number of N-Back levels needed to be sampled (1–4-Back), the N-Back performance and decision-making tasks were tested in two separate sub-experiments (Experiments 3a and 3b).

Methods

Motivated N-Back Task (Experiment 3a)

Thirty-two participants were recruited for this experiment [mean age (stdev) = 23.16 (3.27), 16 females]. Participants performed an N-Back task under four different levels of memory load (1, 2, 3, 4-Back; see **Figure 3A**). Participants were presented with a series of letter stimuli (1-s presentation, 3-s ISI), and had to respond with a target button press if the current letter matched the letter that was presented N positions before the current stimulus. If the current letter did not match the letter N positions back, a non-target button press was required. Each task run consisted of 64 stimuli, 16 of which were targets. The experiment started with a practice phase, in which all levels of N-Back were trained to criterion (>50% correct responses). Subsequently, participants performed two incentivized runs (gain and loss, order counter-balanced) for all N-Back levels. In the gain run, they could earn 2¢ for each correct non-target response and 6¢ for each correct target response. In the loss run, they received $2, and would lose 2¢ for each incorrect non-target response (or non-response), and lose 6¢ for each incorrect target response (or non-response). Given the target/non-target ratio, this incentive scheme neither biased towards more target nor non-target responses. Furthermore, a subjectively experienced effort was assessed after each incentivized run *via* a assessed after each incentivized run *via* a self-report scale (NASA-TLX).

Effort Discounting Task (Experiment 3b)

Thirty independent participants were recruited [mean age (stdev) = 22.53 (3.47), 16 females]. As in Experiment 3a, participants first completed a practice phase for all N-Back levels, after which the discounting task was performed (see **Figure 3F**). Participants were presented with a series of choice trials in which they were given the option between a lower variable amount of money in return for performing a low effort 1-Back, or a higher reward for performing a higher level N-Back (2, 3, 4-Back). In gain trials, higher rewards were fixed at $10, and lower rewards were variable between $0 and $10. In loss trials, participants were first instructed that they could receive $10 and that they would lose money for performing the low effort 1-Back, or lose $0 for performing the higher effort N-Back. Gain and loss trials were intermixed, and the monetary amount was dynamically updated following separate adjusting staircase procedures. Upon completion of all choice trials, one choice was randomly drawn for execution. Participants performed the chosen level of the N-Back task for a fixed duration of 15 min and received the associated reward. As in Experiments 1 and 2, the reward was not dependent on performance levels, but participants were instructed that they had to maintain effort throughout (see **Supplementary Materials** for full instructions).

Results

Motivated N-Back Task (Experiment 3a)

A repeated-measures ANOVA with Effort Level (1, 2, 3, 4-Back), and Incentive Condition (Gain, Loss) yielded a significant main effect of Effort Level ($F_{(3,93)} = 83.28$, $p < 0.001$) on detection sensitivity (d-prime), but no main effect of Incentive Condition ($F_{(1,31)} = 0.997$, $p = 0.326$). Furthermore, there was a significant Effort Level × Incentive Condition interaction ($F_{(3,93)} = 2.825$, $p = 0.043$; see **Figure 3B**). Further deconstruction of this interaction showed no differences between gain and loss in detection sensitivity for the 1-Back ($t_{(31)} = 0.192$, $p = 0.849$), 2-Back ($t_{(31)} = 1.93$, $p = 0.063$), and 3-Back levels ($t_{(31)} = -1.38$, $p = 0.178$). However, for the 4-Back level, d-prime was significantly higher for the loss condition compared with the gain condition ($t_{(31)} = -2.21$, $p = 0.034$). Signal detection bias, on the other hand, increased with higher N-Back levels ($F_{(3,93)} = 45.78$, $p < 0.001$; see **Figure 3C**), with no difference between incentive conditions ($F_{(1,31)} = 0.392$, $p = 0.536$). Although bias was numerically higher in the Gain condition compared to the Loss for 4-Back condition, the Level × Incentive interaction did not reach significance ($F_{(3,93)} = 2.371$, $p = 0.076$). The increase in detection sensitivity at 4-Back level was primarily due to an increased hit rate for the loss condition (mean = 0.68, stdev = 0.18), compared to the gain condition (mean = 0.60, stdev = 0.20; $t_{(31)} = -2.56$, $p = 0.016$; see **Figure 3D**), but no difference in false alarm rate (gain: mean = 0.08, stdev = 0.097; loss: mean = 0.07, stdev = 0.067; $t_{(31)} = 0.688$, $p = 0.497$; see **Figure 3E**). Subjective effort did increase with higher N-Back levels ($F_{(3,87)} = 22.81$, $p < 0.001$), but not with incentive condition (main-effect: $F_{(1,29)} = 1.29$, $p = 0.265$; interaction: $F_{(3,87)} = 0.41$ $p = 0.742$).

Effort Discounting Task (Experiment 3b)

For decision making, reward value was discounted when higher levels of effort were required (higher N-Back levels; see **Figure 3G**. Furthermore, effort discounting was more pronounced for gain-framed decisions than loss-framed decisions ($t_{(29)} = -3.091$, $p = 0.004$; see **Figure 3H**), indicating robust loss aversion in effort-based decision-making.

Discussion

Results from Experiment 3 replicated and extended findings in Experiments 1 and 2. In particular, participants were more willing to invest cognitive effort when decisions were framed as losses, rather than gains. Central to the aims of Experiment 3, the effort was operationalized as working memory load on an N-Back task. This indicates that the influence of loss framing on effort-based decision making generalizes across different cognitive domains (i.e., sustained attention and working memory). Results from Experiment 3a showed that loss incentives led to better cognitive performance at the highest effort level of the N-Back task (4-Back). At other N-Back levels, detection sensitivity was similar in the gain and loss conditions.

COMPUTATIONAL MODELING

To characterize the shape of the discounting function underlying the choice data, five different discounting functions were fit to the individual choice data (see **Figure 4A**; hyperbolic, exponential, linear quadratic and sigmoid; Klein-Flügge et al., 2016; see **Supplementary Materials** for analysis details). Comparison of model fit indicated that in all three experiments the choice data were best modeled by a quadratic discounting function (see **Figure 4B**; Hartmann et al., 2013; Chong et al., 2016; Chen et al., 2020), both in the gain and in the loss conditions (see **Figures 4C–H**). Resulting discounting parameters (k) were compared between Gain and Loss conditions (square root transformed to correct for non-normality). Although average discounting rates were higher in the Gain compared to the Loss condition in all Experiments, this difference did not reach significance for Experiment 1 ($t_{(29)} = 1.14$, $p = 0.265$) and Experiment 2 ($t_{(29)} = 1.77$, $p = 0.088$). In Experiment 3b, however the Gain-Loss difference was significant ($t_{(29)} = 2.357$, $p = 0.025$). Moreover, when combining the samples across all experiments a significant Gain-Loss difference was confirmed ($t_{(89)} = 2.645$, $p = 0.0097$).

GENERAL DISCUSSION

We found that losses motivate cognitive effort expenditure more strongly than gains during decision-making. Loss aversion was consistently observed in all three effort-based decision-making experiments. Participants were more willing to invest effort when avoiding losses compared to when equivalent outcomes were

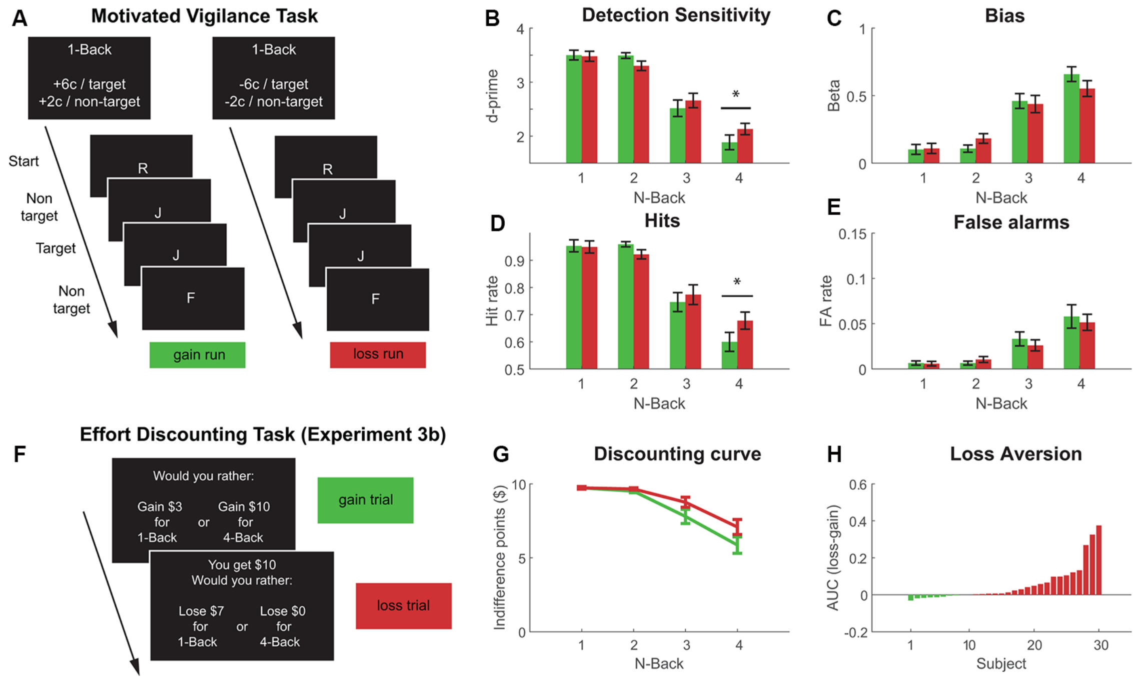

FIGURE 3 | Results from Experiments 3a and 3b with **(A)** schematic of the incentivized N-Back task in Experiment3a, **(B)** detection sensitivity (d-prime) in the N-Back task for gain and loss conditions, **(C)** detection bias (beta), **(D)** hit rate, **(E)** false alarm rate, **(F)** example trials in the Effort Discounting Task in Experiment 3b **(G)** effort-discounting indifference points and **(H)** loss-gain difference in the area under the discounting curve (AUC; positive difference scores denote less discounting for loss vs. gain choices). $^*p < 0.05$.

framed as gains. This loss aversion effect may be dependent on the cognitive domain or the level of effort required.

Effort-Based Decision Making Is Influenced by Loss Aversion

The first main finding of this study was that participants discounted loss-framed outcomes less than gain-framed outcomes. Individuals were willing to exert more effort to fend off a loss than to gain a reward. This loss aversion effect was present across cognitive domains (sustained attention and working memory), underlining the robustness of this effect. These results further expand the scope of loss aversion effects from risky and intertemporal decision making to effort-based choice. Only a few previous studies have explored the effects of loss aversion in effort-based decision-making. One study found that, in agreement with the current findings, people were more willing to invest the physical effort to avoid losses, compared to pursuing gains (Chen et al., 2020). Other studies, however, did not find such asymmetry (Nishiyama, 2016; Lockwood et al., 2017) or only in some populations (i.e., elderly, Byrne and Ghaiumy Anaraky, 2019). Importantly, the current effects were not confounded by delay or probability discounting, as these factors were strictly controlled. Moreover, computational modeling demonstrated that individual choice patterns were the best fit by a parabolic discounting function which has specifically associated with effort-discounting in previous studies (Hartmann et al., 2013; Chen et al., 2020).

Losses Enhance Working Memory Performance Only at a High Cognitive Load

The effect of loss aversion effect on performance, however, was different for the sustained attention task vs. the working memory task. In Experiments 1 and 2, there was no difference in sustained attention performance for losses compared to gains. Concurrent pupillometry also showed no indications of higher effort in loss blocks (Experiment 1), or on loss trials (Experiment 2) compared to gains. In Experiment 3 on the other hand, losses were associated with better working memory performance only at the highest effort level (4-Back). These mixed findings concur with previous studies, some of which found no difference in performance between gain and loss conditions in a 3-Back task (Belayachi et al., 2015), while other studies found that loss incentives could even impair performance on other tasks (switch task, Stroop task, flanker task; Paschke et al., 2015; Carsten et al., 2019; Cubillo et al., 2019). Possibly, the effects of loss incentives may depend on the nature of the task (e.g., differentially affecting proactive vs. reactive control processes; Chiew and Braver, 2013; Botvinick and Braver, 2015).

Alternatively, the effects of loss aversion may only show at higher levels of effort. In Experiment 3a, working memory performance was not different between the gain and loss conditions on the lower effort levels (1–3-Back). Only at the

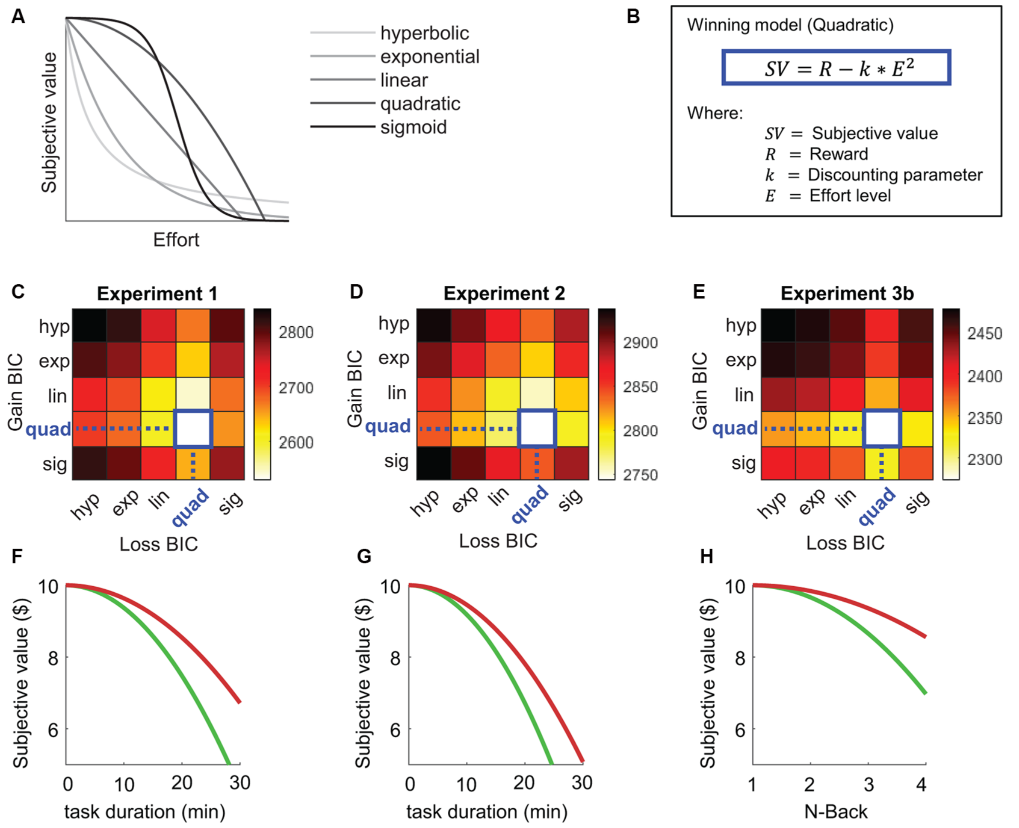

FIGURE 4 | Computational modeling results with **(A)** illustration of different discounting models, **(B)** winning model (Quadratic), **(C–E)** model comparison using Bayesian Information Criterion (BIC) in Experiments 1, 2 and 3b, and **(F–H)** average discounting curves for Gain (green) and Loss (red) framing conditions in Experiments 1, 2 and 3b.

highest effort level (4-Back) was performance enhanced for the loss compared to the gain condition. It is, therefore, possible that higher effort levels need to be probed before differential effects of gains and losses become apparent. Future studies could further explore the contributions of task type and effort level on the manifestation of loss aversion in cognitive performance.

Conclusion

In total, this study shows that individuals are willing to invest more cognitive effort to avoid losses, compared to obtaining gains when making effort-based decisions. The effect of loss aversion effect on performance, however, may depend on the cognitive domain and/or task difficulty.

DATA AVAILABILITY STATEMENT

All data and code are available through the Open Science Framework: https://osf.io/fy9ms/.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by National University of Singapore Institutional Review Board. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

SM designed the study, analyzed the data, and wrote the initial manuscript. ZP and CC programmed the experimental scripts, collected and analyzed the data, and edited the manuscript. MC was responsible for funding and revision of the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnhum.2020.00287/full#supplementary-material.

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Resting-State Connectivity of Auditory and Reward Systems in Alzheimer's Disease and Mild Cognitive Impairment

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Music-based interventions (MBI) have become increasingly widely adopted for dementia and related disorders. Previous research shows that music engages reward-related regions through functional connectivity with the auditory system, but evidence for the effectiveness of MBI is mixed in older adults with mild cognitive impairment (MCI) and Alzheimer's disease (AD). This underscores the need for a unified mechanistic understanding to motivate MBIs. The main objective of the present study is to characterize the intrinsic connectivity of the auditory and reward systems in healthy aging individuals with MCI, and those with AD. Using resting-state fMRI data from the Alzheimer's Database Neuroimaging Initiative, we tested resting-state functional connectivity within and between auditory and reward systems in older adults with MCI, AD, and age-matched healthy controls ($N = 105$). Seed-based correlations were assessed from regions of interest (ROIs) in the auditory network (i.e., anterior superior temporal gyrus, posterior superior temporal gyrus, Heschl's Gyrus), and the reward network (i.e., nucleus accumbens, caudate, putamen, and orbitofrontal cortex). AD individuals were lower in both within-network and between-network functional connectivity in the auditory network and reward networks compared to MCI and controls. Furthermore, graph theory analyses showed that the MCI group had higher clustering and local efficiency than both AD and control groups, whereas AD individuals had lower betweenness centrality than MCI and control groups. Together, the auditory and reward systems show preserved within- and between-network connectivity in MCI individuals relative to AD. These results motivate future music-based interventions in individuals with MCI due to the preservation of functional connectivity within and between auditory and reward networks at that initial stage of neurodegeneration.

Keywords: resting-state fMRI, auditory, reward, dementia, Alzheimer's disease, mild cognitive impairment

INTRODUCTION

Alzheimer's disease (AD) is a severe and rapidly increasing problem, with over 5 million Americans suffering from this illness. Individuals with AD manifest variable but significant impairments in multiple cognitive, functional, and behavioral domains, including changes in mood and anxiety as well as the loss of memory and executive functions, which together affect activities of daily living (Marshall et al., 2011). While AD affects 10% of adults over age 65, an additional 15–20% of people above age 65 have mild cognitive impairment (MCI). MCI is defined as a noticeable decrement in cognitive functioning that goes beyond normal changes seen in aging and may progress to dementia (Petersen et al., 2009). Individuals with Amnestic MCI are at the highest risk of developing AD (Petersen et al., 2009). Because of this increased risk, early intervention is most likely to affect the temporal cascade of subsequent effects that lead to dementia (Vega and Newhouse, 2014).

In recent years, music-based interventions (MBIs) have become increasingly adopted for patients with AD and related disorders. Several randomized controlled trials have shown positive results in the effect of receptive MBIs on alleviating symptoms of cognitive decline, especially in improving mood and reducing stress when listening to familiar music. However, findings to date have been mixed—partly because of variability between subjects, small sample size, and because of differences between intervention protocols across studies (Vink and Hanser, 2018). Part of the challenge in understanding MBIs in neurodegenerative disease is that we do not yet know the influence of cognitive decline on brain networks that are involved in music processing. Advancing this knowledge could help researchers target more precisely when and how to administer MBIs and music therapy.

To date, the best available evidence suggests that music listening may motivate behavior through interactions between brain networks necessary for auditory predictions (such as predictions for melody, harmony, and rhythm) and the brain's reward system. The auditory system is organized in subdivisions and processing streams that include cortical as well as subcortical regions. Cortical regions include bilateral Heschl's and superior temporal gyri, but also extend towards superior temporal sulci and middle temporal gyri (Kaas and Hackett, 2000). Lesions to the right auditory cortex, encroaching into the right Heschl's gyrus, results in perceptual deficits in perceiving pitch, while left temporal-lobe damage affects behavioral tasks that involve fine-grained temporal discrimination (Zatorre et al., 2002). There is abundant evidence showing that listening to music that we enjoy engages the dopaminergic reward system, indicating that rewarding music has similar properties to other rewarding experiences such as monetary gain and social stimulation (Salimpoor et al., 2013; Ferreri et al., 2019; Gold et al., 2019). When listening to personally pleasurable music, task fMRI has shown that cortical structures in the superior temporal lobe, which constitute an auditory brain network, are correlated in activity with areas in the reward system centering around the ventral striatum (Salimpoor et al., 2013; Martínez-Molina et al., 2016; Gold et al., 2019). Findings from structural neuroimaging have linked white matter connectivity between auditory and reward-related areas, specifically the posterior superior temporal gyrus to the anterior insula and ventromedial prefrontal cortex (vmPFC), to individual differences in reward sensitivity to music (Sachs et al., 2016; Loui et al., 2017; Martínez-Molina et al., 2019). These findings suggest that there is a neuroanatomical network that is known to be involved in deriving rewards from music listening (Belfi and Loui, 2020). Altogether, these two networks are well associated with behavioral data supporting their roles in the emotional processing of music.

In contrast to the structural neuroimaging and task neuroimaging literature, less is known about the intrinsic functional connectivity of the auditory and reward systems, and even less is known about how these patterns of intrinsic functional connectivity may vary in different stages of neurodegeneration. In a landmark study, Jacobsen et al. (2015) compared the brain activity of young adults listening to familiar and unfamiliar music in functional Magnetic Resonance Imaging (fMRI) and found that a specific region within the anterior cingulate cortex (ACC) was more active when listening to familiar music, likely part of the auditory prediction network. The authors then analyzed PET data of essential AD biomarkers in a region of interest derived from musical memory findings which included the caudal ACC and ventral pre-supplementary motor area. They showed that this musical memory region was relatively spared in AD, with minimal cortical atrophy and minimal disruption of glucose metabolism. These findings support the potential efficacy of MBIs in engaging these relatively preserved brain regions in individuals with AD. Overall, these findings raise the intriguing possibility that music processing might engage brain networks that are relatively spared in neurodegeneration. However, the fMRI results from music listening in this study were obtained from a healthy group of young adults. Thus, results could be explained by intrinsic differences between the different age groups rather than by the specific effects of music *per se*.

Another study specifically conducted resting-state fMRI (rsfMRI) and task fMRI during music listening in the same group of AD patients. King et al. (2019) showed that after listening to familiar music, patients with AD had increased functional connectivity in multiple regions including the default mode network (DMN) as well as the auditory and reward networks. The DMN is a resting state network that is involved in autobiographical memory, mind-wandering, and stimulus-independent thought, and has become a subject of intense interest especially as its connectivity is disrupted in AD (Greicius et al., 2004). Listening to familiar music has been associated with increased connectivity within the DMN, suggesting that music may aid autobiographical memory, a hypothesized role of the DMN (Kay et al., 2012). In this regard, the DMN may also play a role in enhancing the effects of music-based interventions through the activations of autobiographical memories by music listening. While these results provide strong evidence for the use of familiar music in music-based interventions, it remains unclear to what extent these differences in brain connectivity relate to symptom severity and stage of illness in AD. Taken together, it is clear that understanding the intrinsic functional connectivity of the auditory and reward systems, their connectivity to other areas such as the DMN, and how they change in the aging brain and in different clinical stages of AD may shed light on how and why music listening could help dementia and promote healthy aging.

The study of intrinsic functional brain networks is aided by recent developments in open science and open data sharing initiatives. The Alzheimer's Disease Neuroimaging Initiative (ADNI) is a multicenter project that shares neuroimaging data from patients with AD, patients with MCI, and older adult controls (Jack et al., 2008). Data from ADNI offer a starting point from which to investigate intrinsic functional networks at different stages of cognitive decline. The overarching goals of the ADNI study are: (1) to detect AD at the earliest possible stage (pre-dementia) and identify ways to track the disease's progression with biomarkers; (2) to support advances in AD intervention, prevention, and treatment through the application of new diagnostic methods at the earliest possible stages (when intervention may be most effective); and (3) to continually administer ADNI's innovative data-access policy, which provides all data without embargo to all scientists in the world.

Here we ask how the auditory and reward systems are intrinsically connected in the healthy older adult brain, and how these connectivity changes at different stages of neurodegeneration. We compare resting-state networks of three age-matched groups: AD patients, MCI patients, and healthy controls (CN). We identify networks of regions with known roles in auditory prediction and reward and use them as seed regions of interest (ROIs) to compare the three groups in seed-based connectivity across the brain, in whole-brain second-level contrasts to assess between-group differences in resting-state functional connectivity, and in ROI-to-ROI connectivity within and across brain networks. Finally, we apply measures from graph theory to describe the complex network properties of the auditory and reward systems and to see how these networks change in different stages of dementia. Although data on responsiveness to MBI are not available in the ADNI dataset, we hope that the results from our analyses will inform future MBIs by characterizing the requisite auditory and reward networks and their trajectory in neurodegenerative disease.

MATERIALS AND METHODS

Sample

We used open-source data from ADNI (Jack et al., 2008). From the available data, we limited our sample to patients who had magnetization-prepared, rapid-acquisition, gradient echo (MPRAGE) and rsfMRI scans that were free of artifacts, both of which met the specific scan parameters listed in the Procedures: MRI Acquisition. This resulted in 105 older adults (ages 55–90) matched in age and gender that were selected from the ADNI study set. In the Control group ($N = 47$), ages ranged from 56 to 86, with 27 females; in the MCI group ($N = 47$), ages ranged from 56 to 88, with 27 females; and in the AD group ($N = 11$), ages ranged from 55 to 86, with three females. The smaller sample of AD patients is due to lower data quality because of movement or noise artifacts from the available data. For each individual, two types of data were extracted for use in data analysis: structural MRI (MPRAGE) and functional MRI (fMRI).

Procedures

MRI Acquisition

High-resolution T1 and resting-state images were acquired in a 3T SIEMENS scanner at multiple locations in the United States and Canada. The anatomical images were acquired using a T1-weighted, 3D, MPRAGE volume acquisition with a voxel resolution of $0.8 \times 0.8 \times 0.8$ mm^3 (TR = 2.3 s, TE = 2.95 ms, flip angle = 9°, Matrix X = 240 pixels, Matrix Y = 256 pixels, Matrix Z = 176 pixels, Mfg Model = Prisma_fit, Pulse Sequence = GR/IR, Slice Thickness = 1.2 mm).

Resting-state MRI was acquired as 197 contiguous echo-planar imaging (EPI) functional volumes, totaling to 9.85 min of resting-state fMRI data acquired from each subject (TR = 3 s; TE = 30 ms; flip angle = 90°; acquisition voxel size = $3.4375 \times 3.4375 \times 3.4375$ mm^3). Participants kept their eyes open during resting-state data acquisition.

MRI Preprocessing

Structural and functional MRI preprocessing were carried out with the CONN Toolbox[1] (Whitfield-Gabrieli and Nieto-Castanon, 2012). In order, this consisted of functional realignment and unwarp (subject motion estimation and correction); functional centering to (0, 0, 0) coordinates (translation); functional slice-timing correction; functional outlier detection [Artifact Detection and Removal Tool (ART)-based identification of outlier scans for scrubbing]; functional direct segmentation and normalization (simultaneous grey/white/cerebrospinal fluid segmentation and Montreal Neurological Institute normalization); functional smoothing (spatial convolution with 8 mm Gaussian kernel); structural center to (0, 0, 0) coordinates (translation); structural segmentation and normalization (simultaneous grey/white/CSF segmentation and MNI normalization). An interleaved slice order was used for Siemens scans, intermediate settings (97th percentiles in normative samples), a global-signal z-value threshold of 9, subject-motion mm threshold of 2, structural target resolution of 1 mm, functionals target resolution of 3.4375 mm, and a bounding box of (90 −126 −72; 90 90 108) mm. Denoising steps for functional connectivity analysis included corrections for confounding effects of white matter and cerebrospinal fluid (Behazdi et al., 2007), and bandpass filtering to 0.008–0.09 Hz, which are the default values in CONN (Whitfield-Gabrieli and Nieto-Castanon, 2012).

Regions of Interest (ROIs) Selection

When choosing the ROIs for seed-based connectivity measures, we chose ROIs from the CONN default atlas (Whitfield-Gabrieli and Nieto-Castanon, 2012) which contains 185 ROIs and 32 networks. We selected 18 ROIs as auditory cortex regions based on previous literature which included all ROIs in the superior, middle, and inferior temporal lobes (Kaas and Hackett, 2000; Rauschecker and Tian, 2000): right anterior Superior Temporal Gyrus (aSTGR), left anterior Superior Temporal

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[1] http://www.nitrc.org/projects/conn

Gyrus (pSTGR), right posterior Superior Temporal Gyrus (pSTGR), left posterior Superior Temporal Gyrus (pSTGL), right anterior Middle Temporal Gyrus (aMTGR), left anterior Middle Temporal Gyrus (aMTGL), right posterior Middle Temporal Gyrus (pMTGR), left posterior Middle Temporal Gyrus (pMTGL), right temporooccipital Middle Temporal Gyrus (toMTGR), left temporooccipital Middle Temporal Gyrus (toMTGL), right anterior Inferior Temporal Gyrus (aITGR), left anterior Inferior Temporal Gyrus (aITGL), right posterior Inferior Temporal Gyrus (pITGR), left posterior Inferior Temporal Gyrus (pITGL), right temporooccipital Inferior Temporal Gyrus (toITGR), left temporooccipital Inferior Temporal Gyrus (toITGL), right Heschl's Gyrus (HGR), and left Heschl's Gyrus (HGL).

Then, we selected 18 ROIs as valuation and reward-related regions based on the previous literature (Belfi and Loui, 2020): right Insular Cortex (InsulaR), left Insular Cortex (InsulaL), Anterior Cingulate Gyrus (AC), Posterior Cingulate Gyrus (PC), right Frontal Orbital Cortex (FOrbR), left Frontal Orbital Cortex (FOrbL), right Caudate (CaudateR), left Caudate (CaudateL), right Putamen (PutamenR), left Putamen (PutamenL), right Pallidum (PallidumR), left Pallidum (PallidumL), right Hippocampus (HippocampusR), left Hippocampus (HippocampusL), right Amygdala (AmygdalaR), left Amygdala (AmygdalaL), right Accumbens (AccumbensR), left Accumbens (AccumbensL).

Finally, we combined the 18 auditory ROIs into an *Auditory Network*, and the 18 rewards ROIs together into a Reward/Valuation Network (hereafter *Reward Network*). **Figure 1** shows the auditory and reward network ROIs.

Seed-Based Connectivity Analyses

Within-Group Seed-Based Connectivity

Since we were interested in whole-brain connectivity patterns of the auditory and reward networks, we first seeded the auditory and reward networks defined above, and for each group of subjects, we extracted all voxels that were significantly functionally connected (using bivariate correlation) to the seed ROIs at the $p < 0.05$, Family Wise Error corrected level, to examine the connectivity patterns of each network in each group. Slices were chosen at the peak cluster for all three groups.

Between-Group Seed-Based Connectivity

Having identified seed-based connectivity patterns for each group, we then contrasted the three groups pairwise to test for between-group differences in seed-based connectivity from the auditory and reward networks for all pairs (i.e., CN > MCI, MCI > CN, CN > AD, AD > CN, MCI > AD, and AD > MCI). We used $p < 0.05$ family-wise error correction whenever possible. However, in contrasts where FWE correction did not show significant between-group differences in seed-based connectivity, we lowered the threshold to examine the contrasts at the less conservative $p < 0.05$ false discovery rate (FDR) cluster-size corrected level.

ROI-to-ROI Analyses

For pairwise correlations, ROI-to-ROI brain connectomes were created for all three groups that included all 36 ROIs. All significant positive T-values from the seed ROIs were extracted into 36 × 36 matrices.

Graph Theory Analyses

To compare the functional networks between groups, we utilized small-world brain networks which provide a useful approach to the investigation of functional connectivity (Bassett and Bullmore, 2006; Reijneveld et al., 2007; Hagmann et al., 2008; Ginestet and Simmons, 2011). Network analysis using graph theory measures yield powerful information about the community structure of brain regions in different groups of subjects, that cannot be accomplished using conventional measures of functional connectivity. We chose to focus on four graph parameters: clustering coefficients, strengths, betweenness centrality, and local efficiency. These parameters have been used to characterize brain networks and their degeneration in AD (Agosta et al., 2013; Brier et al., 2014; Khazaee et al., 2015). Furthermore, previous studies in music cognition have found these network statistics to be sensitive to musical training and musical aptitude (Loui et al., 2012; Belden et al., 2020). The *clustering coefficient* is a measure of functional segregation, indicating the fraction of neighboring nodes of each node that are also neighbors of each other, i.e., the cliquishness of a node (Watts and Strogatz, 1998). *Strength* is the sum of weights of links connected to each node (Latora and Marchiori, 2001). *Betweenness centrality* is a measure of centrality and denotes the number of shortest paths that pass through a given node (Hagmann et al., 2008). Finally, *local efficiency* is another measure of segregation; it is the inverse of the average shortest distance between each node in a subgraph and reveals the efficiency of each node within the network in transporting information (Ajilore et al., 2014).

Pairwise correlation coefficients (r values) for each of the 36 ROIs from the CONN atlas were extracted for every participant and averaged across each group to compute pairwise correlations and graph theory analyses. First, pairwise correlation matrices were extracted for all 36 ROIs from the CONN atlas, resulting in a 36 × 36 matrix for each participant in each group. These matrices were then analyzed using the Brain Connectivity Toolbox in MATLAB (Rubinov and Sporns, 2010). For each group, a series of proportional thresholds were tested, ranging from 5% to 100% of the overall connections. At each threshold level, the four network statistics were computed for each ROI and then averaged across participants for each group. We show graph theory statistics from thresholds ranging from 0.05 to 1.0 to visually show how group differences persist across a range of correlation thresholds. To avoid issues with multiple comparisons from performing tests at every threshold, we chose a proportional correlation threshold of 45% of the strongest connections for statistical analysis, as this captured a representative pattern of graph theory metrics for each group. To confirm that the variance of graph theory metrics was similar across the three groups (despite the smaller sample size in the AD group), two-sample Kolmogorov–Smirnov tests were used to compare the distributions of graph theory metrics

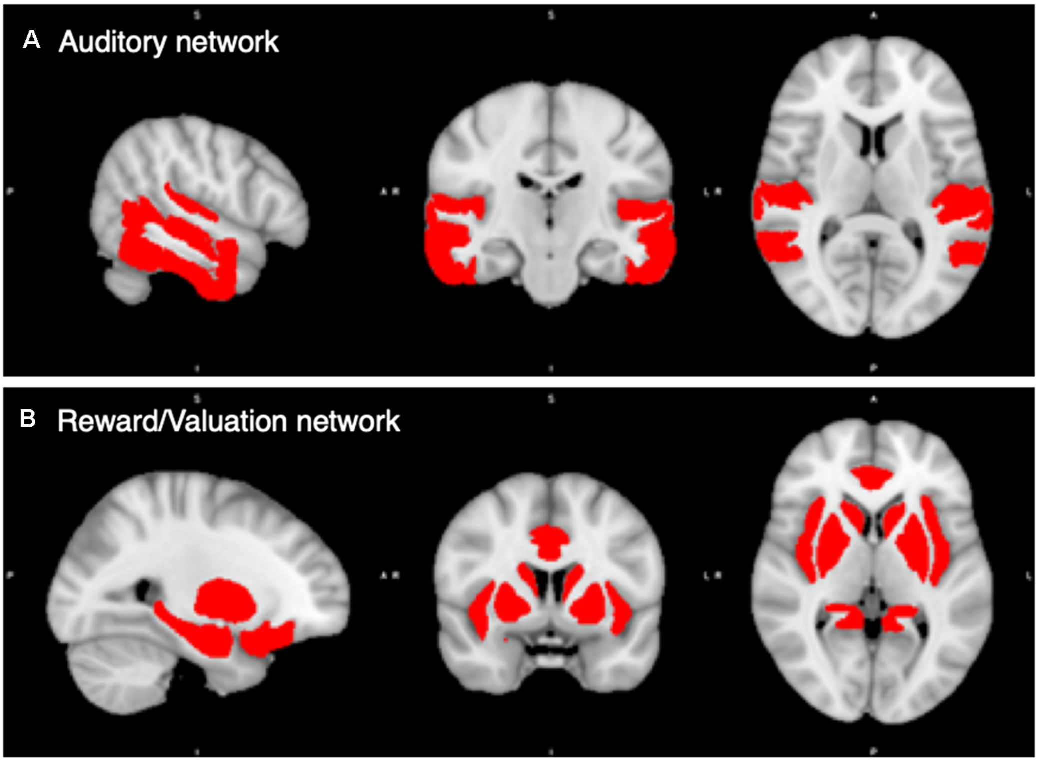

FIGURE 1 | Regions of Interest (ROIs) in the auditory and reward/valuation networks from the CONN Toolbox. **(A)** Compilation of the 18 auditory ROIs from CONN. **(B)** Compilation of the 18 reward ROIs from CONN. See **Supplementary Table S1** for a list of the ROIs used. The Auditory and Reward/Valuation networks in the figure become the two ROIs that we carry the rest of our analysis upon in this article.

between groups. All Kolmogorov–Smirnov tests were not significant (all $p > 0.2$); thus the network statistics did not appear to be differently distributed between groups. These group averages were then compared between groups using one-way ANOVAs to determine group differences in each network measure while correcting for a false-discovery rate of 0.05 for comparisons across the four network measures (Benjamini and Hochberg, 1995).

RESULTS

Seed-Based Connectivity Analyses

Within-Group Seed-Based Connectivity

Seed-based connectivity patterns from the auditory network for each group are shown in **Figure 2**. All groups showed highly significant auditory network functional connectivity to the auditory areas, including the STG, MTG, and ITG, at the $p < 0.05$ FWE-corrected level. The control and MCI groups additionally showed significant functional connectivity in the parietal, occipital, and frontal lobes. The AD group showed less significant functional connectivity than the other two groups, with the significant functional connectivity only observed in the temporal lobe, and not in the other lobes.

Seed-based connectivity from the reward network showed significant functional connectivity within areas of the reward network in all groups at the $p < 0.05$ FWE-corrected level. CN and MCI groups both have significant functional connectivity to the auditory network ROIs including the MTG and ITG, as well as significant overlap in areas that are functionally connected to auditory and reward ROIs in the frontal, parietal, and occipital lobes. In contrast, the AD group did not show connectivity in lateral frontal, parietal, or occipital lobes from the reward network ROIs.

Between-Group Seed-Based Connectivity

From the auditory network seed, between-group comparisons showed higher functional connectivity in the CN group compared to the AD group ($p < 0.05$ FDR cluster-size corrected) in the precuneus. From the reward network seed, between-group comparisons showed higher functional connectivity in the CN group compared to the AD group at the $p < 0.05$ FDR cluster-size corrected level in six regions: the cingulate cortex, the medial prefrontal cortex, the left lingual gyrus, the bilateral fusiform gyri, and superior parietal lobule. No other between-group differences were significant in seed-based connectivity.

ROI-to-ROI Analyses

We further characterized within- and between-network connectivity across the 36 ROIs from the auditory and reward networks. **Figure 3** shows the positive T-values of bivariate correlations between each pair of ROIs in each group. All

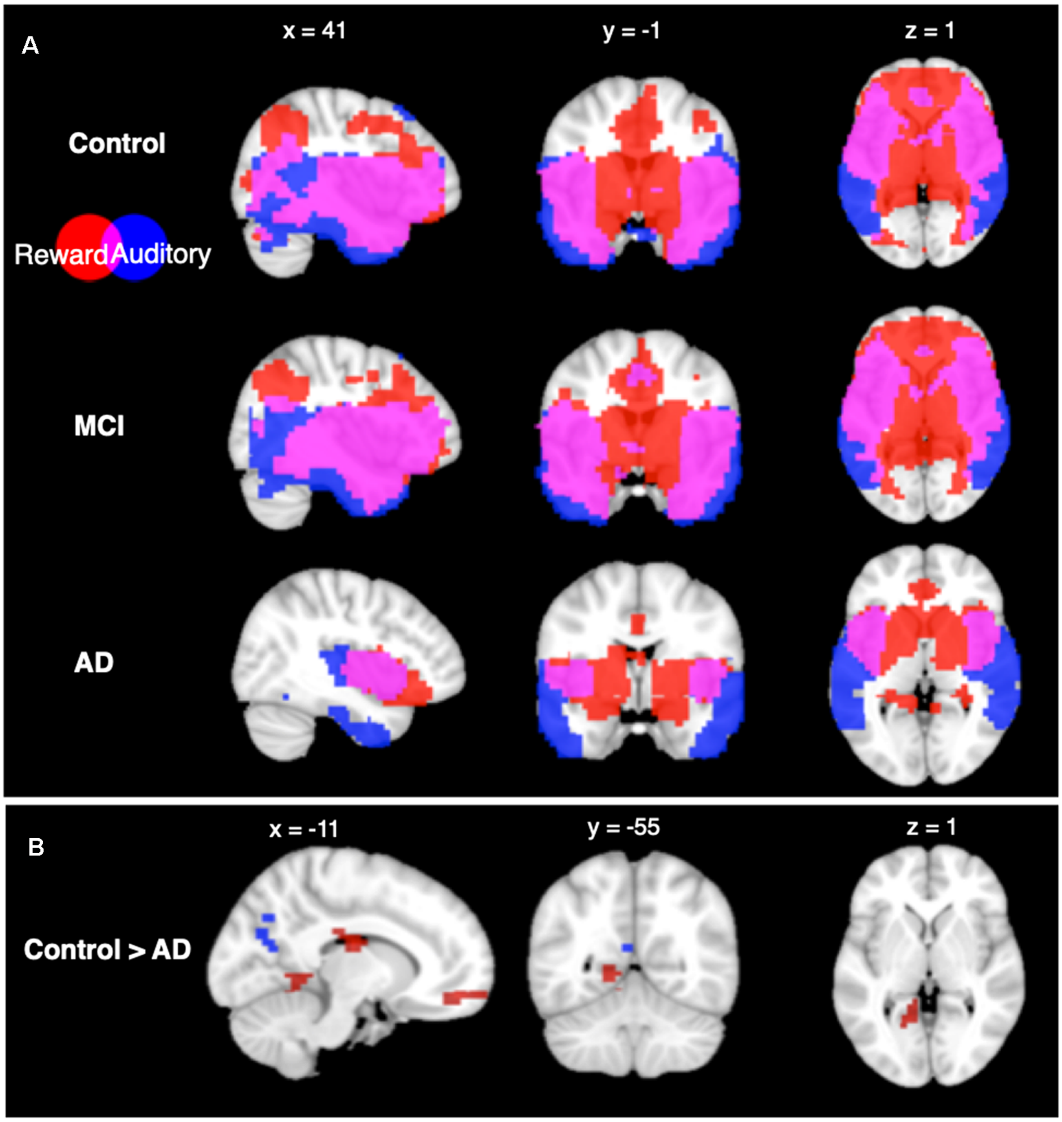

FIGURE 2 | Seed based connectivity analysis. **(A)** Connectivity profiles of Control group (top row), mild cognitive impairment (MCI) group (middle row), and Alzheimer's disease (AD) group (bottom row) for the auditory (blue) and reward (red) networks seed regions ($p < 0.05$, voxel-wise FWE corrected). **(B)** Connectivity profile differences comparing Control and AD groups seeded from auditory (blue) and reward (red) networks [$p < 0.05$, false discovery rate (FDR) cluster-size corrected].

three groups show higher connectivity within each network (auditory-auditory, reward-reward) than between networks (auditory-reward), as shown by higher T values within the diagonal quadrants (which represent auditory-auditory and reward-reward connectivity) than in the off-diagonal quadrants (which represent auditory-reward connectivity). The T-values are generally similar between CN and MCI groups. In contrast, the AD group has lower network connectivity overall.

Graph Theory Analyses

Figure 4 shows graph theory measures for the three groups across a range of proportional thresholds. The main effects of the group were observed at a proportional threshold of 0.45 for betweenness centrality, clustering coefficient, and local efficiency, but not for strengths. Betweenness centrality showed significant group differences ($F_{(2,105)} = 6.01$, $p = 0.0045$, Benjamini-Hochberg corrected, **Figure 4A**), with the AD group showing significantly lower betweenness centrality while CN and MCI individuals did not differ. There was also a main effect of group for clustering coefficient ($F_{(2,105)} = 15.08$, $p = 0.00000175$, Benjamini-Hochberg corrected, **Figure 4B**) and for local efficiency ($F_{(2,105)} = 11.57$, $p = 0.000028$, Benjamini-Hochberg corrected, **Figure 4C**), with the MCI group showing highest clustering and local efficiency, followed by the CN and then AD group. Taken altogether, the MCI group is higher than the CN group in clustering and local efficiency and is

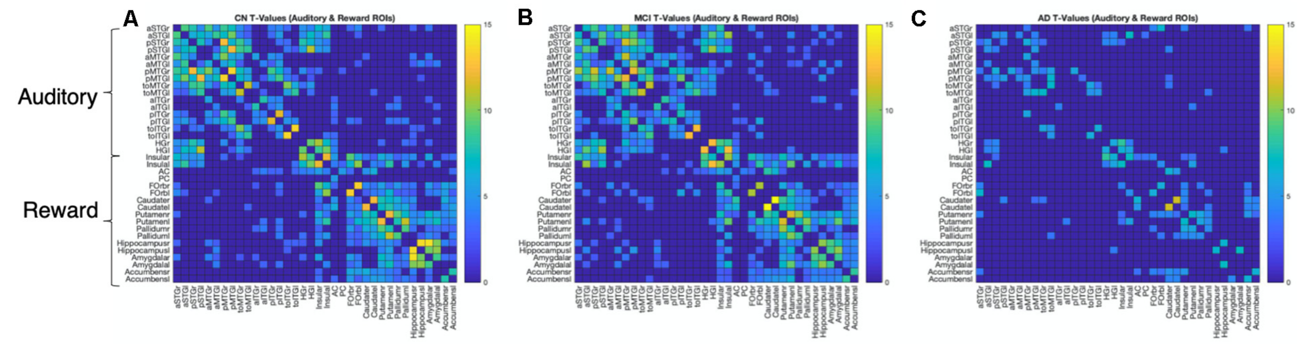

FIGURE 3 | ROI-to-ROI connection matrices and corresponding brain connectomes. **(A)** Control group, **(B)** MCI group, **(C)** AD group showing significant positive correlations ($p < 0.05$, FDR corrected) between the auditory and reward regions. The colors correspond to the strength of the correlation between the two ROIs.

similar to the CN group in betweenness centrality. The AD group is statistically indistinguishable from MCI and CN groups in strengths (**Figure 4D**) while being lower than others in clustering and local efficiency, and much lower than both other groups in betweenness centrality. In summary, the pattern of graph theory results show that MCI individuals are similar or even higher than CN individuals in clustering, local efficiency, and betweenness centrality, and have consistently high clustering and within the reward network relative to controls and AD individuals.

DISCUSSION

Although abundant research supports the interaction between auditory and reward systems in enabling pleasure in music listening, little is known about the intrinsic functional connectivity between the auditory and reward systems. Here, we defined an auditory network and a reward network based on previous studies and characterized their intrinsic functional connectivity using resting-state fMRI from a sample of AD, MCI, and age-matched controls. We found decreased functional connectivity within and between the two systems in AD individuals. These differences are observable in seed-based as well as ROI-to-ROI connectivity, and also in disruptions that affect clustering, local efficiency, and betweenness centrality of the overall network.

Importantly, we observe an overlap between seed-based connectivity patterns from the auditory network and the reward network. This overlap was observed in all three groups, centering around the anterior insula. Notably, there was no overlap among the ROIs chosen as the seed regions of the auditory and reward networks; thus the results are due to similar patterns in functional connectivity between the anterior insula and both the auditory and reward regions. The anterior insula is part of the salience network, which has been posited as a hub that enables alternating between default mode and executive control networks (Menon and Uddin, 2010). The present results extend that previous work by suggesting that the salience network, with the anterior insula at its core, may be key to interactions between large-scale brain systems more generally. This result has important implications. First, it supports the neuroanatomical model for the reward of music listening and music-based interventions, as laid out in Belfi and Loui (2020), which posits that the anterior insula is connected to both auditory and reward systems. This finding is also consistent with lesion mapping studies: cases of acquired musical anhedonia (i.e., the lack of emotional responses to music due to brain injury) mostly have lesions in the anterior insula (Griffiths et al., 2004; Satoh et al., 2011). Thus, the anterior insula seems to be a key region for deriving rewards from music listening.

The AD group showed less functional connectivity from the auditory network to the precuneus, and from the reward network to the cingulate cortex, the medial prefrontal cortex, the left lingual gyrus, the bilateral fusiform gyri, and superior parietal lobule. The precuneus is one of the most metabolically active areas in the brain (Cavanna and Trimble, 2006). The posterior precuneus (which is showing the difference in our study) is associated with episodic memory retrieval in fMRI studies (Cavanna and Trimble, 2006). In this context, the finding of lower auditory-seeded functional connectivity in the precuneus among AD individuals is consistent with less successful episodic memory retrieval in AD. The fact that this reduction is observed from auditory seeds suggests that the decrease in episodic memory retrieval may be specific to auditory access. On the other hand, findings in the precuneus may be more general, relating to the DMN which is disrupted in AD individuals (Greicius et al., 2004; Buckner et al., 2008).

Findings in the reward-seeded connectivity differences between the control group and AD group consisted of the cingulate cortex, the medial prefrontal cortex, the left lingual gyrus, the bilateral fusiform gyri, and superior parietal lobule. The medial prefrontal cortex, bilateral fusiform gyri, and lingual gyrus are also part of the DMN (Buckner et al., 2008; Christoff et al., 2016). The lingual gyrus is also coupled with the DMN as part of the overall brain system involved in mind-wandering or stimulus-independent thought (Christoff et al., 2016) and is also associated with better performance on creativity tasks (Belden et al., 2020). The superior parietal lobule, part of the dorsal attention network (Dixon et al., 2017), is related to memory, especially in music (Klostermann et al., 2009). Taken together, the regions

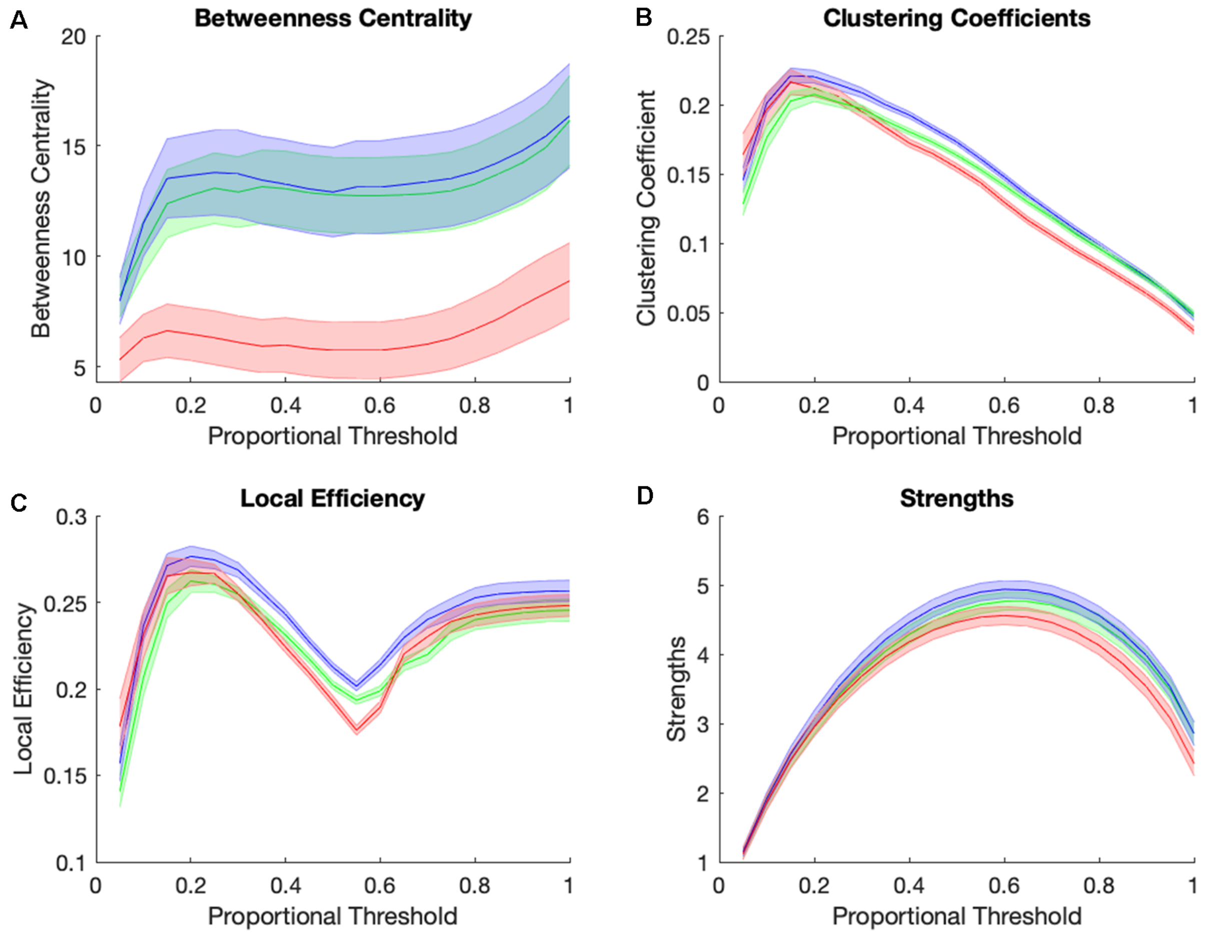

FIGURE 4 | Group differences in small-world brain connectivity. Network measures of betweenness centrality **(A)**, clustering coefficients **(B)**, local efficiency **(C)**, and strengths **(D)** for Control group (green), MCI group (blue), and AD group (red) across a range of proportional thresholds (solid line = mean of all subjects' ROIs for each group, error bar = standard error for all 36 CONN ROI's averaged across subjects for each group).

that are under-connected to the reward network in the AD group are broadly consistent with brain networks associated with memory and stimulus-independent thought. These results are especially relevant in the present context as music-based interventions may draw upon both of these constructs (Hanser and Thompson, 1994).

Relative to AD individuals, MCI individuals show preserved functional connectivity, with no significant between-group differences in auditory-seeded or reward-seeded connectivity patterns from age-matched controls. Graph theory results showed higher degrees, strengths, clustering, and local efficiency in the MCI group than in both the AD and the control groups. Thus, the relationship between dementia severity and network connectedness appears to follow an inverse u-shaped curve, with the slightly impaired MCI group showing the strongest and most efficient connections across all the ROIs of the auditory and reward networks. This is different from previous findings in graph theory analysis of resting-state networks of MCI, AD, and CN groups (Seo et al., 2013). Using FDG-PET data, previous work has shown lower clustering in both MCI and AD groups compared to the CN group. However, those with very mild AD had lower clustering compared to those with mild AD (Seo et al., 2013). On the other hand, a more recent study found that the small world index, a summary network statistic, was significantly decreased in MCI converters who progressed to AD compared to stable MCI individuals who did not progress to AD (Miraglia et al., 2020). Taken together, the distinctions between MCI and AD may be more fine-grained than are captured in our study. Furthermore, as we were specifically interested in the auditory and reward networks we used only a subset of ROIs that represented these networks rather than ROIs covering the whole brain. Thus, our results should not be interpreted as generalizable towards the whole brain in all MCI individuals, but rather as results of a specific hypothesized network of regions important for deriving rewards from music listening.

In the present study, the finding of higher network statistics in auditory and reward network ROIs among MCI individuals may suggest that auditory and reward regions more readily connect in the MCI brain. This may have important implications for music therapy. As music-based interventions rely on the participants' engagement with music and the activity and connectivity of the reward system are reflective of engagement in music and other domains (Kampe et al., 2001; Tamir and Mitchell, 2012; Salimpoor et al., 2013; Martínez-Molina et al., 2016; Ferreri et al., 2019), the current results may suggest that targeting individuals with MCI can capitalize on the heightened auditory-reward connectivity in MCI, thus offering the best chance for effective intervention.

AD individuals have less functional connectivity overall; however, this may be confounded by the fact that, due to limitations in data quality within the ADNI dataset, we had a smaller sample size of only 11 AD individuals, compared against $n = 47$ in control and MCI groups. Nevertheless, the AD group still shows some preserved overlap between auditory and reward systems in the anterior insula. This finding may also have implications for music-based interventions. Specifically, it may be possible to identify specific experiences that also engage the insula, and tailor music-based interventions to maximize these experiences. For example, the anterior insula has been implicated in specificity for voice processing and has been described as part of a voice-selective cortex (Abrams et al., 2013). Perhaps listening to music with the voice, or even engaging in vocalization in an active music-based intervention, maybe specific ways to tap into the reward system. Since the dopaminergic reward system is crucial for motivating behavior, understanding its connectivity patterns to the rest of the brain, and in different stages of the disease, offers insight into the design of effective interventions for diseases and disorders.

CONCLUSION

We have identified an anatomical model of auditory and reward systems and characterized the functional connectivity within and between these systems in healthy older adults and older adults with MCI and AD. Results inform music-based interventions by highlighting the importance of focusing on the MCI population, as they have the most functional connectivity in their auditory and reward systems.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

PL conceptualized the idea behind this manuscript. DW acquired and preprocessed the behavioral and neuroimaging data, performed data analyses, and wrote the first draft. AB, SH, and MG provided feedback, guidance, and support on the conceptual and technical aspects of the study. All authors revised the manuscript and approved the submission.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnhum.2020.00280/full#supplementary-material.

TABLE S1 | Auditory and reward brain regions and the XYZ-coordinates of their centers of gravity. The 36 ROI's are from the default atlas in the CONN Toolbox (Whitfield-Gabrieli and Nieto-Castanon, 2012). Coordinates in millimeters in the Montreal Neurological Institute space.

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Influence of Reward Motivation on Directed Forgetting in Younger and Older Adults

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An important feature of the memory system is the ability to forget, but aging is associated with declines in the ability to intentionally forget potentially due to declines in cognitive control. Despite cognitive deficits, older adults are sensitive to affective manipulations, such as reward motivation, and reward anticipation can improve older adults' memory performance. The goal of the current studies was to examine the effect of reward motivation on directed remembering and forgetting. Participants were healthy CloudResearch/Turk Prime workers aged 18–35 and 60–85. In Experiment 1, we conducted a typical item-method directed forgetting task using neutral words presented one at a time followed by a to-be-remembered (TBR) or to-be-forgotten (TBF) cue. A recognition memory test followed that included all words from the encoding task, as well as new words. We replicated prior findings of better memory for TBR compared to TBF items, but not typical age-related differences in recognition of TBF items. In Experiments 2–4, we repeated this paradigm except that in the second block of trials, each word was presented with a high ($0.75) or low ($0.01) reward cue indicating the value that could be earned if the item was successfully Remembered or Forgotten (depending on cue). During recognition, correct responses to target items (both TBR and TBF) resulted in the associated reward, but incorrect "old" responses resulted in a loss of $0.50. In three experiments, high rewards led to better memory for younger and older adults compared to low rewards, regardless of the directed cue to remember or forget the word. In Experiments 3 and 4, older adults showed typical deficits in directed forgetting, but this was across reward conditions. For older adults, there was no evidence that including reward motivation improved cognitive control abilities as high value reward anticipation did not improve directed forgetting. Instead, in line with hypotheses, high compared to low value reward anticipation leads to engagement of processes that result in better memory regardless of the TBR or TBF cue, and reward anticipation bolsters memory in a relatively automatic, rather than strategic, fashion that overrides one's ability to cognitively control encoding processes.

Keywords: directed forgetting, reward anticipation, aging, memory, reward motivation

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INTRODUCTION

An important and adaptive feature of the memory system is the ability to forget irrelevant or unwanted information. Forgetting can occur *unintentionally*, due to decay of a memory trace, but there are also circumstances that necessitate *intentional* forgetting—for example, to avoid interference with similar or overlapping information, to update incorrect or missing information in memory with new information, or as an emotion regulation strategy for memories that evoke negative affect. To study intentional forgetting in the lab, directed forgetting paradigms indicate to participants that some stimuli are to-be-remembered (TBR) and other stimuli are to-be-forgotten (TBF) via cues presented after each stimulus presentation (MacLeod, 1998). Aging is associated with well-documented increases in unintentional forgetting (Maylor, 1993), but when older adults are directed to intentionally forget information, they often have difficulty doing so compared to younger adults (Zacks et al., 1996; Titz and Verhaeghen, 2010). The cognitive and neural mechanisms responsible for the directed forgetting effect are hotly debated (Anderson and Hanslmayr, 2014; Aguirre et al., 2017), but a prevailing hypothesis concerning older adults' paradoxical forgetting abilities is that age-related declines in cognitive control lead to reductions in goal-directed memory processes and the inability to inhibit unwanted information which leads to continued encoding of items they have been instructed to forget (Sahakyan et al., 2008; Titz and Verhaeghen, 2010; Gallant et al., 2018). In other words, to intentionally forget, one must engage inhibitory cognitive control and resist goal-irrelevant TBF stimuli, but as we age, the ability to inhibit attention to distracting or unnecessary information declines, thereby leading older adults to remember TBF items to a greater extent than younger adults. Neuroimaging evidence provides additional support for this hypothesis as reduced intentional forgetting in older adults is associated with reduced engagement of frontal lobe inhibitory control regions (Rizio and Dennis, 2014).

While executive function and other cognitive processes are associated with an age-related decline (Salthouse, 2010; Murman, 2015; Salthouse, 2019), affective functioning, such as sensitivity to rewards, is relatively preserved or maintained in healthy aging (Harada et al., 2013; Mather, 2016). In several contexts, older and younger adults show similar activation in the reward network to gain and loss anticipation (Samanez-Larkin et al., 2007; Spaniol et al., 2015; Geddes et al., 2018; Bowen et al., 2020) and gain and loss feedback (Bowen et al., 2019), but valence differences have also been reported in striatal regions that respond robustly to rewarding outcomes compared to loss outcomes (Samanez-Larkin et al., 2007, 2014; Schott et al., 2007; Vink et al., 2015). Memory performance has been shown to be enhanced by high compared to low reward anticipation (Castel et al., 2002; Castel, 2007; Spaniol et al., 2014; Cohen et al., 2016; Bowen et al., 2020), as well as positive feedback (Eppinger et al., 2011; Mather and Schoeke, 2011), in younger as well as older adults.

Reward can enhance older adults' ability to remember, so the critical question in this set of studies is whether it could also improve directed forgetting. One interpretation of the memory findings reported above is that even in older adults who suffer cognitive deficits, intact reward anticipation increases cognitive control over episodic memory formation. When motivated by a reward cue, cognitive control processes are engaged to successfully remember the high- compared to low-value items to a greater extent (see Cohen et al., 2014; Eich and Castel, 2016, for a discussion of this). Neuroimaging evidence supports this idea that reward motivation increases cognitive control due to projections between the ventral tegmental area of the reward network to the prefrontal cortex during reward processing (for a review, see Ferdinand and Czernochowski, 2018). Since cognitive control is thought to underlie older adults' reduced ability to intentionally forget, rewards could potentially increase goal-directed remembering *and* forgetting. A second interpretation for the motivated memory findings above is that reward motivation enhances processing of high-value compared to low-value stimuli, but this processing is relatively automatic, rather than controlled (e.g., Cohen et al., 2019; Bowen et al., 2020). Neuroimaging provides evidence for this interpretation as reward anticipation boosts activation in the ventral tegmental area and triggers dopaminergic modulation of hippocampal consolidation processes. Presenting reward cues during stimulus presentation (i.e., before remember/forget instructions) may make forgetting even more difficult due to the relatively automatic cascade of processes within and between the ventral tegmental area and hippocampus during reward anticipation (e.g., Adcock et al., 2006; Bowen et al., 2020). Furthermore, reward anticipation has been shown to increase semantic processing of word stimuli—which are typically employed as stimuli in directed forgetting paradigms—in particular when a high reward is at stake. This results in elaborative encoding and increased memory for high- compared to low-value information (Cohen et al., 2016).

Considering reported age-related impairments in directed forgetting (Titz and Verhaeghen, 2010), it is important to determine whether older adults' ability to intentionally forget could be improved by extrinsic motivation via monetary reward, like it has been shown to increase remembering of high- compared to low-value information. A few prior studies have demonstrated that reward motivation does influence the directed forgetting effect in younger adults. In an effort to empirically test the possibility that participants' lack of motivation to search and recover TBF items may actually be driving the directed forgetting effect, Macleod (1999) offered participants a reward ($0.50) for any additional TBF words they could recall after an initial recall test for all TBR and TBF items. Despite this added motivation, participants reported very few additional TBF words during the second recall task, suggesting that the directed forgetting effect may not be driven by differential withholding of recovered TBF words. Macleod (1999) implemented reward motivation during the retrieval phase, so it is unclear from these results whether reward anticipation could influence cognitive control processes engaged during the encoding phase of the directed forgetting task. To answer this question, Friedman and Castel (2011) used a directed forgetting task where remember and forget cues were replaced with numerical values and participants were told to try and maximize their points with the following instructions: Words followed by +5, if recalled, would result in a gain of 5 points, but words followed by −5, if recalled, would result in a loss of 5 points, effectively making these words TBR and TBF, respectively. The authors found a stronger directed forgetting effect in the motivation block compared to a baseline block with no motivation manipulation. Finally, in a recent study, instead of replacing remember/forget cues with reward values, Ren et al. (2018) orthogonalized remembering/forgetting and reward/loss, by presenting TBR and TRF cues along with reward and loss cues, after presentation of each stimulus during encoding. The reward cues indicated how many points would be rewarded for successful remembering and forgetting on the subsequent recognition task as well as how many points would be lost for unsuccessful remembering and forgetting. They found that words associated with rewards led to a typical directed forgetting effect with better memory for TBR items compared to TBF items, but the threat of losses made it difficult for participants to forget, and there was no significant difference in recognition between TBR and TBF words.

The Current Studies

The goal of the current set of studies was to examine the effect of reward anticipation on age differences in directed forgetting in healthy younger and older adults. Hypotheses and a power analysis were preregistered on the Open Science Framework[1]. In Experiment 1, we wanted to establish directed forgetting effects in an online sample of younger and older adults recruited from CloudResearch/Turk Prime (Litman et al., 2017). This first study was done using a typical item-method directed forgetting task with neutral words without any motivational incentives. Based on prior research, we expected an age-related decline in the overall directed forgetting effect (i.e., the difference between memory for TBR vs. TBF words). In Experiment 2, we tested the effect of high-and low-value motivational incentives (monetary rewards) on directed forgetting in younger and older adults. Based on research described above, we suspected that high rewards would increase memory for TBR items compared to low or no reward in all participants. Compared to younger adults, we predicted that high rewards would also reduce the directed forgetting effect compared to a baseline condition of no reward in older adults, making TBF words even harder to forget. In Experiment 3, we investigated participant strategy during the recognition task, specifically whether they intentionally withheld their memory of TBF words in order to receive a reward. Experiment 3 followed the same procedure as Experiment 2, but after the recognition task, participants were offered an additional reward for each TBF word that they could freely recall to determine if they were intentionally withholding their memory for TBF words. While we did not have age-related hypotheses about this third experiment, given Macleod's (1999) findings, we hypothesized that participants would freely recall very few TBF items, which would be indicative of a cognitive strategy employed during encoding to modulate remembering and forgetting abilities, rather than a motivational strategy on the part of the participant to increase earnings. Finally, Experiment 4 followed the same procedures as Experiment 3 with the exception that participants were asked multiple choice questions during instructions to ensure that they understood the reward contingencies. We expected the findings from Experiment 3 would replicate, indicating the effects were reliable.

EXPERIMENT 1

While an age-related decline in directed forgetting has been shown (Titz and Verhaeghen, 2010), this has yet to be established in an online sample of young and older adults. Although participants recruited through crowdsourcing platforms like Amazon's Mechanical Turk (MTurk) are diverse, they do not necessarily represent the general population, which may reflect that Internet users typically differ from non-Internet users in systematic ways (Paolacci and Chandler, 2014). For example, there is some evidence that MTurk workers tend to be more educated, underemployed, more liberal, less extraverted, and more socially anxious than the general population (Shapiro et al., 2013). Given these potential differences between online and lab-based samples, the goal of Experiment 1 was to determine baseline directed forgetting effects in an online sample of young and older adults. During the study, participants completed an item directed forgetting task for neutral words. We predicted that young adults would show a larger directed forgetting effect than older adults.

Method

Participants

A power analysis using G*Power (Faul et al., 2007) indicated that a sample size of $n = 48$ in each group would provide 95% power to detect a within–between interaction effect of $\eta_p^2 = 0.08$ with $\alpha = 0.05$. The effect size $\eta_p^2 = 0.08$ is a conservative estimate (60%) of an effect size $\eta_p^2 = 0.14$ reported from an Age × Reward × Recognition interaction in a study with a similar design (Spaniol et al., 2014). We chose this conservative estimate to deal with potentially inflated effect sizes due to underpowered samples in the prior work. In Experiment 1, the final sample after exclusions included 50 young adults ranging in age from 22 to 29 years (*M* = 26.18, *SD* = 2.21) and 51 older adults ranging in age from 60 to 77 years (*M* = 65.37, *SD* = 4.49). All participants were recruited via CloudResearch/Turk Prime (Litman et al., 2017) and located in the United States. Participants were compensated $5 USD for approximately 45 min of participation. All participants provided informed consent in accordance with procedures approved by the Institutional Review Board at Southern Methodist University.

To ensure data quality, participants were required to complete attention checks that were dispersed throughout the survey to make sure they were reading task instructions (Oppenheimer et al., 2009). This included multiple choice questions in which specific responses were required such as, "Please select option three" and "What was this experiment about?," with the options "Current events," "Marketing," "Products," and "Other." The instructions for the latter question told participants to select "Other" and type the word "Silver" in the response box (e.g., Gallant et al., in press; Mather et al., 2012). At the end

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[1] https://osf.io/3pe9d/

of the task, participants were also asked to indicate whether they wrote down any of the words during encoding to help their performance on the memory task. If participants did not pass these attention checks or indicated that they had written down words, their data were excluded from analysis. Data were also excluded if participants learned English after the age of 7, had fewer than 12 years of education (to better match in-lab samples of older adults who typically have at least some post-secondary education), indicated a diagnosis of a psychiatric and/or neurological disorder, or were taking psychoactive medications. Based on these criteria, nine young adults and 11 older adults were excluded from analyses.

Characteristics of the final sample are displayed in **Table 1**. Older adults had more years of education, $t(97) = 2.14$, $p = 0.04$, and scored higher on the Shipley Vocabulary test, $t(99) = 3.51$, $p = 0.001$. These are age differences that are commonly reported in the literature (e.g., Gallant and Yang, 2014; Gallant et al., 2018). Older adults had lower rates of anxiety, $t(99) = 2.13$, $p = 0.04$, but there were no age differences in depression or stress, $ts \leq 1.55$, $ps \geq 0.13$; based on Depression, Anxiety, and Stress Scale-21 items (DASS-21) scoring, these scores were all within the "Normal" range (Lovibond and Lovibond, 1995). We also sought to characterize age differences in motivational behavior using the Behavioral Inhibition System/Behavioral Activation System (BIS/BAS) scales (Carver and White, 1994), which is theorized to be composed of separate behavioral inhibition and activation systems. Relative to young adults, older adults showed lower levels of behavioral inhibition, $t(99) = 2.31$, $p = 0.023$. In terms of activation, older adults had lower levels of drive, $t(99) = 2.01$, $p = 0.04$, and fun seeking than young adults, $t(97) = 2.71$, $p = 0.008$, but—importantly—they did not differ in reward responsiveness, $t = 0.29$, $p = 0.77$.

Materials

The experiment was programmed and run using Qualtrics survey software (Qualtrics, Provo, UT, United States). A total of 90 neutral nouns were selected from the word list provided by Janschewitz (2008) and split into three lists of 30. During the item directed forgetting task, participants saw 60 words, evenly split across two encoding blocks followed by a recognition task that was composed of the 60 old words and 30 new words as lures. As such, the three stimuli lists were counterbalanced as old words that were presented across the two encoding blocks and lure words presented only during the recognition task. Each of

TABLE 1 | Sample characteristics.

	Experiment 1 (*n* = 101)		Experiment 2 (*n* = 96)		Experiment 3 (*n* = 95)		Experiment 4 (*n* = 85)	
	Younger adults	**Older adults**	**Younger adults**	**Older adults**	**Younger adults**	**Older adults**	**Young adults**	**Older adults**
Characteristic	***M (SD)***	***M (SD)***	***M (SD)***	***M (SD)***	***M (SD)***	***M (SD)***	***M (SD)***	***M (SD)***
Age	26.18 (2.21)	65.37 (4.49)	26.02 (2.37)	65.81 (3.93)	25.69 (2.90)	65.09 (5.14)	25.87 (3.55)	65.69 (5.05)
Years of Education	14.84 (2.08)	*15.97 (3.09)	15.33 (1.69)	15.02 (2.28)	15.45 (1.60)	15.47 (2.57)	14.90 (2.12)	15.66 (2.48)
Shipley	32.80 (3.28)	**35.12 (3.36)	32.31 (3.85)	**35.67 (2.89)	31.58 (5.40)	**34.47 (3.90)	31.80 (4.25)	**35.38 (3.36)
BAS Drive	*11.60 (2.43)	10.65 (2.33)	*11.04 (2.45)	9.77 (2.61)	**11.74 (2.57)	9.68 (2.18)	11.44 (2.64)	10.40 (2.69)
BAS FS	*11.49 (2.07)	10.36 (2.08)	*11.13 (2.27)	9.83 (2.81)	**11.57 (2.32)	10.23 (2.36)	10.95 (2.35)	9.96 (2.55)
BAS RR	16.82 (2.07)	16.94 (1.99)	16.60 (2.52)	16.28 (2.51)	17.17 (2.11)	16.45 (2.10)	16.75 (2.32)	17.04 (2.32)
BIS	*21.24 (4.79)	19.10 (4.54)	*20.89 (5.43)	18.49 (4.96)	[b] –	[b] –	20.25 (5.55)	19.78 (3.79)
DASS: Anxiety[a]	*3.14 (3.77)	1.76 (2.64)	**3.08 (3.71)	0.77 (1.52)	**3.06 (3.46)	0.89 (1.40)	**4.42 (4.68)	1.44 (1.97)
DASS: Depression	3.98 (5.21)	2.61 (3.83)	**5.00 (5.86)	2.23 (3.67)	*4.06 (4.87)	1.96 (3.86)	**6.05 (5.92)	2.22 (2.83)
DASS: Stress	4.38 (4.57)	3.14 (3.42)	**5.15 (4.67)	2.60 (3.21)	**5.19 (4.34)	1.80 (1.85)	**6.38 (5.34)	2.56 (3.05)
	n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Sex								
Female	27 (54)	37 (72.5)	27 (56.3)	34 (70.8)	28 (58.3)	30 (66.7)	19 (47.5)	26 (57.8)
Male	23 (46)	14 (27.4)	21 (43.8)	14 (29.2)	20 (41.7)	14 (31.1)	21 (52.5)	18 (40)
Ethnicity								
Hispanic	4 (8)	0 (0)	5 (10.4)	0 (0)	5 (10.4)	3 (6.7)	4 (10)	0 (0)
Not Hispanic	46 (92)	51 (100)	43 (89.6)	48 (100)	42 (87.5)	40 (88.9)	36 (90)	44 (97.8)
Racial Group								
African American	7 (14)	2 (3.9)	3 (6.3)	0 (0)	5 (10.4)	3 (6.7)	9 (22.5)	4 (8.9)
American Indian	0 (0)	0 (0)	1 (2.1)	0 (0)	0 (0)	1 (2.2)	0 (0)	0 (0)
Asian/Pacific Islander	5 (10)	1 (1.9)	5 (10.4)	0 (0)	3 (6.3)	0 (0)	4 (10)	0 (0)
Caucasian	37 (74)	47 (92)	36 (75)	48 (100)	35 (72.9)	40 (88.9)	26 (65)	41 (91.1)
Other	1 (2.0)	0 (0)	3 (6.3)	0 (0)	5 (10.4)	1 (2.2)	1 (2.5)	0 (0)

*BAS FS, Behavioral Activation System (BAS) Fun-Seeking subscale; BAS RR, BAS Reward-Responsivity subscale; BIS, Behavioral Inhibition System subscale; DASS, Depression, Anxiety, and Stress Scale (21-item). *This age group had a significantly higher score than the other age group within experiments, at $p < 0.05$; ** at $p < 0.01$. [a] Older adults in Experiment 1 vs. Experiment 2 had significantly higher mean anxiety scores, $p = 0.04$. There were no other significant group differences in sample characteristics across experiments. [b] A programming error led to omission of BIS scores in Qualtrics for Experiment 3.*

the old word lists were further randomly split into two sets of 15 words, which were each paired with a TBR cue (RRRR) or a TBF cue (FFFF).

Three questionnaires were administered at the end of the experiment. The Shipley Institute of Living Vocabulary task (Shipley, 1940) measures crystallized intelligence with a 40-item vocabulary test. The BIS/BAS (Carver and White, 1994) is a 24-item self-report questionnaire designed to measure the complementary motivational systems. The DASS-21 (Lovibond and Lovibond, 1995) assesses emotional states of depression, anxiety, and stress.

Procedure

Participants first completed the item directed forgetting task. They were told that the purpose of the study was to understand their ability to selectively prioritize and remember some words over others. Participants were instructed to study a series of words for a later memory task, some of which would be followed by the cue "RRRR," which meant they should remember the word, or the cue "FFFF," which meant they should forget the word. Participants first completed six practice trials to familiarize themselves with encoding. Each trial began with a fixation cross in the center of the screen for 500 ms, followed by a word for 1,500 ms. To discourage participants from writing down the words, they were asked to use the mouse to check a box located directly below the word once they had finished studying it. After the word, a blank screen as an interstimulus interval (ISI) appeared for 500 ms, immediately followed by either the RRRR or FFFF cue for 1,000 ms. During encoding, words were presented in a pseudo-randomized order across two blocks of 30 trials, which each included 15 TBR and 15 TBF words. There was a 30-s break between blocks.

Following encoding, participants completed a non-verbal distractor task for approximately 5 min. The recognition task followed during which participants saw a series of 90 words (60 old words intermixed with 30 lures) and were instructed to indicate whether the word was old, meaning they previously studied it regardless of the cue it was associated with, or new, meaning they did not study it. Responses were self-paced and made via a mouse click. After recognition, participants completed the questionnaires and demographic information.

Results

Results were analyzed using SPSS and interpreted in terms of statistical significance ($\alpha = 0.05$) and effect size using partial eta square (η_p^2). Bonferroni-corrected pairwise comparisons were modeled into the analyses. Data were visualized using ggplot2 (Wickham, 2016) in R Studio. To determine how recognition was affected by the memory cue, we analyzed hits to correctly recognize words as old as well as false alarms to incorrectly classify new words as old as a measure of guessing. Average hit rates were submitted to a 2 (Age Group: Young, Older) × 2 (Cue: TBR, TBF) repeated-measures ANOVA (**Figure 1**), with age as the only between-subjects factor. A main effect of cue, $F(1,99) = 35.53$, $p < 0.001$, $\eta_p^2 = 0.26$, showed that hit rates were higher for TBR words ($M = 0.74$, $SD = 0.18$) than for TBF words ($M = 0.59$, $SD = 0.22$; **Figure 1**). The main effect of age and the interaction was not significant, $Fs \leq 0.02$, $ps \geq 0.89$.

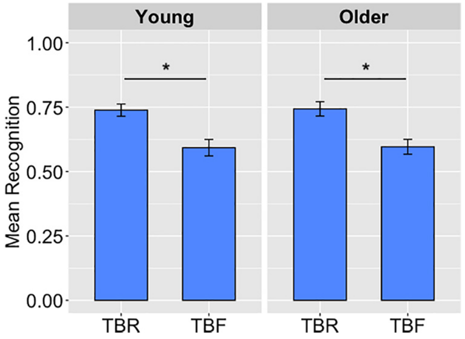

FIGURE 1 | The average hits to recognize to-be-remembered (TBR) and to-be-forgotten (TBF) words in Experiment 1, displayed as a function of age group, illustrate a main effect of cue ($p < 0.001$) in which both age groups showed better recognition of TBR than TBF words. Error bars represent standard error of the mean. *$p < 0.001$.

An independent-samples *t*-test on average false alarm rates across age groups showed that young adults had higher false alarm rates ($M = 0.22$, $SD = 0.18$) than older adults ($M = 0.09$, $SD = 0.12$), $t(99) = 3.54$, $p < 0.001$.

Discussion

In Experiment 1, both age groups were similar in their ability to remember TBR words and intentionally forget TBF words, which suggests there may be no age difference in directed forgetting when young and older adults are sampled from online crowdsourcing platforms. This contradicts our hypothesis as well as the findings of previous studies (Zacks et al., 1996; Sahakyan et al., 2008; Gallant et al., 2018) and meta-analyses (Titz and Verhaeghen, 2010) that have demonstrated smaller directed forgetting effects in older relative to young adults in laboratory-based tasks.

One possible explanation for age-equivalent finding is that older adults using CloudResearch/Turk Prime have higher cognitive abilities (e.g., greater cognitive reserve, more computer savvy, more motivated to seek out opportunities) than the average older adult participating in laboratory studies. Consistent with this notion, there is evidence that digital literacy (e.g., Internet and e-mail use) may positively impact cognitive performance in older adults by reducing cognitive decline (Xavier et al., 2014; Klimova, 2016). However, young adults in the current study showed a lower hit rate for TBR words ($M = 0.73$) when compared to previous investigations ($M = 0.87$ in Collette et al., 2014; $M = 0.89$ in Gallant et al., 2018) and also showed a higher false alarm rate than older adults, an age difference that is typically reversed (e.g., Huh et al., 2006). This finding might imply that our young adults were not fully attending to the encoding task and, as a result, did not encode the words as well as older adults. Prior work has shown that, relative to lab-based participants, young adults completing studies via MTurk are more likely to be distracted by other activities such as using their cell phone, watching television, browsing the Internet, or talking with friends (Clifford and Jerit, 2014). By dividing their attention among other tasks, young adults from online settings may be inadvertently reducing their cognitive performance.

In the second experiment, we investigated the effect of reward motivation on young and older adults' directed forgetting performance. However, prior to implementing reward incentives, we had participants complete a baseline item directed forgetting block with no rewards to see if we could replicate the age-equivalent directed forgetting effect observed in Experiment 1.

EXPERIMENT 2

In Experiment 2, we modified the procedure of Experiment 1 to include high and low rewards for memory performance. During encoding, participants first completed a no-reward block to establish baseline directed forgetting. In the second block, each stimulus was paired with either a high ($0.75) or low reward ($0.01) prior to the memory cue, which indicated how much money could be earned if TBR words were successfully remembered or TBF words were successfully forgotten. We expected that high rewards would increase memory for TBR words compared to low or no reward in all participants. We also predicted that high rewards would reduce older, but not younger, adults' directed forgetting effect relative to a no-reward baseline condition by making TBF words even harder to forget.

Method

Participants

Based on the exclusion criteria used in Experiment 1, 24 young adults and 26 older adults were excluded from analyses. The final sample after exclusions included 48 young adults ranging in age from 19 to 29 years ($M = 26.02$, $SD = 2.38$; 27 females) and 48 older adults ranging in age from 60 to 75 years ($M = 65.81$, $SD = 3.93$; 34 females). All participants were recruited via CloudResearch/Turk Prime (Litman et al., 2017) and provided informed consent for their participation. Participants were compensated $4 USD for approximately 45 min of work in addition to the incentives they received based on their memory performance.

The final sample characteristics are displayed in **Table 1**. There was no age difference in education, $t = 0.76$, $p = 0.45$, but older adults scored higher on the Shipley vocabulary test than young adults, $t(94) = 4.82$, $p < 0.001$. Relative to young adults, older adults had lower levels of depression, $t(94) = 2.78$, $p = 0.007$, anxiety, $t(94) = 3.99$, $p < 0.001$, and stress, $t(94) = 3.11$, $p = 0.002$; all scores fell in the "Normal" range. On the BIS/BAS, older adults showed lower behavioral inhibition than young adults, $t(91) = 2.18$, $p = 0.03$, as well as lower total activation, $t(91) = 2.11$, $p = 0.04$, including lower drive, $t(92) = 2.35$, $p = 0.02$, and fun seeking, $t(92) = 2.42$, $p = 0.02$. Age groups did not differ in reward responsiveness, $t(91) = 0.46$, $p = 0.65$.

Materials

The experiment was programmed and run using Qualtrics survey software (Qualtrics, Provo, UT, United States). A total of 120 neutral nouns were selected from the word list provided by Janschewitz (2008) and split into four lists of 30 words. During the directed forgetting task of Experiment 2, participants again completed two encoding blocks, which included a no-reward block of 30 words, followed by a reward block that included 30 words paired with a high reward intermixed with 30 words that were paired with a low reward. During the recognition task, participants viewed 90 old words intermixed with 30 new lure words. The four word lists were counterbalanced such that they equally served as no reward, high reward, low reward, and new words across participants. Each list of 30 words was further randomly split into two subsets of 15 words, which were each paired with a TBR or TBF cue.

Procedure

The directed forgetting task followed the same procedure as Experiment 1, except that participants first completed an encoding block with no rewards, followed by an encoding block in which words were equally paired with high- or low-reward values. Participants were not informed that they could receive a reward for their performance until the second block. This was done to ensure that knowledge of monetary incentives did not influence performance on the no-reward block, which provided a baseline measure of directed forgetting. Each trial of the no-reward block proceeded the same as in Experiment 1. Participants completed eight practice trials followed by the no-reward block, which included 15 TBR words intermixed with 15 TBF words. After a 30-s break, participants started the second block, in which each word was presented with a monetary cue indicating the reward that they could earn if the word was successfully remembered or forgotten. Reward-block trials proceeded the same as no-reward trials, except that each word was paired with a reward, either $0.75 or $0.01, that appeared directly above the word. To differentiate rewards, high rewards appeared in green colored font (RGB decimal: 50, 205, 50), whereas low rewards appeared in blue colored font (RGB decimal: 52, 152, 219). Reward-block trials included 15 high-reward TBR words, 15 high-reward TBF words, 15 low-reward TBR words, and 15 low-reward TBF words.

After encoding, participants completed a non-verbal filler task for 5 min followed by a recognition task for the 90 old words intermixed with 30 new lures. They were told to indicate whether each word was old or new and that the reward for each word they correctly identified as old would be based on the monetary cue ($0.75 or $0.01) it was associated with during encoding. To discourage participants from committing a false alarm to new words to increase their reward, they were told they would lose $0.50 for each new word incorrectly identified as old. The recognition task followed the same procedure as that of Experiment 1, after which participants completed the Shipley Vocabulary Task, BIS/BAS, DASS-21, and a demographic questionnaire.

After the experiment, rewards were calculated based on performance and administered to participants' CloudResearch/Turk Prime account. Rewards for TBR words were calculated based on the total number of words that were successfully remembered (i.e., identified as old). In contrast, rewards for TBF words were calculated based on the total

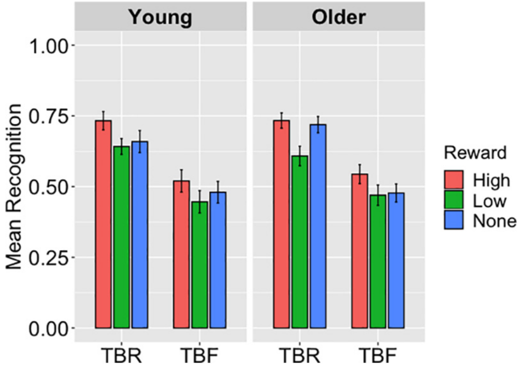

FIGURE 2 | The average hits for to-be-remembered (TBR) and to-be-forgotten (TBF) words in Experiment 2, displayed as a function reward magnitude and age group, illustrate a main effect of cue, with more TBR words recognized than TBF words in both age groups ($p < 0.001$). A main effect of reward ($p < 0.001$) is also apparent, with high-reward words recognized more than low- and no-reward words. Error bars represent standard error of the mean.

number of words that were successfully forgotten (i.e., identified as new). The false alarm penalty was calculated based on the total number of new words recognized as old and was subtracted from their overall reward.

Results

Recognition performance is displayed in **Figure 2**. Average hit rates were submitted to a 2 (Age Group: Young, Older) × 3 (Reward: No Reward, High Reward, Low Reward) × 2 (Cue: TBR, TBF) ANOVA. A main effect of cue, $F(1,94) = 81.33$, $p < 0.001$, $\eta_p^2 = 0.46$, showed that hits were higher for TBR ($M = 0.68$, $SD = 0.17$) than for TBF words ($M = 0.49$, $SD = 0.22$). There was also a main effect of reward, $F(2,188) = 11.96$, $p < 0.001$, $\eta_p^2 = 0.11$. Pairwise comparisons showed that high-reward words ($M = 0.73$, $SD = 0.21$) were better recognized than low-reward words ($M = 0.63$, $SD = 0.22$, $p < 0.001$) and no-reward words ($M = 0.69$, $SD = 0.24$, $p = 0.04$). The difference between recognition of low-reward and no-reward words was not significant ($p = 0.08$). There were no other significant main effects or interactions in the ANOVA, $Fs \leq 2.19$, $ps \geq 0.11$.

Age differences in false alarms to incorrectly identify new words as old were also analyzed. The *t*-test showed that older adults made fewer false alarms ($M = 0.13$, $SD = 0.14$) than young adults ($M = 0.22$. $SD = 0.20$), $t(94) = 2.39$, $p = 0.02$.

Discussion

Like Experiment 1, young and older adults in Experiment 2 were similar in their overall directed forgetting performance, recognition was higher for TBR than TBF words, and older adults again showed a tendency for fewer false alarms. As mentioned previously, one possibility is that online samples of young adults are dividing their attention among other tasks (Clifford and Jerit, 2014), reducing their ability to pay full attention during encoding. As such, in Experiment 3, we repeated the procedure of Experiment 2, but we added an additional task to the encoding phase that required participants' attention. Following each cue, participants were required to indicate whether an arrow cue (presented as "<" or ">") was pointing to the left or right side of the screen. This task was intended to be simple enough to keep participants' attention engaged, but to not detract from the cognitive processes required to intentionally remember and forget words.

Experiment 2 also partially supported our hypotheses as recognition was better for high-reward than for low- or no-reward words, but this did not vary as a function of whether words were cued as TBR or TBF. With regard to the effect of reward on directed forgetting, one possibility is participants are intentionally withholding their memory of high- and low-reward TBF words in order to maximize their overall payout. This would imply a motivational explanation for participants' forgetting rates as opposed to a process-based explanation in which participants are using cognitive resources to limit encoding of TBF words (Macleod, 1999). A second goal of Experiment 3 was therefore to better understand participant strategy during the motivated directed forgetting task.

EXPERIMENT 3

The purpose of Experiment 3 was two-fold: first, to increase participant engagement during encoding and, second, to further investigate the effect of rewards on participants' memory for TBF words. We modified the directed forgetting task by including a simple arrow-detection task following the presentation of each memory cue during encoding. We also implemented a surprise recall task for TBF words, modeled after Macleod (1999). Specifically, following an initial memory task, participants were offered an additional reward for every TBF word that they could freely recall. If participants show better recall of high- and low-reward TBF words relative to no-reward TBF words, this might imply that they were intentionally withholding their memory of TBF words to receive a higher payout.

Method

Participants

Based on the exclusion criteria described in Experiments 1 and 2, 23 young adults and 13 older adults were excluded from analyses. The final sample after exclusions included 49 young adults ranging in age from 18 to 31 years ($M = 25.69$, $SD = 2.90$; 28 females, one unidentified sex) and 46 older adults ranging in age from 59 to 79 years ($M = 65.09$, $SD = 5.14$; 30 female, three unidentified sex). All participants were recruited via CloudResearch/Turk Prime (Litman et al., 2017) and provided informed consent for their participation. Similar to Experiment 2, participants were compensated $4 USD for approximately 45 min of work in addition to the incentives they received based on their memory performance during the recognition and recall task.

Characteristics of the final sample are displayed in **Table 1**. Older adults scored higher than young adults on the Shipley Vocabulary test, $t(93) = 2.88$, $p = 0.005$, but age groups did not differ in total years of education, $t = 0.05$, $p = 0.96$. Older adults showed lower levels of depression, $t(93) = 2.29$, $p = 0.02$, anxiety,

$t(93) = 3.84$, $p < 0.001$, and stress, $t(93) = 4.96$, $p < 0.001$, than young adults, but all scores fell within the "Normal" range. On the BIS/BAS, older adults scored lower on overall behavioral activation, $t(87) = 3.51$, $p = 0.001$, including drive, $t(89) = 4.12$, $p < 0.001$, and fun seeking, $t(88) = 2.72$, $p = 0.008$; there was no age difference in responsiveness to reward, $t = 1.62$, $p = 0.11$. Due to a programming error, one item from the behavioral inhibition scale was not presented to participants and so it was not possible to compute this score for either age group.

Procedure

Experiment 3 used the same materials and protocol as Experiment 2 with a few modifications. Each encoding trial followed the same procedure except that after the memory cue (RRRR or FFFF), an arrow (< or >) appeared in the center of the screen and participants were required to indicate the direction of the arrow via button press. This was done to ensure that participants stayed engaged with the task and to discourage them from selectively writing down TBR words. Following encoding and a 5-min filler task, the same recognition test as Experiment 2 was administered. After recognition, participants were told they could earn an additional $0.10 for each TBF word that they could recall. They were invited to recall any words that they could remember, including TBR words, but they were only rewarded for recall of TBF words. They had 1.5 min to type their responses into a response box. After the recall task, participants completed the same questionnaires and tasks as Experiments 1 and 2. Their rewards were calculated based on memory performance and administered to their CloudResearch/Turk Prime account.

Results

Recognition performance is displayed in **Figure 3**. Average hit rates were entered to a 2 (Age Group: Young, Older) × 3 (Reward: High, Low, None) × 2 (Cue: TBR, TBF) repeated-measures ANOVA. This analysis showed a main effect of reward, $F(2,186) = 9.04$, $p < 0.001$, $\eta_p^2 = 0.09$. According to pairwise comparisons, hit rates were reduced for low-reward words ($M = 0.53$, $SD = 0.21$) relative to high-reward ($M = 0.60$, $SD = 0.20$; $p < 0.001$) and no-reward words ($M = 0.59$, $SD = 0.19$; $p = 0.009$); hit rates for high-reward words did not differ from no-reward words ($p > 0.99$). A main effect of cue, $F(1,93) = 69.54$, $p < 0.001$, $\eta_p^2 = 0.42$, also showed that hit rates were higher for TBR words ($M = 0.65$, $SD = 0.17$) than for TBF words ($M = 0.50$, $SD = 0.21$). The main effect of age was not significant, $F = 1.25$, $p = 0.26$.

There was a significant two-way interaction of age group and cue, $F(1,93) = 6.68$, $p = 0.01$, $\eta_p^2 = 0.07$. Pairwise comparisons showed that older adults recognized more TBF words ($M = 0.55$, $SD = 0.19$) than young adults ($M = 0.46$, $SD = 0.22$; $p = 0.04$), suggesting they were less able to intentionally forget TBF words than their young counterparts. Hits for TBR words did not differ, $p = 0.75$. The age group-by-reward interaction was also significant, $F(2,186) = 2.94$, $p = 0.05$, $\eta_p^2 = 0.03$, such that recognition of no-reward words was higher in older adults ($M = 0.64$, $SD = 0.17$) than young adults ($M = 0.55$, $SD = 0.20$), $p = 0.01$; there was no age difference between the other reward conditions. The remaining interactions were not significant, $Fs \leq 1.31$, $ps \geq 0.27$.

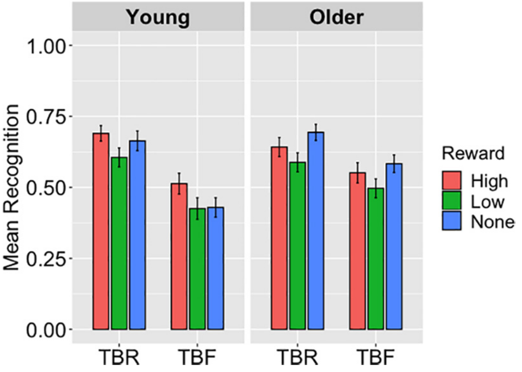

FIGURE 3 | The average hits for to-be-remembered (TBR) and to-be-forgotten (TBF) words in Experiment 3, displayed as a function of reward magnitude and age group, illustrate a main effect of cue ($p < 0.001$) with better recognition of TBR than TBF words as well as an effect of reward ($ps < 0.01$), such that low-reward words were recognized to lesser extent than both high- and no-reward words. The age-by-cue interaction is also apparent as older adults recognized more TBF words than young adults ($p = 0.04$), but the same proportion of TBR words. The figure further shows the age-by-reward interaction in which older adults had superior recognition of no-reward words versus young adults ($p = 0.01$) but similar recognition of high- and low-reward words. Error bars represent standard error of the mean.

The *t*-test on false alarm rates across age groups showed no difference between young ($M = 0.21$, $SD = 0.18$) and older adults ($M = 0.25$, $SD = 0.20$), $t = 1.05$, $p = 0.29$.

Proportional recall rates were analyzed in a 2 (Age Group: Young, Older) × 3 (Reward: High, Low, None) × 2 (Cue: TBR, TBF) ANOVA. In general, recall was low ($M = 0.04$, $SD = 0.04$). There was a marginal main effect of cue, $F(1,93) = 3.51$, $p = 0.06$, $\eta_p^2 = 0.04$, which showed that recall rates were higher for TBR ($M = 0.04$, $SD = 0.06$) than for TBF words ($M = 0.03$, $SD = 0.04$). The remaining effects and interactions were not significant, $Fs \leq 1.11$, $ps \geq 0.33$.

Discussion

The results of Experiment 3 revealed an age-related difference in the directed forgetting effect consistent with prior in-lab experiments (Sahakyan et al., 2008; Titz and Verhaeghen, 2010; Gallant et al., 2018). Older adults had more difficulty cognitively controlling their memory and therefore recognized more TBF items compared to younger adults, but recognition of TBR items did not differ between age groups. Unlike Experiments 1 and 2, younger adults did not commit more false alarms than older adults. We believe that age differences in directed forgetting, but no age differences in false alarm rates, emerged in this experiment, and not in Experiment 1 or 2, because of the arrow task that was added to increase participant engagement, particularly for younger adults. As noted, when doing online versus in-lab experiments, young adults often divide their attention, potentially reducing their ability to pay attention to the task and key instructions, like remember or forget cues. This inclusion of the arrow task seems to have increased younger adults' ability to intentionally forget which is driving the age-related interaction. One concern was that adding this task would reduce performance overall, especially for older adults, but across all three experiments, the recognition rates for both age groups are relatively consistent. Like Experiment 2, high-reward led to better memory than low-reward items, but in Experiment 3, there were no differences between high-reward and no-reward trials. This boost for no-reward trials in Experiment 3 may also be related to greater task engagement particularly in the first block of trials when there were fewer competing trials and less memory interference.

Finally, replicating the findings from Experiments 1 and 2, recognition was better for TBR compared to TBF words. We added the surprise rewarded recall task after recognition to understand whether this was strategic. Participants may have intentionally withheld their memory for TBF words in order to maximize their overall payout, indicative of a motivational retrieval strategy rather than a process-based explanation in which participants are limiting encoding of TBF words. The recall task was based on the design from Macleod (1999) and in agreement their results, we found that participants freely recalled very few words, but did recall slightly more TBR than TBF words, providing evidence against the motivational prediction that participants were withholding their memory at the time of retrieval.

EXPERIMENT 4

The results of Experiments 2 and 3 imply that high rewards do not enhance the ability to intentionally forget TBF words and, instead, enhance overall remembering. Given that these experiments were conducted online without an experimenter present to explain instructions, it is possible that participants may have misunderstood how rewards would be administered for TBF words. Specifically, participants may have thought that rewards were only associated with remembering *in general*, thus assuming they would forgo \$0.75 if they forgot TBF words. This could explain why high rewards had a general effect on overall memory rather than a differential effect on remembering or forgetting (a reward-by-cue interaction). To rule out this possibility, in Experiment 4, we repeated Experiment 3 and added comprehension questions during the instructions to ensure that participants understood how rewards would be administered for TBR and TBF trials. We also sought to replicate the age-by-cue interaction that we observed in Experiment 3 when we added the arrow detection task to increase participant engagement.

Method

Participants

The same exclusion criteria from Experiments 1–3 were applied to Experiment 4, resulting in the exclusion of 31 young adults and 19 older adults from analyses. The final sample after exclusions included 40 young adults ranging from 18 to 30 years of age (M = 25,88, SD = 3.55; 19 females) and 45 older adults ranging from 61 to 89 years of age (M = 65.59, SD = 5.06; 26 females, one unidentified sex). All participants were located in the United States, recruited from CloudResearch/Turk Prime (Litman et al., 2017), and provided informed consent for their participation. They were compensated \$4 USD for approximately 45 min of work plus the incentives received based on their memory performance.

Sample characteristics are displayed in **Table 1**. Whereas there was no age difference in years of education, $t(83) = 1.50$, $p = 0.14$, when compared to young adults, older adults scored higher on the Shipley Vocabulary test, $t = 4.32$, $p < 0.001$, as well as had lower levels of depression, $t(83) = 3.87$, $p < 0.001$, anxiety, $t(83) = 3.89$, $p < 0.001$, and stress, $t(83) = 4.11$, $p < 0.001$. On the BIS/BAS, there were no age differences in drive, $t(82) = 1.77$, $p = 0.08$, fun seeking, $t(83) = 1.86$, $p = 0.07$, reward responsiveness, $t(83) = -0.59$, $p = 0.56$, and behavioral inhibition, $t(59) = 0.39$, $p = 0.70$.

Procedure

Experiment 4 used the same materials and protocol as Experiment 3—the only changes were made to the task instructions for the reward block of the directed forgetting task. After reading encoding instructions for this block, participants completed two multiple choice comprehension questions. In the first question, a sample trial was presented in which a \$0.01 reward was paired with a TBR word. Participants were asked to indicate what the outcome would be if they remembered the TBR word from the following options: "You would win \$0.01," "You would lose \$0.01," or "You would not receive anything." In the second question, the sample trial presented a \$0.75 reward paired with a TBF word and participants selected what the outcome would be if they forgot the TBF word from the options: "You would win \$0.75," "You would lose \$0.75," or "You would not receive anything." To ensure participants understood the retrieval instructions and the financial penalty for a committing a false alarm, they were asked to indicate what the outcome would be if they incorrectly identify a NEW word as one that they previously studied from the following options: "You will lose \$0.50," "You will win \$0.50," or "Nothing will happen." If participants answered any of the questions incorrectly, the survey presented the correct answer and reiterated the instructions.

Results

With regard to our comprehension check questions, nine older adults responded incorrectly to the TBF trial—three indicated they would lose \$0.75 and six indicated they would receive no reward if they forgot the word. Two older adults also responded incorrectly to the TBR trial, indicating they would receive no reward if they remembered the word. Seven young adults incorrectly responded to the TBF trial—one indicated they would lose \$0.75, and six indicated they would receive no reward. Regarding false alarm instructions, 10 older adults and eight younger adults incorrectly indicated that nothing would happen to their earnings for committing a false alarm, and five older adults and six younger adults indicated they would win \$0.50.

Recognition performance is displayed in **Figure 4**. Average hit rates were submitted to a 2 (Age Group: Young, Older) × 3 (Reward: High, Low, None) × 2 (Cue: TBR, TBF) repeated-measures ANOVA, which showed a main effect of reward,

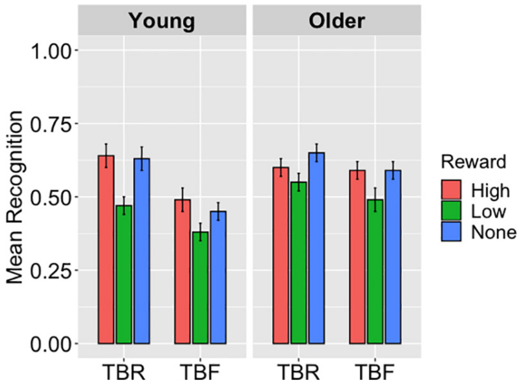

FIGURE 4 | The average hits for to-be-remembered (TBR) and to-be-forgotten (TBF) words in Experiment 4, displayed as a function of reward magnitude and age group, illustrate a main effect of cue ($p < 0.001$) with better recognition of TBR than TBF words as well as an effect of reward (*ps* < 0.001), such that low-reward words were recognized to a lesser extent than both high- and no-reward words. An age-by-cue interaction is also displayed, as older adults recognized more TBF words than young adults ($p = 0.01$), but the same proportion of TBR words.

$F(2,166) = 25.73$, $p < 0.001$, $\eta_p^2 = 0.24$. According to pairwise comparisons, low-reward words ($M = 0.47$, $SD = 0.21$) were recognized to a lesser extent than high-reward ($M = 0.58$, $SD = 0.19$; $p < 0.001$) and no-reward words ($M = 0.58$, $SD = 0.21$; $p < 0.001$). There was also a main effect of cue, $F(1,83) = 32.07$, $p < 0.001$, $\eta_p^2 = 0.28$, with better recognition of TBR ($M = 0.59$, $SD = 0.19$) than TBF words ($M = 0.50$, $SD = 0.21$). The main effect of age was not significant, $F = 2.77$, $p = 0.10$.

Replicating Experiment 3, there was a significant age group-by-cue interaction, $F(1,83) = 9.31$, $p = 0.003$, $\eta_p^2 = 0.10$. Pairwise comparisons showed that older adults recognized more TBF words ($M = 0.55$, $SD = 0.20$) than young adults ($M = 0.44$, $SD = 0.20$; $p = 0.01$), but a similar proportion of TBR words ($p = 0.70$), implying that older adults were less able to intentionally forget TBF words than young adults. There were no other significant interactions, $Fs \leq 2.77$, $ps \geq 0.10$.

The comparison of false alarm rates across age groups showed that there was no difference between young ($M = 0.29$, $SD = 0.27$) and older adults ($M = 0.27$, $SD = 0.18$), $t = 0.49$, $p = 0.61$.

The proportion of words recalled was analyzed in a 2 (Age Group: Young, Older) × 3 (Reward: High, Low, None) × 2 (Cue: TBR, TBF) ANOVA. Like Experiment 3, overall recall was low ($M = 0.05$, $SD = 0.04$). The ANOVA revealed a main effect of reward, $F(2,166) = 4.75$, $p = 0.01$. Pairwise comparisons confirmed that recall was better for high-reward words ($M = 0.07$, $SD = 0.09$) than for no-reward words ($M = 0.04$, $SD = 0.06$), $p = 0.04$; there was no difference in recall between high- and low-reward words ($M = 0.04$, $SD = 0.05$), $p = 0.08$, nor between low-reward and no-reward words, $p = 1.00$.

Discussion

The results of Experiment 4 replicate those of Experiment 3, revealing the typically reported age difference in directed forgetting. Along with prior work (e.g., Titz and Verhaeghen, 2010), these results imply that older adults are less able to control their memory to intentionally forget TBF words. Further like Experiment 3, high rewards enhanced memory relative to low-reward items, but there was no difference in memory for high- and no-reward items. This effect of reward magnitude also did not vary based on memory instruction, suggesting that rewards had a general effect on memory performance as opposed to a differential effect on remembering and intentional forgetting.

The novel component of this experiment was the addition of comprehension checks, in which we probed whether participants understood how rewards would be administered based on performance (i.e., that they would win a reward for remembering TBR words as well as for forgetting TBF words and be penalized for committing a false alarm). Only 20% of older adults and 17.5% of young adults incorrectly answered these questions about encoding, and 33% of younger and older adults incorrectly answered the question at retrieval, all of whom were required to reread the instructions prior to beginning the experiment. Given that our results were consistent with Experiment 3, it does not seem likely that the effect of our reward manipulation (or lack thereof) on intentional forgetting can be attributed to misunderstanding instructions.

GENERAL DISCUSSION

Prior in-lab experiments have established that age is associated with decreased abilities to intentionally forget (Zacks et al., 1996; Titz and Verhaeghen, 2010). Across four experiments, we assessed the directed forgetting effect in an online sample of younger and older adults recruited from CloudResearch/Turk Prime with the main objective of elucidating whether reward anticipation could positively impact older adults' reduced ability to intentionally forget.

This is the first study to establish a directed forgetting effect in an online sample. In all four experiments, we replicated the typical directed forgetting effect of better recognition memory for TBR words than for TBF words. The cognitive and neural mechanisms responsible for directed forgetting are still debated (Anderson and Hanslmayr, 2014; Aguirre et al., 2017), but one hypothesis is that participants simply do not search their memory as long for TBF words or choose to withhold retrieved information. It was unclear from the results of Experiment 2 when participants were rewarded for successful intentional remembering and forgetting, whether participants were withholding their memory or suppressing retrieval to increase their performance-based rewards. Replicating findings from Macleod (1999), in Experiments 3 and 4, we found little evidence of this as participants did not freely recall very many words overall, but recalled more TBR words, despite an added monetary bonus to recall TBF words. We chose to probe memory for additional TBF items with a free recall task instead of a recognition task to avoid source confusion. Results from a second recognition task would be unclear because it would not be able to tease apart memory for words that were encoded in the original encoding session and those encoded during the first recognition test. Recall is a cognitively harder task, especially for older adults, so some TBF items may have been missed by employing this method, but it avoids the confounds of a second recognition task.

Only in Experiments 3 and 4 did we find typical age-related reductions in directed forgetting. There were few age differences or interactions overall across the experiments, including no main effects of age. As crowdsourcing platforms like MTurk and CloudResearch/Turk Prime are utilized more often in psychological research, findings that have been well-documented in the lab may not replicate in online samples due to systematic differences between these samples (Paolacci and Chandler, 2014). Interestingly, our results suggest that this may not be because of differences in older adults who participate in-lab versus online, but because of younger adults. The age-related reductions in directed forgetting that we found in Experiments 3 and 4 seem to be driven by the amount of task engagement by younger adults. In online studies, younger adults are known to divide their attention between the task and other distractions such as their phone or television (Clifford and Jerit, 2014). In Experiments 3 and 4, when a detection task was included to increase engagement during encoding, younger adults showed a stronger directed forgetting effect than older adults, but both groups recognized TBR stimuli to the same extent. These findings suggest that online data collection might require that younger adult participants be given a more engaging encoding task that prevents divided attention, but not so cognitively demanding so as to decrease overall performance.

Turning to our main objective, in Experiments 2–4, we included a reward manipulation to determine whether added motivation might help older adults' ability to intentionally forget by increasing cognitive control and goal-directed remembering *and* forgetting, or whether rewards may potentially hinder directed forgetting because of processes that unfold during reward anticipation that prioritize high value information in memory rather automatically, thereby making any stimuli associated with a high reward value during encoding more likely to be remembered. We found evidence across experiments that high-value reward anticipation boosted recognition memory for both younger and older adults compared to low-reward (Experiments 2–4) and compared to no-reward (Experiment 2), regardless of the memory cue to remember or forget. In other words, this evidence supports the latter hypothesis that reward anticipation increases the ability to encode and remember information but does not seem to help with intentional forgetting abilities. It has been suggested that age-related declines in cognitive control are responsible for the inability to inhibit unwanted information, and this leads to continued encoding of items they have been instructed to forget (Sahakyan et al., 2008; Gallant et al., 2018). Despite evidence that reward anticipation can improve cognitive control abilities in other tasks (Ferdinand and Czernochowski, 2018), our findings do not support that this is occurring in this paradigm. We found no evidence that high reward led to better intentional forgetting compared to low or no reward, ergo reward anticipation did not increase cognitive control abilities in the task for younger or older adults.

Instead, evidence from this set of studies was generally in support of our preregistered hypothesis (see footnote 1) that high-value reward anticipation boosts overall remembering and does not lead to increased goal-directed forgetting, but this was true for both younger and older adults. It is important to note that in Experiment 2, high-reward words were better recognized than low-reward and no-reward words which we had additionally hypothesized, but in Experiments 3 and 4, hit rates for high-reward did not differ from no-reward words. These differences in results may be accounted for by the change in encoding conditions with participants being more engaged (particularly younger adults) during Experiments 3 and 4 than in Experiment 2. Although speculative, this increased engagement may be coupled with psychological differences between the two experimental blocks. In block 1, there was no reward manipulation and participants were unaware that the next block of trials would include performance-based rewards. This may have led to more cognitive resources available to encode the stimuli in the no-reward block of Experiments 3 and 4 since interference from other trials is low at this early stage of the task. In block 2, when cognitive resources become limited due to processing the reward cue and stimulus simultaneously, as well as the sheer number of trials that have occurred at that point, participants may expend more cognitive effort on high-reward compared to low-reward trials, leading to no statistical differences in recognition memory for high- and no-reward trials. We intentionally did not counterbalance the no-reward/reward blocks to ensure that knowledge of monetary incentives did not influence performance on the no-reward block. Future studies that are able to counterbalance block order, or that include the same number of trials, but all associated with rewards, will be able to test the idea of these psychological differences and the role of interference on this pattern of results.

An additional difference between the blocks is that the reward cue appears on the screen during stimulus presentation during block 2. The purpose of presenting the reward cue during stimulus presentation was to test the effect of reward anticipation on the ability to control memory by either intentionally remembering or forgetting the word. Reward anticipation has been shown to engage the reward network but also other brain regions that could either increase inhibitory cognitive control of memory that would benefit both goal-directed remembering and forgetting (e.g., Cohen et al., 2016; Ferdinand and Czernochowski, 2018) or more automatic episodic memory formation (e.g., Spaniol et al., 2014; Cohen et al., 2019; Bowen et al., 2020) that would benefit remembering only, making forgetting more difficult. This is the first study to examine the role of monetary reward anticipation and its interaction with memory cues in a directed forgetting paradigm, adding to a small literature examining the effect of motivation on directed forgetting, more broadly. In an early study, Macleod (1999) found that monetary reward during a surprise free recall test did not elicit additional TBF words from memory. Utilizing points as a proxy for remember and forget cues presented after stimulus encoding, Friedman and Castel (2011) found a stronger directed forgetting effect when participants were motivated by these points compared to baseline. Finally, presenting reward cues along with memory cues after stimulus presentation led to increased directed forgetting when the rewards were gains, but a reduced ability to forget when participants were expecting a loss

(Ren et al., 2018). There are still many unanswered behavioral questions, such as whether the timing of the reward cue matters to intentional forgetting processes (i.e., cueing rewards before, during, or after stimulus encoding or cueing during retrieval). Perhaps reward anticipation during stimulus encoding in the current study reduced the ability for older adults to cognitively control their memory because it was too cognitively taxing to read the stimulus, pay attention to the reward cue, and then engage with the TRB or TBF cue. Future studies that manipulate this aspect of the experimental design will be able to answer these questions and align the findings with other studies that have examined the role of reward on directed forgetting. Further, and of importance for elucidating the role of cognitive control, individual differences in older adults' executive function may also be a predictor of reward effects on directed forgetting. As noted, we did not find evidence that reward was leading to increased cognitive control in this paradigm when participants were put into a state of reward anticipation during stimulus encoding, but it is still unclear from this set of studies how reward is influencing these different effects. An interesting future experiment would be to use neuroimaging to further clarify the role of prefrontal cortex and cognitive control regions, reward network activation and dopaminergic modulation of hippocampal consolidation processes (e.g., Adcock et al., 2006; Spaniol et al., 2014; Bowen et al., 2020), and/or left lateral prefrontal cortex engagement indicative of increased semantic processing of the verbal stimuli at the time of encoding (Cohen et al., 2016) to test how each supports the relationship between reward anticipation and directed remembering and forgetting.

CONCLUSION

In four experiments, we tested directed remembering and forgetting abilities in an online CloudResearch/Turk Prime sample of younger and older adults. We replicated typical age-related deficits in forgetting, but only when younger adults were obliged (via button press) to stay cognitively engaged in the task. This highlights the importance of task demands in online studies—not only to be mindful of cognitive limitations of older adults but also to prevent possible divided attention in younger adult samples. In line with our preregistered hypotheses, across three experiments, we found evidence that high-value reward anticipation led to better memory overall compared to low reward, for younger and older adults, but this was regardless of the directed forgetting cue. If reward anticipation increased cognitive control in this paradigm, this would have modulated the directed forgetting effect, not general memory overall. High-value reward anticipation may strengthen memory relatively automatically, rather than strategically, possibly via dopaminergic activation of memory formation processes. Moreover, bonus rewards for successful recall of TBF words revealed that participants were not strategically withholding their memory of TBF words in the service of a higher payout, giving strength to the idea that directed forgetting effects are not driven by a motivational retrieval strategy, but by processes that unfold at the time of encoding. Future studies aimed at uncovering the cognitive and neural mechanisms responsible for these effects will be necessary to understand how these processes remain relatively stable across the life span.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on the Open Science Framework https://osf.io/3pe9d/.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Southern Methodist University Institutional Review Board. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

HB and SG contributed to the conception and design of the study. SG programmed the study, organized the online data collection, maintained the participant data, and performed the statistical analysis. DM performed the statistical analyses. HB and SG wrote the first draft of the manuscript. All the authors wrote sections of the manuscript, contributed to manuscript revision, read and approved the submitted version.

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ORIGINAL RESEARCH
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Psychosis and Psychotic-Like Symptoms Affect Cognitive Abilities but Not Motivation in a Foraging Task

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Background and Objective: Goal-directed behavior is a central feature of human functioning. It requires goal appraisal and implicit cost-benefit analyses, i.e., how much effort to invest in the pursuit of a certain goal, against its value and a confidence judgment regarding the chance of attainment. Persons with severe mental illness such as psychosis often struggle with reaching goals. Cognitive deficits, positive symptoms restricting balanced judgment, and negative symptoms such as anhedonia and avolition may compromise goal attainment. The objective of this study was to investigate to what degree symptom severity is related to cognitive abilities, metacognition, and effort-based decision-making in a visual search task.

Methods: Two studies were conducted: study 1: $N = 52$ (healthy controls), and study 2: $N = 46$ (23 patients with psychosis/23 matched healthy controls). Symptoms were measured by the CAPE-42 (study 1) and the PANSS (study 2). By using a visual search task, we concomitantly measured (a) accuracy in short-term memory, (b) perceived accuracy by participants making a capture area or confidence interval, and (c) effort by measuring how long one searched for the target. Perseverance was assessed in trials in which the target was omitted and search had to be abandoned.

Results: Higher levels of positive symptoms, and having a diagnosis of psychosis, were associated with larger errors in memory. Participants adjusted both their capture area and their search investment to the error of their memory. Perseverance was associated with negative symptoms in study 1 but not in study 2.

Conclusion: By simultaneously assessing error and confidence in one's memory, as well as effort in search, we found that memory was affected by positive, not negative, symptoms in healthy controls, and was reduced in patients with psychosis. However, impaired memory did not concur with overconfidence or less effort in search, i.e., goal directed behavior was unrelated to symptoms or diagnosis. Metacognition and motivation were neither affected by cognitive abilities nor by negative symptoms. Clinically, this could indicate that struggles with goal directed behavior in psychosis may not solely be dependent on primary illness factors.

Keywords: metacognition, goal-directed behavior, schizophrenia, short-term memory, decision-making

INTRODUCTION

Motivation and goal-directed behaviors are complex phenomena. Consider the following: You meet four students and all tell you that they are motivated to pass an important exam. Student A is very smart, she knows she is high performing, and she spends some time but not all day on studying for the exam. Student B is smart, and she knows she can pass the exam if she studies all day. Student C is not as smart as students A and B, but she still wants to pass the exam and she, too, studies all day. Student D is as smart as student C but thinks of herself as being as smart as student A and does not spend all day studying for the exam. This example illustrates the interplay of cognitive ability, knowing about one's ability, and effort (here the amount of learning spent) affecting goal-directed behavior. Without asking about motivation, only measuring the outcome or the effort, we would draw different conclusions. Students A and D would appear as not having spent much effort, hence not being motivated. Students C and D may appear not motivated as they might not have passed the exam.

We often infer motivation from the intensity, e.g., speed or vigor, with which a person tries to achieve a goal and how much effort she invests in a task, respectively. However, this equates motivation with effort, while effort depends on knowing one's abilities and chances of reaching the goal. For physical effort this is obvious: A well-trained person needs less energy to catch the last bus into town than an untrained person, but both can be similarly motivated. A person using crutches may also be similarly motivated to catch the last bus but knows they cannot make it and hence is not running to the bus. This knowing of what one can achieve requires metacognition (Norman et al., 2019).

Goal-directed behavior, which is an operationalization of motivation (Hebb, 1955; Duffy, 1957), requires knowledge about one's abilities (metacognition), and the effort needed for reaching the goal. The latter can be, for example, how fast (latencies, vigor) or how hard (perseverance) one tries to reach the goal (Salamone and Correa, 2012). Conversely, if one overcomes the costs of effortful actions to achieve a desired outcome (Chong et al., 2016), the costs will depend on one's abilities. It is rational to not spend any effort on a too costly or fruitless task (Pfuhl et al., 2009), or alternatively, to try solving the task in a cheaper manner (Pfuhl, 2012; Mækelæ et al., 2018). Thus, to infer about a person's motivation, we have to know the relative effort spent. Only measuring absolute effort spent does not suffice.

Amotivation and effort-related impairments are common symptoms in many mental disorders, including schizophrenia (Fervaha et al., 2015) and depression (Clery-Melin et al., 2011). Both are associated with a lack of goal-directed behavior, impeding daily functioning (Barch et al., 2014; Bergé et al., 2018). However, effort-related impairments are sensitive to the tasks in question (Horan et al., 2015; Reddy et al., 2015). Often tasks used in research or clinical practice do not control for cognitive abilities and metacognition, which is known to also be affected in these mental disorders (Moritz et al., 2015; Sun et al., 2017; Norman et al., 2019). Indeed, if a person is like student D, then it is metacognition, not effort spending, that is aberrant. Students C and D need in absolute terms to spend more effort.

To tease apart which factors contribute to motivation and goal-directed behavior, we developed a foraging task that simultaneously measures how good a person's visual short-term memory is, how good a person thinks their memory is (metacognition), and, consequently, how much effort they spend in finding a predefined target. By using a mathematical model, we can also infer the costs of foraging and thereby calculate the relative effort spent. We tested this in two studies. In study 1 we recruited healthy participants from the general population that varied in the severity of dysphoria and psychotic-like experiences. We thereby aimed to have a larger variation in cognitive abilities and metacognitive abilities than found in a pure student sample. In study 2 we recruited patients with a diagnosis of schizophrenia and related psychoses, as there is inconsistency in the literature (Gold et al., 2015; Green et al., 2015; McCarthy et al., 2016; Culbreth et al., 2018) in whether they lack effort or not, and whether this is due to cognitive dysfunctions, aberrant metacognition, or true amotivation, i.e., no desire to reach the goal. In both studies we used the same paradigm to measure concomitantly cognitive ability, here visual short-term memory, implicit metacognition (Honig et al., 2020), and effort in a foraging task (Pfuhl et al., 2009, 2013). We first present the task before we review relevant clinical literature.

The Precision and Motivation Task – A Simple Foraging Task

In an attempt to disentangle the various components inherent in tasks involving goal-directed behavior, we developed the Precision and Motivation Task (PMT). The task is based on a mathematical model (Pfuhl et al., 2009), trying to quantify the question of how much effort one should invest in an activity (effort estimation), and when to abandon it in relation to how likely it is to find reward relative to the cost of searching (reward valuation and memory estimation).

To illustrate, imagine a treasure hunt where you hide a small cache with sweets for a children's party somewhere in a nearby park in the morning. At lunch time you check on the cache and find it again. In the late afternoon you (with the children) go out to find the cache. Since you are distracted on your way to the location you have a hard time finding the exact location. You don't want to embarrass the children and continue searching but you also see families with dogs, and after a while consider the option that the cache got raided and abandon the treasure hunt.

In between the extremes of knowing for sure and having no idea, there is an optimal limit of investing in the search. As you forget (memory of the location of the cache becomes less precise), the optimal search limit first rises, but then it declines steeply. Furthermore, your investment depends also on the probability of it being there, and not having been removed by a third party (here: cache raided by a dog). This probability of a third party is never zero. However, the closer it is to zero, the longer you should search irrespective of the precision of your memory. If the probability of the target being gone is high, you should–as in the case of having poor memory–not start searching at all (Pfuhl et al., 2009). This cognitive weighing of pros and cons of investing effort is an example of effort-based decision making.

In this foraging task the investment in search depends on how well one thinks one's memory is, and how likely one thinks that no third party raided the cache. In our task, we inform about the probability of the cache being raided, and measure directly how well a person thinks she remembers the cache. We refer to how well one thinks one remembers as meta-cognitive ability in the remainder of the article.

In sum, this task allows us to measure how precise a person's memories for a target actually are (visual short-term memory), how precise they believe those memories are (meta-cognitive ability), and how much effort they invest in searching for the target, respectively (Pfuhl et al., 2013). We also measured perseverance, latencies, and vigor. Vigor has been found to be an implicit measure for the subjective utility of the outcome (Shadmehr et al., 2019). Perseverance is the duration of search relative to one's metacognitive ability.

Motivation, Vigor, and Effort-Based Decision Making in Psychosis and Schizophrenia

It has previously been thought that motivational deficits in schizophrenia were linked to the anhedonia and the blunting of affect seen in negative symptoms (Rømer Thomsen et al., 2015). However, it appears that in-the-moment hedonic experiences are in fact intact (Llerena et al., 2012). This has led researchers to explore other possibilities, now suggesting that individuals with negative symptoms have deficits in a range of reward-related processes, making it difficult to translate reward information into motivated behavior (Blanchard and Cohen, 2006; Whitton et al., 2015; Barch et al., 2016). This has been proposed as a deficit of vigor, the speed of activities toward a goal, dependent on the computation of reward expectation, i.e., subjective goodness of an option, and effort (Shadmehr et al., 2019).

Others have linked negative and depressive symptoms, both prevalent in schizophrenia (an der Heiden et al., 2016) to amotivation (Pelizza and Ferrari, 2009), and accordingly to a lack of goal-directed behavior (Brown and Pluck, 2000). A range of studies have found that individuals with psychotic disorders or schizophrenia have effort-related impairments (Barch et al., 2014; Whitton et al., 2015) and that there is an association between the degree of negative symptoms and these impairments (Bergé et al., 2018). In healthy populations similar findings have been reported for negative symptom-like phenomena (Stefanis et al., 2002; Terenzi et al., 2019).

Cognitive Abilities in Psychosis and Schizophrenia

Research on cognitive dysfunctions in psychosis in general, and schizophrenia in particular, is abundant, as these have been considered core features for at least the last century (Mesholam-Gately et al., 2009). They have been studied in relation to negative symptoms, which are characterized by a lack of interest in goal-directed behavior and affective expression (Andreasen et al., 1995), as well as psychomotor poverty (Liddle and Barnes, 1990), and in relation to positive symptoms (Moritz et al., 2008), characterized by unwilled mental experiences such as hallucinations or paranoia. They are known to appear before psychosis onset (Barragan et al., 2011; Bora and Murray, 2014) and have also been found in first-degree relatives of persons with psychosis (Snitz et al., 2006; Montag et al., 2012).

Deficits are most prominent in memory (working memory, verbal, and visual memory), processing speed, and visuospatial abilities (Mesholam-Gately et al., 2009). Severity of general symptom load appears to be related to severity of general cognitive deficits in some studies (Barder et al., 2013), but minimally so in others (Dominguez Mde et al., 2009). Negative symptoms specifically appear to be associated with poorer memory (both verbal and visual), verbal fluency and executive functions (O'Leary et al., 2000), and with poorer motor and information processing speed (Rund et al., 2016), or movement vigor. However, some researchers have proposed that it might not be negative symptoms in themselves that drive cognitive dysfunction–or the other way around–but that this relation is moderated by psychological factors such as a defeatist belief (Grant and Beck, 2009) and an underconfidence in one's abilities (Szu-Ting Fu et al., 2012). The observed overlap of negative with depressive symptoms (an der Heiden et al., 2016) supports this. Both the memory dimension of deficits and negative symptoms are particularly important for daily life functioning, and therefore, highly relevant foci of study (Fu et al., 2017). Both negative symptoms and cognitive deficits are longitudinally more stable compared to positive symptoms, which are more likely to wax and wane (Harvey et al., 2006), leading to the widely held belief that these are the more trait-like core characteristics of schizophrenia.

In sum, motivation, effort-based decision making, and goal-directed behavior in psychosis and schizophrenia appear to be linked through cognitive (working memory, processing speed), vigor (the reflection of the economic evaluation of cost vs. benefit as speed toward a goal), and symptom (especially negative) factors. Several paradigms have been developed to be able to more objectively measure motivation and effort (Gorissen et al., 2005; Horan et al., 2015; Reddy et al., 2015; Bergé et al., 2018). These tasks measure how much effort one is willing to exert across different reward amounts and reward probability conditions. They do not measure effort relative to one's cognitive abilities and belief in one's abilities. Hence, analyzing the various components involved remains a challenge.

In two studies we investigated the role of the various components in our PMT. Our aim is identifying which component(s) contributes to effort-based decision-making in psychosis. In detail:

> As **hypothesis 1a)** we predicted neurocognitive deficits in participants to be associated with load of symptoms and symptom-like phenomena. In **hypothesis 1b)** we predicted a difference in metacognitive ability among individuals: On the one hand we expected dysphoric participants to be underconfident (Szu-Ting Fu et al., 2012) and participants with psychotic-like experiences to be overconfident about their memory (Moritz et al., 2015).
>
> In **hypothesis 2a)** we expected that participants with many symptoms will search less than needed to find the target. In **hypothesis 2b)** we expected reduced speed and vigor

among participants with predominantly negative symptoms and symptom-like phenomena and dysphoria compared to participants scoring predominantly high on positive symptoms and symptom-like phenomena and to the control group with no symptoms.

STUDY 1 – INVESTIGATING GOAL-DIRECTED BEHAVIOR ALONG THE PSYCHOSIS SPECTRUM

The aim of this study was to identify which of the several psychosis-like phenomena contribute the most to a lack of motivation and goal-directed behavior in a non-clinical sample. We aimed to recruit healthy, not at risk, participants with a first-degree relative diagnosed with a psychotic disorder to increase the odds that our sample varies in the severity of psychosis-like symptoms.

PARTICIPANTS

Fifty-three individuals with no current or prior history of mental illness were recruited through social media and on a volunteer basis. Twelve of the participants had first-degree relatives with mental illness history, of whom four reported a relative with a schizophrenia diagnosis and eight with a first-degree relative with a bipolar diagnosis. The age ranged from 18 to 49 years, with mean age of 26 (*SD* = 7.1). Thirty-seven (70%) of the participants were women. Participants were excluded if they presented a substance use disorder (except nicotine), clinically significant psychiatric symptoms, or if they had neurological disorders. One participant was excluded due to abandoning testing after two tasks, leaving 52 participants.

Participation was rewarded with a gift certificate worth 150 NOK, approximately $16.

Materials

Neurocognitive Tests

We used the Trail Making Test (TMT) A and B (Reitan and Wolfson, 1985). TMT A yields an indication of psychomotor speed and visual processing, which is an attention and processing speed measure, whereas TMT B is an estimate of mental flexibility and inhibition, central compounds of cognitive control and executive function. The task was administered and interpreted as described in Bowie and Harvey (2006). We used the Digit Symbol Substitution Task (DSST), a test that is sensitive to psychomotor speed and general speed of information processing. The score is computed by counting the number of correct pairings completed in 90 s.

Precision and Motivation Task

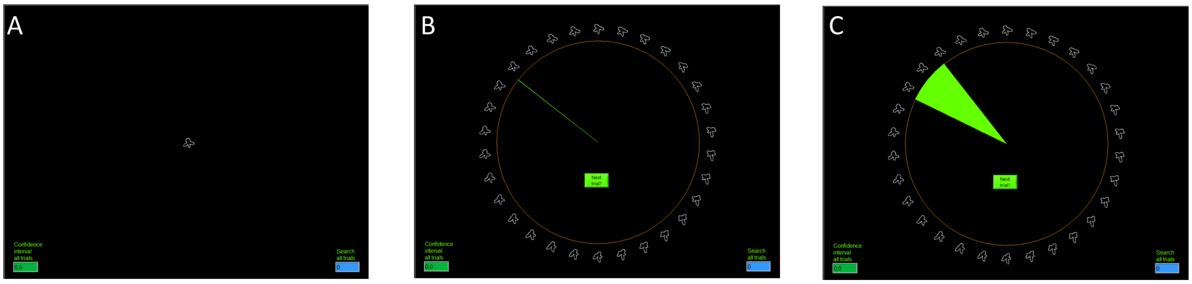
We developed an effort-based decision-making paradigm, where one has to search for a previously seen shape (visual short-term memory), indicate how well one thinks that one remembers the shape (implicit metacognitive assessment), and decide to search for it with the probability of succeeding in finding the shape signaled (effort-based decision). There are points to be scored for correct responses. We presented the task as a computer game with a background story of squirrels hiding nuts and other squirrels stealing them. The game has four stages.

Stage 1: An abstract shape (the "nut") is shown for 2 s (**Figure 1A**). The participant is instructed to remember the shape.

Stage 2: The participant must indicate where, among 30 similar shapes arranged continuously on a circle, the previously seen shape is located. If she does not remember, she can move on by clicking the "next trial" button. This stage measures the error of one's memory as the deviation between the chosen shape and the target shape, measured in degrees (**Figure 1B**).

Stage 3: From the indicated location of the shape the participant draws a capture area (**Figure 1C**). The participant is instructed to make the area large enough so that she is sure the shape is located somewhere inside the capture area (Graf et al., 2005; Pfuhl et al., 2013; Honig et al., 2020). The size of the capture area can be considered an implicit measure of confidence. Points are received depending on the size of the capture area in relation to one's error in memory. The maximum score is 10 points in each trial, with points subtracted if the capture area is made too large, but no points earned if the capture area is made too small. The points are presented after each trial (stage 5). Metacognitive error is calculated as the ratio of the logs of the size of the capture area and the memory (stage 2). A ratio of 1 indicates perfect calibration between real and perceived precision of memory. A ratio larger than 1 indicates underconfidence whereas a ratio smaller than 1 indicates overconfidence.

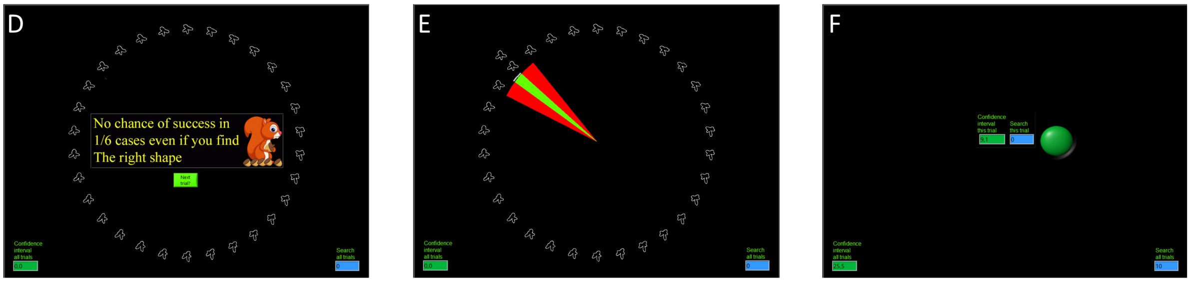
Stage 4: The participant searches for the shape after being presented with information about the probability of finding it, represented by a mean or a kind squirrel (**Figure 1D**). The mean squirrel is hungry and steals the nut in 1 out of 3 cases. The kind squirrel is less hungry and steals the nut in 1 out of 6 cases (representing 67 and 83% probability of success or finding the nut). The participant was informed that the nut will be found if searched long enough but that search has to be abandoned if she thinks the nut got stolen. These stolen trials are referred to as no-target trials and are not signaled. Search was done by clicking the left mouse key repeatedly. The search started where the participant indicated she thinks the nut is located (same as for stage 3) and expanded equally to each side (**Figure 1E**). The search ended either when the search radius reached the location of the nut in all but no-target trials, or the participant abandoned search by clicking "next trial." Ten points were received if the nut was found, otherwise the search yielded zero points. Hence, in each trial, participants earned points for their metacognitive ability (stage 3, point amount variable) and success (10 or 0 points). The search phase represents goal-directed behavior and has to be seen in relation to the capture area. Searching less than the indicated capture area means that one spends less effort than one's belief or (meta-) memory indicates. Accordingly, we calculated a perseverance score as the ratio of logs of search radius in no-target trials and the size of the capture area. A number larger than 1 means that participants searched longer than indicated by the capture area made. Conversely, a score below 1 indicates searching less than announced by the capture area made.



Stage 1: encoding, 1 sec

Stage 2: indicate best guess

Stage 3: make capture area



Information about p(success)

Stage 4: search + feedback

Stage 5: points earned

FIGURE 1 | Precision and motivation task. **(A)** Sample phase, here a squiggly shape is shown for 2 s. **(B)** Retrieval phase, 30 similar shapes are organized in a circle. The participant indicates the location of the shape looking most alike as the one seen in the sample phase. **(C)** Confidence phase, participants make a capture area large enough to be certain that the shape from the sample phase is included in the area. **(D)** The chances of reward are signaled. The probability of not finding the "nut" is indicated by the squirrel, either 1/6 or 1/3. **(E)** Search phase, the participant searches for the "nut," starting at the indicated location from the retrieval phase. **(A)** White line stretches in both directions for each click, indicating the search. When found or abandoned, the program provides visual feedback on the capture area with red indicating excess area. **(F)** Points earned for making a well-calibrated capture area (shown in the green rectangle), and points earned for search (shown in the blue rectangle) are presented. Total earnings are always presented in the bottom, bottom left for capture area and bottom right for search. Apart from the sample phase, all other phases were self-paced. Abandoning retrieval, confidence judgment, and search was possible by clicking on the "next trial" button (no points earned).

Stage 5: presented the earned points, i.e., feedback on how many points participants earned in stage 3 for making a capture area, where the maximum was 10 points and points less than 0 (negative points) were possible if an excessive large capture area was made, and in stage 4 where one either received 10 points or no points (**Figure 1F**). There was no incentive for abandoning a trial.

The PMT had 45 trials, 30 trials with 1/6 probability of the nut being stolen, 15 trials with 1/3 probability of the nut being stolen. In stolen (no target) trials one sees the maximal effort a participant is willing to exert for a reward. The task was programmed in Labview.

The task measured precision in visual short-term memory, perceived precision, hit rate, absolute and relative search effort, latencies and vigor by which participants searched.

CAPE-42

To measure subclinical symptoms, the participants completed the Norwegian version of the Community Assessment of Psychic Experiences (CAPE-42) (Stefanis et al., 2002) questionnaire. The CAPE-42 was developed to measure the lifetime prevalence of psychotic experiences in the general population. The CAPE has three subscales: positive (CAPE-P), negative (CAPE-N) and depressive (CAPE-D). The questionnaire was implemented in Qualtrics.

Internal consistency for the CAPE-42 total score ($\alpha = 0.94$), as well as for the positive symptom subscale ($\alpha = 0.84$), the negative symptom subscale ($\alpha = 0.90$), and the depressive symptom subscale ($\alpha = 0.87$), were high. CAPE negative and CAPE depressive subscale correlated highly, $\rho = 0.823$, $p < 0.001$. Because of this correlation and the significant conceptual overlap (an der Heiden et al., 2016), and to maximize the probability of score variability in a healthy population, we created a new subscale CAPE-ND being the sum of those two subscales.

Procedure

Participants read and signed the consent form and completed a survey asking about education and employment, alcohol habits, medication and substance use habits, mental health, and neurological disorders. Thereafter they performed the TMT A and B and the DSST. These tests were done with pen and paper and a stopwatch. Next, we demonstrated the PMT introducing the stages and point structure step-wise in six demonstration trials. The task took approximately 22 min to complete. Lastly, participants answered the CAPE-42.

Ethics

The project was approved by the Regional Committee for Medical and Health Research Ethics Norway, Region West (2011/1198/REK Vest).

Statistical Analyses

We used multiple regression for TMT A, TMT B, DSST with CAPE-P, CAPE-ND, and age as predictors. The results do not change when including education (Tombaugh, 2004).

For the PMT we calculated the average latency to start a trial and vigor (speed at which the search clicks were made). Average error in memory was the absolute error of memory in all 45 trials. Similarly, the average size of the capture area was based on all trials where a participant made a capture area. Metacognitive error was the relative size of the capture area to one's error in memory.

Search radius was calculated separately for trials with a high or low probability of finding the target, and for trials where the target could be found, and where it could not be found. In trials where the shape could not be found we calculated the perseverance score, which expressed search investment relative to perceived error. Hits are all trials where the search was long enough to include the target shape, and a high hit rate suggested a decision criterion based on low effort sensitivity.

Finally, we calculated the costs of searching by using the 1D approach described in Pfuhl et al. (2009). The cost function depends on one's perceived error and search as well as the probability of success. Details of the mathematical derivation and code to evaluate the costs of searching can be found here: https://osf.io/9bfxt/.

We used multiple regression for the indices of the PMT with the CAPE-P, CAPE-ND, and age as predictors. Data was analyzed in R and JASP (JASP Team, 2020).

Results

None of the participants had psychiatric symptoms indicative of mental disorder; however, 13 participants reported feeling depressed or dysphoric at a sub-clinical level.

Hypothesis 1a predicted that neurocognition as measured by the TMT A and B, the DSST and error in the visual short-term memory task would be impaired in participants with high CAPE-42 scores. **Table 1** provides the descriptives for those four tests, as well as for the symptom severity in this sample.

There was no significant relationship between TMT A and CAPE-P ($\beta = 0.18$, $t = 1.07$, $p = 0.29$) or CAPE-ND ($\beta = -0.07$, $t = -0.42$, $p = 0.68$), but there was a significant relationship of age and TMT A ($\beta = 0.50$, $t = 3.83$, $p < 0.001$), i.e., younger people were faster. There was a significant relationship of TMT B performance with lower levels of CAPE-P ($\beta = 0.39$, $t = 2.09$, $p = 0.042$), but not with CAPE-ND ($\beta = -0.22$, $t = -1.23$, $p = 0.22$) or age ($\beta = 0.13$, $t = 0.91$, $p = 0.37$).

TABLE 1 | Symptom severity and neurocognitive task performance ($N = 52$) in study 1.

	M(*SD*)	Minimum	Maximum
CAPE-P	25.62 (4.9)	20.00	41.00
CAPE-ND	42.64 (11.1)	26.00	69.00
TMT-A	24.74 (5.9)	14.37	38.18
TMT-B	59.16 (16.6)	30.49	100.85
DSST	57.48 (7.9)	37.00	73.00
Error in PMT	18.29 (7.3)	7.23	40.47

CAPE-P, positive symptom scale from the CAPE-42. CAPE-ND, negative/depressive symptom scale. TMT A and TMT B is measured in seconds, DSST is measured as number of correct symbols. Error in PMT is measured in degrees. Means (M; with standard deviations SD).

There was a significant negative relationship between CAPE-P and completed pairings in DSST ($\beta = -0.53$, $t = -3.29$, $p = 0.002$) and between age and DSST ($\beta = -0.39$, $t = -3.10$, $p = 0.003$), i.e., more positive symptoms and older age were associated with fewer completed pairings. There was no significant relationship between DSST and CAPE-ND ($\beta = 0.08$, $t = 0.52$, $p = 0.60$).

The error in memory was statistically significantly associated with CAPE-P ($\beta = 0.672$, $t = 4.406$, $p < 0.001$), i.e., the more positive symptoms, the poorer visual short-term memory. There was no significant relationship between visual short-term memory and CAPE-ND ($\beta = -0.227$, $t = -1.517$, $p = 0.136$) or age ($\beta = 0.141$, $t = 1.141$, $p = 0.259$).

Hypothesis 1b predicted aberrant metacognition in participants scoring high on symptoms, i.e., participants reporting positive symptom-like experiences would be overconfident whereas participants high on depression/negative symptoms would be underconfident.

Metacognitive Error

On average participants were well calibrated, i.e., the size of the capture area corresponded well to their error, $M = 1.037$, $SD = 0.122$. The predictors explained only 11.4% of the variance, $F = 2.053$, $p = 0.119$. The mean *hit rate*, searching long enough to find the target, was 0.66 ($SD = 0.11$), ranging from 0.42 to 0.96. The predictors explained only 11% of the variance, $F = 1.977$, $p = 0.13$.

Thus, we found that symptom severity and age did not relate to how well people assess their memory to be; there was no clear indication of over- or underconfidence, i.e., aberrant metacognition, in participants with psychotic-like experiences or those with dysphoria.

Hypothesis 2a predicted that goal-directed behavior would be diminished in people scoring high on negative or depressive symptoms, i.e., that they would search less than indicated by the capture area. Since the search radius depends on how well a person thinks she remembers the shape, we used the perseverance score. A score larger than 1 indicates searching beyond the capture area made. In the high probability condition the perseverance score was 1.24 ($SD = 0.166$), and in the low probability condition the perseverance score was 1.191 ($SD = 0.168$), indicating that participants searched beyond the capture area made in both the high and the low probability conditions. One sample t-test confirmed that the search exceeded the capture area made [high probability condition: $t(51) = 10.4$, $p < 0.001$, $d = 1.443$; low probability condition: $t(51) = 8.21$, $p < 0.001$, $d = 1.138$]. Perseverance was lower in the low probability condition, $t(51) = 2.968$, $p = 0.005$, $d = 0.412$ than in the high probability condition. Next, we performed stepwise multiple regressions with positive and negative/depressive symptom scores and age as predictors. In the high probability condition, the remaining predictor was the CAPE-P, $\beta = -0.305$, $t = -2.264$, $p = 0.028$, indicating less perseverance associated with higher positive symptom scores. In contrast, for the low probability condition, only the CAPE-ND remained, $\beta = -0.324$, $t = -2.417$, $p = 0.019$, indicating less perseverance for higher negative/depressive symptoms. Since CAPE-P and CAPE-ND correlated highly ($\rho = 0.616$, $p < 0.001$), general symptom severity (total CAPE-42 score) related to search investment, i.e., the more symptoms a participant reported, the less was their relative search investment.

Hypothesis 2b predicted that individuals with many negative or depressive symptoms show longer latencies and lower vigor. The average latency to start a trial was 2.76 s (*SD* = 1.14), ranging from 1.18 to 6.26. The average vigor in high probability trials was 0.25 (*SD* = 0.09), ranging from 0.15 to 0.64. In the low probability trials the mean vigor was 0.26 (*SD* = 0.07), ranging from 0.16 to 0.59. That is on average a participant made four clicks per second. There was no relationship between latency, vigor, and symptom severity or age, all $p > 0.05$.

Finally, we calculated the costs of searching and found that it did not relate to symptom severity or age, $p > 0.4$. **Figure 2** summarizes the relationship between the CAPE-42 subscores and error in memory, perceived error in memory, and relative investment in search (perseverance).

STUDY 2 – ASSESSING GOAL-DIRECTED BEHAVIOR IN PATIENTS WITH SCHIZOPHRENIA OR RELATED PSYCHOSIS

Study 1 recruited participants along the psychosis continuum. Cognitive abilities were lower among those with more symptoms, and symptom severity was associated with diminished effort spent, despite similar costs.

We therefore predicted that: **H1a**: Patients perform worse on the neurocognitive tests compared to matched controls. **H1b**: Patients have an aberrant meta-cognitive ability compared to healthy controls. **H2a**: Goal-directed behavior is reduced, i.e., search is less than indicated by the capture area, in patients compared to controls, and is associated with negative symptoms. **H2b**: Latency and vigor is reduced in patients compared to controls, and is associated with negative symptoms.

PARTICIPANTS

Study participants (*N* = 23) for the clinical group were recruited from the on-going TIPS 2 (early Treatment and Intervention in Psychosis, start in 2002) study, and invited to partake in this sub-study by one of the research clinical team members, which consists of highly trained psychiatric nurses. Recruitment was conducted between 2015 and 2019, and assessments consisted of the standard TIPS protocol described elsewhere (Melle et al., 2004), with additional assessments as described above. The main inclusion criteria, described in detail elsewhere, were having a first episode of non-affective or affective mood incongruent, non-organic psychosis, and age between 15 and 65 years. Main exclusion criteria were suffering from neurological disorder, primary substance use disorder, or IQ below 70. The patients agreed to baseline assessment, and follow-up after 3 months and 1, 2, and 5 years. Mean duration since inclusion and baseline assessment was 4 years (minimum: 1 year, maximum: 5 years). We recruited 23 age and gender matched participants as healthy controls. One recruited participant had a first-degree relative with psychosis and was excluded. We replaced this participant with one healthy control recruited in study 1. Inclusion criteria for healthy controls were no first-degree relative with a mental health diagnosis, no substance use disorder (except nicotine), no clinically significant psychiatric symptoms, and no neurological disorders. All participants gave informed written consent.

Materials

We used the same neurocognitive tests and the same PMT as in study 1. Symptoms were assessed by using the Positive and Negative Syndromes in Schizophrenia interview (PANSS) (Kay et al., 1987). The interview, the neurocognitive tests, and the computer task were conducted by three psychologists, under supervision from author WH. The TIPS team holds regular reliability trainings to avoid drift, and previous reliability assessments have proven good reliability (Hegelstad et al., 2012). Patients only received the PANSS.

Procedure

Patients were first interviewed with the PANSS before starting the behavioral tasks. Matched control participants were not interviewed, however, demographics were recorded (age, gender, education, medication, and handedness).

Ethics

This study was approved by the Regional Committee for Medical and Health Research Ethics Norway, Region West (2011/1198/REK Vest).

Statistical Analyses

The indices are similarly calculated as in study 1. Group comparisons are done with t-tests, test of equality of variances done with Levene's test, and effect of symptom severity on outcomes assessed with regression analysis.

Results

Sample characteristics of study 2 are summarized in **Table 2**. **Hypothesis 1a** was confirmed: The patient group was significantly slower on the TMT A and TMT B, and they completed fewer pairings in the DSST and had larger errors in memory. Patients needed on average 30.83 s (*SD* = 8.7) on the TMT A, and 98.1 s (*SD* = 45.1) on the TMT B, whereas controls needed 23.24 s (*SD* = 4.8) and 56.88 s (*SD* = 14.45), respectively. Patients solved on average 55.4 (*SD* = 15.1) pairings, and controls solved on average 65.35 (*SD* = 16.3) on the DSST. Patients had larger errors of their visual short-term memory in the PMT. The mean deviation in degrees for patients was 27.5 (*SD* = 11.18), and for controls 22.12 (*SD* = 10.01). Since we had directional predictions we used one-sided Welch's t-test, and all comparisons were statistically significant (**Table 3**). There was a significant

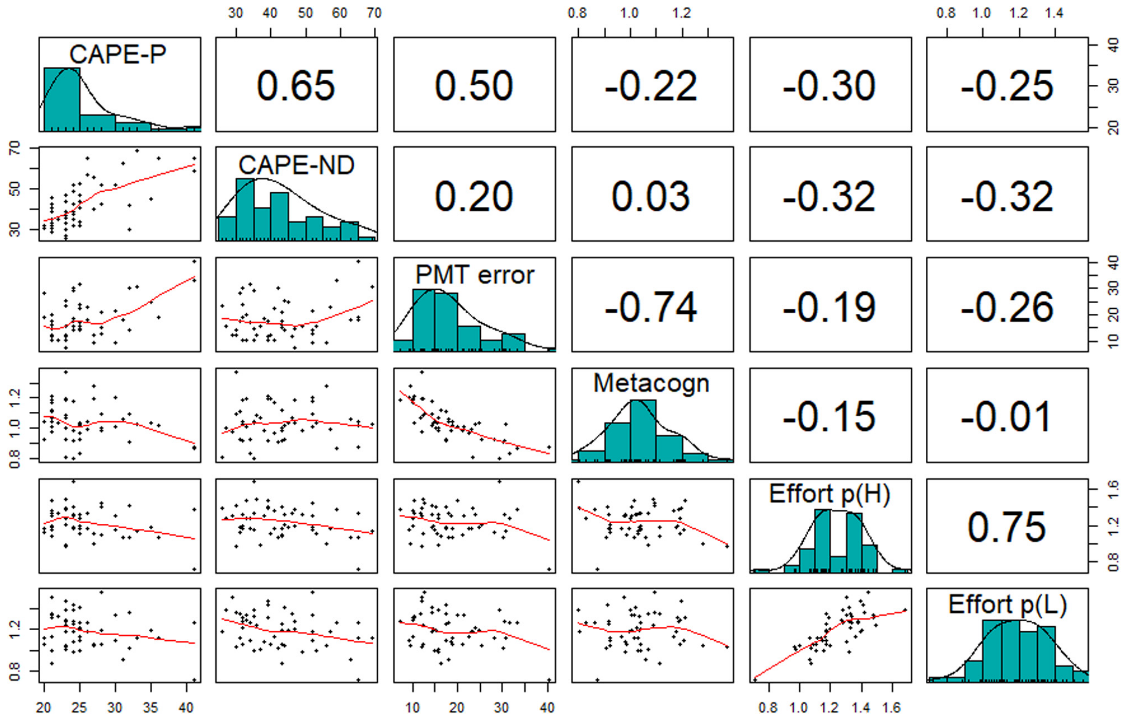


FIGURE 2 | Association of symptom severity with error in memory (deviation), metacognitive error, and investment in search in study 1. Numbers represent Pearson's correlation coefficients, and asterisks indicate a *p*-value below 0.05. The more positive symptoms the more errors in memory (Pearson's $r = 0.5$, $p < 0.001$) and also the more negative/depressive symptoms ($r = -0.65$, $p < 0.001$). The more negative/depressive symptoms a participant had, the less the person invested in searching relative to the belief in their memory ($r = -0.32$ $p = 0.02$). General symptom severity (CAPE-P and CAPE-ND) related to relative effort in both probability conditions (not shown). Perseverance (effort) in the high and low probability condition were highly correlated ($r = 0.75$, $p < 0.001$). Finally, the worse the memory (larger PMT error) the more overconfident participants were ($r = -0.74$, $p < 0.001$).

TABLE 2 | Sample characteristics study 2.

	Patients (*n* = 23)		**HC (*n* = 23)**	
	N (%)		**N (%)**	
Gender, female	8 (34.7)		7 (30.4)	
Gender, male	15 (65.3)		16 (69.6)	
Diagnosis				
Schizophrenia spectrum	16 (69.6)		n/a	
Affective psychosis	1 (4.3)		n/a	
Other psychosis[1]	6 (26.1)		n/a	
	***M* (SD)**	***Md* (*r*)**	***M* (SD)**	***Md* (*r*)**
Age	27.1 (8.7)	24 (16–48)	26.0 (9.9)	23 (15–52)
Years of education after secondary school total score	2.7 (2.8)	3 (0–7)	4.4 (2.8)	4 (2–11)
PANSS subscale				
Positive[2]	11.9 (4.7)	12 (7–26)	n/a	n/a
Negative[2]	13.5 (6.7)	11 (7–29)	n/a	n/a
General[3]	25.5 (8.9)	24 (16–54)	n/a	n/a
DDD antipsychotic	0.72 (0.77)	0.66 (0–2.7)	n/a	n/a

Means (M; with standard deviations SD) and medians (Md; with range r) are displayed. [1]Delusional disorder, Psychosis NOS. [2]Maximum score 63. [3]Maximum score 112. DDD, defined daily dosis.

larger variation in the patient group for the TMT A ($F = 9.13$, $p = 0.004$) and TMT B ($F = 9.909$, $p = 0.003$) but not for the DSST or error in memory.

TABLE 3 | Independent Samples Welch's *T*-Test, one-sided testing.

	t	***df***	***p***	**Cohen's *d***
TMT A	−3.658	34.288	< 0.001	−1.079
TMT B	−4.177	26.479	< 0.001	−1.232
DSST	2.150	43.776	0.019	0.634
PMT error	−1.717	43.465	0.047	−0.506

Within the patient group we performed step-wise regressions with the three subscales of the PANSS and age as predictors. We found that negative symptoms were associated with lower DSST performance, $\beta = -0.473$, $t = -2.462$, $p = 0.023$. For TMT scores and error in memory, neither age nor symptom severity were statistically significant predictors.

Hypothesis 1b was not confirmed; there was no difference in meta-cognition (e.g., overconfidence in the patient group), $t(44) = 1.019$, $p = 0.157$, $d = 0.301$. Both groups had a ratio slightly smaller than 1, HC group: $M = 0.972$, $SD = 0.128$, SCZ group: $M = 0.937$, $SD = 0.106$. Metacognitive error was not related to PANSS scores in the patient sample, all p-values > 0.2.

The mean *hit rate* was marginally smaller in the SCZ group than the HC group with a medium effect size, $t(44) = 1.552$, $p = 0.064$, $d = 0.458$, where patients found on average

56% (*SD* = 12%) of the targets whereas controls found 61% (*SD* = 13%).

Hypothesis 2a was not confirmed. Goal-directed behavior was similar in both groups. We noted, however, that one patient never started searching. The perseverance score was above 1 for both groups and in both conditions, all four $p < 0.001$. Mixed ANOVA yielded less search in the low compared to the high probability condition, $F(1,43) = 6.653$, $p = 0.013$, $\eta^2 = 0.015$, but no group difference, $F < 1$, or interaction, $F < 1$. Thus, patients and controls alike searched beyond the capture area made and invested more in trials with a higher chance to succeed. We performed a step-wise regression within the patient group. In the high probability condition, age was a statistically significant predictor, $p = 0.049$, but symptom severity did not predict perseverance in high or low probability trials. Finally, we assessed the costs of searching. The two groups had similar search costs, and within the SCZ group search costs did not relate to symptom scores or age, all $p > 0.1$. As can be seen in **Figure 3**, both groups are similar in their error in memory, capture area made, and search performed.

Hypothesis 2b was partly confirmed. There were no group differences for latencies or vigor, all *p*s > 0.1. Within the patient group, step-wise regressions with symptom scores and age as predictors revealed that larger vigor (fewer clicks per minute) was related to higher PANSS general scores in the high probability condition, $\beta = 0.487$, $t = 2.553$, $p = 0.019$, but failed to reach statistical significance in the low probability condition (pair-wise: $r = 0.377$).

Goal-Directed Behavior and Neurocognitive Abilities

After pooling the data from both studies, we explored whether error in memory, metacognitive error, or investment in search and cost of searching are related to the speed in the trail making tasks and the DSST. We also assessed whether perseverance was associated with the error in memory. We used Bonferroni correction (eight tests) and treat $p < 0.006$ as statistically significant.

We found a significant association between speed on the TMT B and error in one's memory, $\beta = 0.334$, $t = 2.978$, $p = 0.004$. TMT-A or DSST were not significant, $p > 0.2$. Metacognitive error, on the other hand, was neither related to TMT-A, TMT-B, nor DSST. These predictors only explained 6.5% of the variance, $F = 2.165$, $p = 0.097$. Goal-directed behavior, as measured with the perseverance score, was not predicted by TMT-A, TMT-B, or DSST, $p > 0.1$. Regarding motor speed, latency to start was positively related with TMT-B, $\beta = 0.258$, $t = 2.264$, $p = 0.026$, but not with TMT-A or DSST, $p > 0.2$. Vigor was not predicted by TMT-A, TMT-B, or DSST, $p > 0.1$. Costs of searching were not related to any of the neurocognitive test scores, $p > 0.1$. Finally, there was also no significant association between the perseverance scores (low and high probability condition) and error in memory, $p > 0.2$.

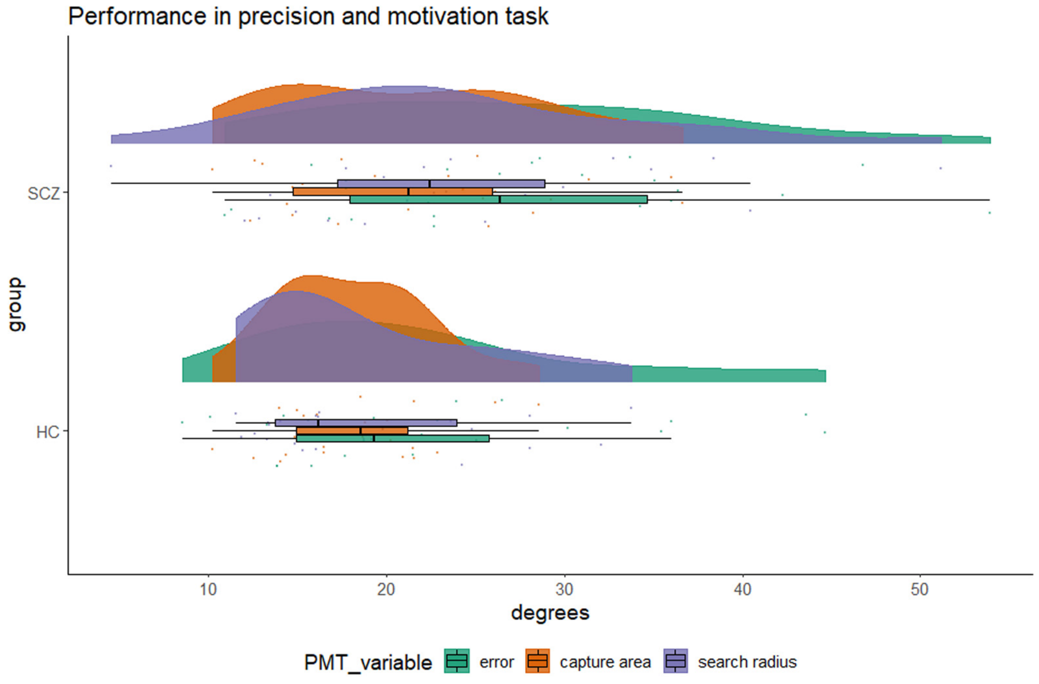


FIGURE 3 | Short-term memory performance expressed as errors in degrees, capture area made (proxy for implicit confidence judgment), and search radii among $n = 23$ patients with a diagnosis of schizophrenia or related psychosis (top row) and $n = 23$ matched healthy controls. The variances between the groups did statistically significantly differ for the capture area made (Levene's test, $p = 0.003$) but note that we use the capture area relative to error in memory (metacognitive ability) and relative to the search radius in no-target trials (perseverance).

DISCUSSION

The hypotheses tested in this study were first, that neurocognition be associated with levels of clinical and subclinical symptoms, and second, that positive symptoms be associated with over- and negative/depressive symptoms with underconfidence regarding memory; that third, symptom levels be associated with search effort, and finally, that negative sub-clinical and clinical symptoms be associated with reduced speed and vigor on an experimental task. Neurocognitive deficits were related to psychotic-like experiences and psychosis. Metacognition, expressed as under- or overconfidence, however, was well calibrated irrespective of diagnosis or symptom severity. Search effort and perseverance was more diminished the more psychotic-like experiences one had (study 1) and vigor was more diminished the more general symptoms a patient had (study 2). Goal-directed behavior as measured by the outcome (hit rate) was reduced in patients, but this finding was not statistically significant when compared to healthy controls.

In study 1 we found that neurocognitive deficits, both in the DSST and error in visual short-term memory, were related to positive, and not negative, symptom-like experiences. Similarly, Rossler et al. (2015) found that processing speed in the DSST was related to anomalous perception in healthy adults. Abu-Akel et al. (2016), though, found that participants with predominantly negative and few positive symptoms were less accurate in a visual-spatial working memory task. This difference might be due to our sample consisting of participants that had either very few symptoms (low CAPE-42 score) or had both many negative/depressive symptoms and positive-like experiences.

In study 2, testing participants with a diagnosis of schizophrenia, we replicated previous findings that patients have slower psychomotor speed and visual processing, i.e., have more problems with interference and mental flexibility and also poorer visual short-term memory (Schaefer et al., 2013). The finding that poorer memory performance was associated with lower scores on TMT-B might be explained by the executive component of both tests, in so far that both place a load on working memory and manipulation of “on-line” information. We found some indication that negative symptoms affect performance in the DSST; however, our sample was small and as for study 1, patients often had either few symptoms or both many negative/depressive and positive symptoms. We can therefore not conclude whether positive or negative symptoms contribute more to neurocognitive deficits.

Regarding meta-cognition, here confidence in one’s own memory, we used a non-verbal assessment of metacognition by asking participants to draw a capture area just large enough that it includes the target. This, in our opinion, yielded a more implicit and observable measure compared to that obtained by inquiring about confidence using rating scales. However, this implicit assessment of confidence yielded neither a group difference nor was it related to symptom-like experiences. Indeed, overconfidence seems not to be linked to delusional symptoms (Balzan, 2016). Furthermore, in a motoric-perceptual task Knoblich et al. (2004) found intact automatic self-correction, but a failure to report mismatches in patients. In line with our findings, this suggests that implicit metacognition is intact in psychosis.

Further, we found no overall association between hit rate and symptoms in study 1. In study 2 there was a small to medium effect size with patients having a lower hit rate than controls. Regarding search in those trials where the target could not be found, we found that symptom load was associated with perseverance among healthy participants in study 1, but not in patients. This could perhaps be explained by symptoms above a clinical threshold level no longer exerting marginally higher effects on perseverance. Furthermore, both participants in study 1 and patients in study 2 with higher symptom severity searched either less in relative terms (study 1) or less vigorously (study 2). In study 1, higher symptom levels predicted lower perseverance overall. For positive symptoms, this was more true for the high, and for negative symptoms, more true for the low probability condition, which might be a spurious effect or reflect subjective beliefs in succeeding. One possible explanation might be found in the underconfidence associated with negative/depressive symptoms: No matter the probability, perseverance is lower, while for positive symptoms, perseverance is not compromised by low probability. However, with high probability, search perseverance in positive symptoms might be influenced by hasty decision making, and consequently, less reflection on the actual probability of attaining the goal (Moritz et al., 2017). Still, we caution these results, as the effects are small. Importantly, despite reduced memory, the costs of searching were not different. The cost function takes into account the belief and the actual search investment. It is not a metabolic cost or based on motor behavior solely. Indeed, due to their less precise memory, patients did search longer and had to make more clicks to reach the goal, respectively.

Our results indicate that patients did value reward equally to healthy controls, as we found no reduced vigor or latency (Shadmehr et al., 2019) among the groups. Vigor was shown to reflect the subjective value, not the salience of the outcome. Such a similar subjective evaluation of the outcome agrees with previous research that found intact hedonic experiences (Llerena et al., 2012).

Our results did not support the hypothesized association of reduced effort with negative symptoms of psychosis, and highlight prior inconsistencies in this literature (Gold et al., 2015; McCarthy et al., 2016). This inconsistency may in part be due to the fact that reduced effort is just one of many components that can affect the expression of negative symptoms. Negative symptom expression depends on a range of psychological, behavioral, motor, cognitive, and biological phenomena. Passivity (due to having assumed a patient-role, for instance) resulting in reduced overall effort, or avolition, are only some of them. To illustrate, in the TIPS early detection mental health system it has previously been shown that early intervention and treatment is associated with less severe negative symptoms over the first 5 years of follow-up and superior vocational outcomes after 10 years compared to control areas. This may possibly be linked to intact effort in general, and one can speculate that relatively low levels of negative symptoms also may explain the lack of difference between patients and controls on the effort measure of the task in this study where patients come from the TIPS center. Indeed, in our study presented here, in spite of no association with negative symptoms specifically, patients had significantly slower speeds on the TMT tasks and DSST compared to healthy controls. Follow-up analyses using data from both studies indicated that speed measured by TMT B predicted latency to start search. TMT B also has an executive component, which may also explain this latency, as well as worse performance in the TMT-B correlated with worse performance in the PMT.

Regarding the analogy with the students, our findings suggest that participants with psychotic-like experiences and patients with a schizophrenia or other diagnosis of psychosis are on average more like student C. That is, our results suggest that neither neurocognitive deficits nor symptom patterns alone predicted metacognition or goal-directed behavior. Possible explanations could be that our task assessed metacognition implicitly and was not an obvious effort task. Finally, our data indicate that the relations between symptoms, cognition and meta-cognition are complex and deserving of further study, as the fact remains that many persons struggling with these symptoms do face difficulties investing effort in day-to-day tasks.

LIMITATIONS

The two studies had small sample sizes but still replicated the neurocognitive deficits. Our sample size provided not enough power to detect subtle motivational differences or find subgroups of patients with aberrant motivation. Further, one cannot directly compare symptom-like experiences from the CAPE-42 to PANSS symptoms. However, this could not be avoided since most healthy controls will score below clinical threshold on the PANSS; rendering this instrument not useful in a healthy population. Future studies should use the CAPE-42 also in patients.

CONCLUSION

By concomitantly measuring cognitive ability, subjective estimation of cognitive ability, and effort we found similar goal-directed behavior irrespective of symptom severity among persons with psychotic-like experiences and participants diagnosed with psychosis. Implicit metacognition was preserved in psychosis.

DATA AVAILABILITY STATEMENT

All data as well as the mathematical model of the Precision and Motivation task are available in an Open Science Framework repository: doi: 10.17605/OSF.IO/9BFXT.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Regional Committee for Medical and Health Research Ethics Norway, Region West (in Norwegian: REK Vest). Written informed consent to participate in this study was provided by the participants.

AUTHOR CONTRIBUTIONS

GP and WH designed the study and supervised the data collection. GP analyzed the data. HT modeled the cost function. GP, IK, and WH wrote the manuscript. All authors contributed to the article and approved the submitted version.

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Dissociable Effects of Monetary, Liquid, and Social Incentives on Motivation and Cognitive Control

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Humans are social creatures and, as such, can be motivated by aspects of social life (e.g., approval from others) to guide decision-making in everyday contexts. Indeed, a common view is that people may have stronger orientation toward social goals or incentives relative to other incentive modalities, such as food or money. However, current studies have only rarely addressed how social incentives compare to other types of rewards in motivating goal-directed behavior. The current study tested this claim; across two separate experiments, the effects of liquid and social incentives were compared in terms of their subsequent impact on task performance and self-reported affect and motivation. Critically, valenced social incentives offered both ecological validity (short video clips—Experiment 1) and continuity with prior stimuli used in the social reward and motivation literature (static images—Experiment 2) when examining their effect on behavior. Across both studies, the results replicate and extend prior work, demonstrating robust effects of liquid incentives on task performance and self-reported affect and motivation, while also supporting an interpretation of weaker motivational and affective effects for social incentives. These patterns of results highlight the complex and wide-ranging effects of social incentives and call into question the effectiveness of social incentives, relative to other incentive modalities, in motivating behavior.

Keywords: social motivation, cognitive control, primary incentives, reward, decision-making

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INTRODUCTION

Incentives are recognized as powerful sources of motivation that support the pursuit of goal-directed behavior. Although most of this evidence comes from studies using monetary incentives (e.g., Braver et al., 2014; Botvinick and Braver, 2015), recent work has begun to highlight the utility of other primary incentive types, such as social and liquid rewards, in motivating goal-directed behavior and decision-making (Krug and Braver, 2014; Tamir and Hughes, 2018). Indeed, social incentives have been shown to increase performance to the same extent as monetary rewards on a cognitive control task (Ličen et al., 2016). Social incentives have also been demonstrated to increase attentional orienting for trials associated with positive social reward (Anderson, 2016; Hayward et al., 2018) and to also increase attentional control (Ličen et al., 2019). Likewise, liquid incentives have been shown to enhance performance on challenging cognitive tasks (Beck et al., 2010; Yee et al., 2016; Yee et al., 2019). Taken together, this work provides initial evidence of the utility of diverse primary incentive modalities in guiding goal-directed behavior.

However, despite the potential utility of both social and liquid incentives in motivating goal-directed behavior and decision-making, an unanswered question is whether both primary incentive types operate equivalently in this regard. Indeed, the few studies that do examine the motivational effects of social incentives, relative to other incentive types, have reported inconsistent motivational effects. For example, both humans and non-human primates have been willing to forgo other types of rewards (e.g., money rewards for humans, juice rewards for primates) to receive social incentives, suggesting that social incentives may hold greater value compared to other types of reward (Deaner et al., 2005; Jones and Rachlin, 2006). In contrast, other recent work suggests that social, consummatory, and monetary rewards operate equivalently in motivating behavior when they are equated in terms of their subjective value (Lehner et al., 2017). Further, some evidence suggests that social incentives *do not* increase task performance to the same extent as monetary incentives, showing higher hit rates for monetary, relative to social, rewards (Rademacher et al., 2014). The heterogeneity in the effects of social incentives has been suggested to be potentially attributed to individual differences in personality (Radke et al., 2016), although there has not yet been strong support for this claim. From these findings, it is evident the literature on social incentives is quite mixed, and that there is not yet a clear understanding of the mechanisms that underlie how social incentives motivate behavior and decision-making, relative to other incentive types. Thus, an important and necessary step for clarifying these mechanisms is the development of experimental paradigms that explicitly compare and measure the effect of social and non-social incentives on task performance and goal-directed behavior.

Nevertheless, evaluating the motivational impact of social incentives solely in terms of task performance (i.e., objective measures) may neglect other important signatures, such as influences on affective/emotional reactions and other metrics of subjective experience. Indeed, there is some evidence to suggest that affect and motivation explain unique variance in modulating cognitive control (e.g., Dreisbach and Goschke, 2004; Chiew and Braver, 2011). In particular, some theoretical accounts postulate that reward incentives could impact dissociable neural pathways related to the hedonic/affective ("liking") and motivational ("wanting") dimensions activated by such incentives (Berridge and Robinson, 2003). Further, other theoretical frameworks highlight the unique contribution affective processes have on decision-making and goal-directed behavior (Winkielman et al., 2007). Based on such accounts, it is plausible that social incentives could elicit affective responses that operate distinctly from their motivational impact on cognitive task performance, which could lead to differential patterns of performance across primary incentive types. For example, it is possible that social incentives might have a similar impact on cognitive task performance compared to primary incentives, such as liquids, but that social incentives would elicit stronger affective and other subjective responses. Likewise, given the increased evolutionary importance of social cognition and social motivation for humans (i.e., Pyszczynski et al., 1997), it is plausible that social incentives could exert a stronger influence over cognitive processing and behavior than other primary incentives, such as liquid.

The current study aimed to test this question by adapting an incentive integration paradigm developed in our lab (Yee et al., 2016, 2019) to investigate how participants integrate the motivational value of monetary incentives with liquid delivery used as performance feedback. This paradigm is an innovative one in that it has demonstrated utility for examining the combined effects of monetary and non-monetary incentives on cognitive task performance, especially for incentives varying across motivational valence (e.g., positive/approach vs. negative/avoidance). The key innovative aspect of the paradigm to highlight is its ability to isolate and quantify the effects of primary (e.g., liquid) incentives on cognitive task performance, separately from the effects of secondary (i.e., monetary) incentives. In the paradigm, monetary reward incentives are offered to participants for fast and accurate performance, with the value of the incentive manipulated on a trial-by-trial basis (i.e., low, medium, or high value). Successful attainment of the monetary reward is signaled to participants via post-trial feedback (e.g., in liquid incentive conditions, oral-delivery of liquid into the participant's mouth). Critically, the meaning of the incentive feedback is purely symbolic (i.e., a drop of liquid signals successful attainment of monetary reward under all conditions regardless of its valence), which makes it possible to examine motivational influences of non-monetary incentives in terms of their incidental, or obligatory, impact on performance. Importantly, the use of monetary rewards as the explicit incentive offered and manipulated across trials biases participants to an approach-motivated state (Bijleveld et al., 2012), which is reflected in overall high-performance levels. Thus, it is possible to quantify the effects of motivational valence of the post-trial feedback on task performance. Indeed, in several prior studies using this incentive integration paradigm with liquid incentives, we found evidence to support that performance is enhanced on positively-valenced (liquid) trials relative to the neutral-valence, and impaired on negatively-valenced trials (relative to positive and neutral; Yee and Braver, 2018).

In the current study, we extended the paradigm to additionally examine the effects of social incentives on task performance (compared to liquid incentive effects) in two parallel and complementary experiments. In particular, we utilized a within-subjects design to enable direct comparison of the two incentive types. In Experiment 1, the social incentives were a novel set of dynamic stimuli (i.e., short video clips) that provided motivationally valenced feedback (positive, neutral, or negative; Tully et al., 2017). These stimuli were chosen to provide an ecologically valid type of social message that participants might experience in daily life when faced with decision-making prospects (e.g., compliments, insults). Ecological validity is a critical consideration when considering extant research on social incentives, since there have been concerns raised as to whether the social content of stimuli being used to investigate social motivation in prior studies might be too simplified and decontextualized to approximate the social feedback individuals experience in daily life (i.e., Tamir and Hughes, 2018). In Experiment 2, the objective was to provide greater continuity with the prior literature, by using static images of valenced facial expressions as social incentives. As these static images form the basis of much of the extant research on social incentives (e.g., Cloutier et al., 2008; Spreckelmeyer et al., 2009), this approach offers a more clear-cut extension and comparison with these prior bodies of work, despite lacking the ecological validity of the stimuli used in Experiment 1. Importantly, we believed that the inclusion of both types of social incentives (static facial expressions, dynamic social messages) would provide a fuller picture of when and how social incentives may be effective in terms of their influence on motivated behavior and affect. Across both studies, we predicted that participants would not only be able to integrate liquid with monetary incentives, as we found in our prior studies (Yee et al., 2016, 2019), but would also show integration effects with social and monetary incentives, providing further evidence of the utility of using both primary incentive types in motivating goal-directed behavior.

Further, we assessed participants' self-reported affect in both liquid and social feedback conditions in order to provide initial information regarding the relationship between affective and motivational dimensions of the feedback. These ratings were only collected in Experiment 1, as data collection was already underway in Experiment 2 when we implemented this portion of the experimental protocol. We predicted that affective modulation would be stronger in the social feedback condition relative to liquid feedback, consistent with a potential dissociation between the role of affect and motivation in modulating cognitive control (e.g., Chiew and Braver, 2011). Obtaining this pattern of results would provide further evidence for the distinct roles of affect and motivation in the recruitment of cognitive control. Conversely, an alternative outcome would be if the liquid feedback condition elicited both a stronger motivational influence on performance and also had a stronger impact on self-reported affect. Such an outcome would indicate that the affective and/or motivational influences of liquid feedback are greater than those for social feedback. To preview, the results from both studies appear to provide greater support for this latter, alternative interpretation, reinforcing the utilization of liquid feedback as an effective motivational incentive for modulating cognitive task performance.

EXPERIMENT 1

In this study, we directly compared the motivational influences of social and liquid incentives when each was used as performance feedback. To investigate this question, we utilized an incentive integration paradigm originally developed by Yee et al. (2016). The key feature of this paradigm is that it provides a means of determining whether valenced performance feedback—positive, neutral, negative—is integrated with pre-trial monetary incentive cues to modulate the motivational value onto task performance. In the original studies (Yee et al., 2016, 2019), liquid incentives were used as feedback, with liquid delivery indicating to the participant that they had successfully obtained the monetary reward available on that trial (through fast and accurate responding). Because the motivational valence of the liquid was manipulated across blocks (positive, neutral, or negative in different blocks), it was possible to detect the additive effect of the liquid on task performance, since performance was better on positive blocks and worse on negative blocks, relative to neutral.

Here, the paradigm was adapted to also compare the effects of liquid and social incentives. In the social incentive condition, short video clips were substituted as performance feedback instead of liquid delivery. Presentation of a video to participants as post-trial feedback had the same meaning in this condition, always indicating success at attaining the monetary reward available on that trial. Yet again, the motivational valence of the video clip was manipulated, such that positive, neutral, or negative messages were delivered in different blocks. This provided the ability to test whether the valence of the video message had a unique impact on task performance. Moreover, by implementing a within-subjects design, it was possible to directly compare social incentive effects with the effects of liquid incentives, as all participants performed both incentive conditions in different experimental sessions.

Materials and Methods

Participants

Forty-one participants (29 females; ages 18–37 years; *M* = 20.71, *SD* = 3.26) were recruited from Washington University Psychology Department and Washington University School of Medicine Volunteers for Health subject pools. Participants completed two separate sessions at Washington University in St. Louis, at least 24 h apart. All participants provided written informed consent and were given payment of $10/h in addition to task-based earnings contingent upon fast and accurate performance in the incentive blocks. Ten participants were excluded from analysis; four only completed one session and did not return for the second, three ended a session prior to completion, one failed to comply with task instructions during the first session and was not invited back to complete the second session, and two participants' data were unable to be analyzed due to experimenter error during data acquisition. Consequently, the final sample subjected to analysis consisted of 31 participants (21 females; ages 18–37 years *M* = 20.81, *SD* = 3.41). All participants were native English speakers, reported no current or previous history of neurological trauma, seizures, or mental illness, and no use of psychotropic medications. The Washington University Human Research Protections Office approved all experimental procedures.

A power analysis was performed using G*Power (Faul et al., 2007) to identify the sample size necessary to detect effects of both monetary and liquid incentives, at the same level of effect size observed in the original work with this paradigm (Yee et al., 2016). The analysis revealed that 28 participants would be necessary for 80% power to detect such effects.

Tasks

All participants performed an incentivized cued-task switching paradigm following the same basic structure as Yee et al. (2016, 2019). The task-switching paradigm was administered using E-Prime Version 2.0.10.242 (Psychology Software Tools, Pittsburgh, PA, United States) and consisted of a series of trials in which participants randomly alternated between performing letter and digit categorization tasks, with the task to be performed on each trial indicated by an advance task cue. Task responses were recorded using an E-prime stimulus response box, via button presses made with their right index and middle fingers, according to response mappings that were counterbalanced across participants. Each trial began with a fixation cross, which was displayed for 300 ms. Next, a task cue was presented for 500 ms, which indicated the categorization task to be performed on that trial. If the cue was "Attend Letter" the participant needed to categorize the letter as being either a vowel or a consonant, whereas the "Attend Number" cue indicated that the participant needed to categorize the number as being either odd or even.

In the primary task conditions, trials were incentivized through monetary rewards available on each trial and indicated through advance reward cues accompanying the task cues. Specifically, monetary reward cues appeared above and below the "Attend Number" or the "Attend Letter" cues ($ = low reward, $$ = medium reward, or $$$$ = high reward). The number of dollar signs varied from trial to trial. During incentive trials, participants were informed that the dollar signs represented the relative monetary worth of that trial (e.g., $$ trials being worth twice as much as $ trials and half as much as $$$$ trials). As described further below, these monetary rewards could be obtained through fast and accurate performance. Thus, participants were incentivized to maximize monetary reward earnings, which occurred by enhancing cognitive task performance (e.g., faster and accurate responses).

Prior to the primary task conditions, participants also performed the task under practice and baseline conditions, in which no rewards were available. The same dollar sign cues were presented, however, but during these trials, participants were told that dollar signs held no significance. Following the task (+monetary reward) cue, a blank screen was presented for 1850 ms, followed by the target stimulus which was presented for up to 2000 ms. The target stimulus was ambiguous as to the relevant tasks, since it always consisted of both a letter and a number, and the same two response buttons were used in each task (e.g., one response mapping might be to respond middle finger for odd, index finger for even in the Digit task, and middle finger for vowel and index finger for consonant in the Letter task). As such, the task placed high demands on cognitive control, requiring participants to mentally update the appropriate task goal and associated response rules on a trial-by-trial basis in order to perform successfully. The baseline condition was used to set an RT criterion for later incentivized trials, as described below.

The key feature of the task was the social or liquid feedback delivered to participants following their response during the primary task conditions. This feedback was delivered only when participants were both accurate and fast on the trial (with the response time cutoff set individually according to baseline task performance; see below). Thus, feedback symbolically indicated to participants that they were successful in obtaining the available monetary reward on that trial (high, medium, or low). However, in different blocks the motivational valence of the feedback was manipulated (positive/appetitive, neutral/neutral, or negative/saltwater). Given that the symbolic meaning of the feedback was positive and held constant across blocks, any further influence of the feedback on performance can be taken as an indicator that it had unique motivational value, over and above the value of the monetary incentive. Indeed, in prior work using liquid feedback (Yee et al., 2016, 2019), there were robust effects of feedback valence on task performance, in that participants received reward feedback at a higher rate when the liquid was of positive/appetitive valence (apple juice) and at a lower rate when the liquid was of negative/aversive valence (saltwater) relative to neutral (tasteless solution). On trials in which the participant made an error or was too slow, they instead received a visual message that read "Next Trial Coming Up"; see **Figure 1** for a schematic diagram. During practice and baseline conditions (when no incentives were available), participants instead received only visual feedback; on practice trials, participants received feedback indicating whether they were correct or incorrect, or did not respond within the available response window. Baseline trials did not provide participants with performance feedback, they instead received a

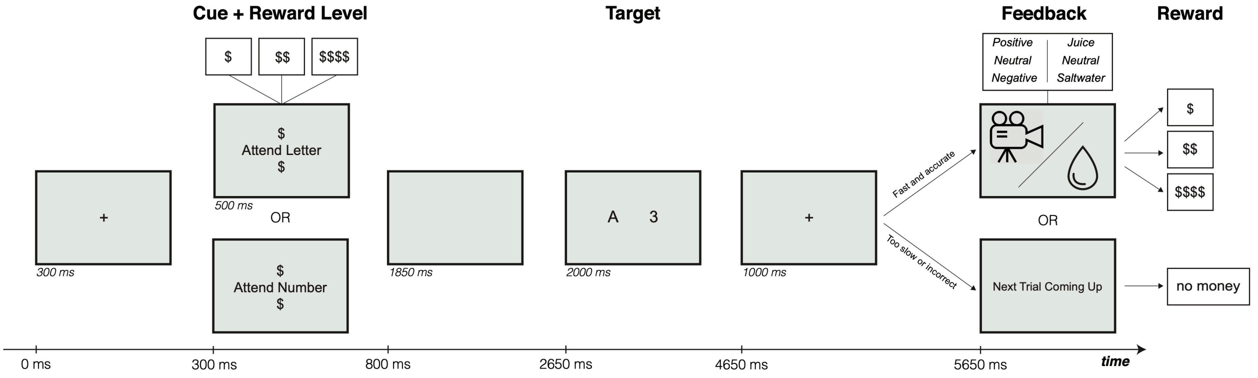

FIGURE 1 | Incentive integration task paradigm. Participants were asked to perform a consonant-vowel odd-even (CVOE) switching task. Reward cues indicated the relative amount of monetary reward available on each trial given fast and accurate performance. If participants were accurate and faster than a subject criterion response time (30% of fastest response times for correct trials during the baseline block), then they received feedback (social or liquid) at the end of the trial. If subjects answered incorrectly, too slowly, or not at all, they received neither monetary reward nor liquid/social incentives.

visual message that read "Next Trial Coming Up," regardless of task performance.

Procedure

Before the start of the experimental session, the neutral and saltwater liquid solution were prepared in a testing room in the lab. The isotonic neutral solution consisted of 1 liter of distilled water, 0.0495 g of NaHCO3 (Sodium Bicarbonate), and 0.4668g of KCl (Potassium Chloride) diluted to 25% for use in the study. The saltwater solution consisted of 250 mL of distilled water and 2.1915 g of non-iodized salt. The juice used was 100% apple juice (Mott's brand) and purchased from the store. To minimize the likelihood that participants were already satiated during the experimental sessions, they were asked to abstain from eating or drinking anything besides water for two hours prior to the session. Upon arrival, participants used REDCap, a secure research and experience management software program (Harris et al., 2009), to complete a contact information questionnaire and pre-task self-report individual difference questionnaires that were not the primary focus of analyses (see **Supplementary Material**).

Each participant performed two experimental sessions that were identical in structure and only differed in the incentive condition being performed (social feedback, liquid feedback). Session order was counterbalanced across participants. Each session began with a practice and baseline phase in which the cued-task switching paradigm was performed under non-incentive conditions. The practice phase consisted of two blocks in which participants practiced only a single task, either the letter or number categorization task. One cue, either "Attend Number" or "Attend Letter," was presented for all trials of the block (12 trials per task, counterbalanced order). A third practice block consisted of both number and letter trials, intermixed (24 trials total). After the practice phase, participants performed a baseline phase, which consisted of three longer blocks mirroring the structure of the practice blocks. During the baseline blocks, participants performed the same tasks as in the practice blocks, and counterbalanced in the same order, but received no feedback after each trial. The first two baseline blocks (either single-task letter or number) consisted of 48 trials each and the third task-switching block (intermixed number and letter trials) consisted of 96 trials. In each of the baseline runs, participants were instructed to perform as quickly and accurately as possible.

Performance on the baseline task-switching block was used to compute the reward cutoff time in subsequent incentive blocks. Specifically, the reward criterion was calculated individually for each participant, based on the 30th percentile of their correct reaction times in the mixed baseline run performed during that session. On incentive trials, participants had to be both accurate and faster than this cutoff time to receive the monetary reward available on that trial. Prior to beginning the incentive blocks, participants were given this information regarding the criteria for being rewarded, and were told that they had the opportunity to earn an additional $14 across the two experimental sessions, in addition to their hourly pay.

The liquid feedback session matched identically the structure used in prior work (Yee et al., 2016, 2019) and consisted of six incentive blocks total, two consecutive blocks each performed with three different liquids associated with a different affect/motivational valence: positive (apple juice), neutral (isotonic tasteless solution), negative (saltwater). The block order of the three liquids was counterbalanced between participants. Each block consisted of 48 trials, and participants were given a rest break between each block. Liquid was dispensed (2 mL per trial) using a digital infusion pump (model SP210iw, World Precision Instruments Inc., Sarasota, FL, United States) with Tygon tubing (United States Plastics Corporation, Lima, OH, United States) delivering liquid directly into the participant's mouth. As described above, on all blocks, participants only received the liquid available for that block on trials in which they were both accurate and their response latency was faster than their individually determined reward cutoff time. Consequently, although the symbolic meaning of the feedback was the same in all cases (indicating success at obtaining the monetary reward), the motivational meaning varied, and was predicted to combine with the monetary reward value in an additive manner, positively in the juice blocks, and negatively in the saltwater blocks, relative to the neutral blocks.

The social feedback session involved a parallel structure, also consisting of six blocks, in sets of two blocks of 48 trials each, performed consecutively, with a rest break provided after each block. Each set was associated with social feedback of a different affect/motivational valence (positive, neutral, and negative), with valence order counterbalanced across participants. The social feedback was presented in the form of a short video clip, selected from the SocialVidStim set (Tully et al., 2017). The SocialVidStim is a collection of short video clips (N = 4,673), each approximately six seconds in length, featuring a single male or female actor facing directly to the screen (i.e., as if speaking to the participant), and delivering an affectively valenced message. Examples of social feedback presented to the participants are as follows (for videos and further information)[1]: "People think positively of you" (positive); "You are a disappointment" (negative); "A minute is a unit of time" (neutral). In brief, validity data collected to date on a subset of videos (N = 1,001; 428 negative; 429 neutral, 144 positive) from 1,781 participants indicate that negative videos are perceived as more negatively valenced (mean difference = −1.21; 95% CI [−1.23, −1.19]) and more arousing (mean difference = 0.68, 95% CI [0.66,0.70]) than neutral videos. Similarly, positive videos are perceived as more positively valenced (mean difference = 0.85, 95% CI [0.82,0.88]) and more arousing (mean difference = 0.59, 95% CI [0.55,0.63]) than neutral videoas. Test-retest reliability data collected on a subset of videos (N = 232; 86 negative, 92 neutral, 54 positive) from 354 participants indicate good-to-excellent reliability of negative and positive videos (ICC negative = 0.93; ICC positive = 0.87) and moderate reliability of neutral videos (ICC neutral = 0.66). For this experiment, we selected 165 videos (55 of each valence type) from the SocialVidStim, which featured 26 different actors (13 females; ages 18–41, M = 25.0, SD = 5.2; 4 Asian, 2 Black, 19 Caucasian, 1 more than one race).

As in the liquid feedback condition, social feedback messages were all of the same category for a given block and were

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[1] https://peplab.ucdavis.edu/videos.php

only received on trials in which the participant was both accurate and faster than their individually determined reward cutoff time. Therefore, paralleling the liquid condition, the symbolic meaning of the social feedback was the same in all cases (indicating success at obtaining the monetary reward), the affective/motivational meaning varied, and was predicted to combine with the monetary reward value in an additive manner, either positively or negatively, relative to neutral as a function of the block condition.

Following each incentive run, participants completed ratings of their current affective state, using a 5-point scale. Participants were instructed to indicate "to what extent you feel this way right now" for each of the 10 valenced words; three terms coded negative affect valence (Ashamed, Irritable, Upset), three coded positive affect valence (Inspired, Content, Excited), and four coded arousal (Fatigued, Alert, Determined, Stressed). The ratings for valence terms were averaged together to create composite positive and negative affect scores in the primary analysis. Additionally, after completing all task blocks, post-task questionnaires were given in each session that assessed ratings of how much participants liked the incentive type (e.g., social or liquid feedback), how intense or arousing they found the stimuli, and also self-reported levels of motivation, liking, and performance for each incentive type (e.g., $-positive social feedback, $$$$-saltwater) using a seven-point Likert scale. A complete description of all self-report questionnaires is provided in the **Supplementary Material**. All relevant experimental scripts, data, and analyses are located in an online repository on the Open Science Framework: https://osf.io/pu9gs/.

Data Analysis

Across both experiments, the primary analysis approach consisted of a 3-factor, within-subject ANOVA [3 monetary reward levels (low, medium, high) × 3 feedback valences (positive, neutral, negative) × 2 incentive types (liquid, social)] in order to test for the effects of the task conditions on the primary dependent measure, reward rate (i.e., the subjective motivation to engage in cognitive control), followed by *post hoc* tests when interactions were identified. In Experiment 1, we also used a 2-factor, within-subject ANOVA design to examine the effects of incentive type (liquid, social) and feedback valence (positive, neutral, negative) on participants' self-reported affect after performing each task block. As such, we present the results from each ANOVA using the test F-statistic, significance level of the effect, and the effect size estimate. The effect sizes for the ANOVAs are reported using the generalized eta squared metric, which is the preferred method for reporting effect sizes of within-subject ANOVA designs (Lakens, 2013). Further, when pairwise comparisons were made using t-tests, we report the results using the t-test statistic, significance level of the effect, and the effect size estimate (Cohen's *d*). No data were excluded, on the basis of outliers, in either study.

Results

Task Performance

We used reward rate (i.e., the percentage of rewarded trials in each incentive condition) to quantify each participant's subjective motivation to implement cognitive control to earn the incentives offered both in the liquid and social feedback tasks. Because the expected reward rate was 0.3, assuming no change in motivation from the baseline condition, the first analysis tested whether the average reward rate obtained in each condition exceeded this value. Indeed, across both the liquid and social feedback sessions, participants exceeded this value (liquid: 31/31, social: 30/31), suggesting that cognitive control was enhanced when participants performed cued task-switching under the heightened motivational context associated with incentives.

The primary analysis was a full 3-factor ANOVA enabling comparisons between all of the task conditions (3 monetary reward levels × 3 feedback valences × 2 incentive types). In this analysis, there was a main effect of monetary reward, $F(2,60) = 18.53$, $p < 0.001$, $\eta^2_G = 0.024$, indicating that reward rate was highest on trials with the highest monetary rewards available ($M = 0.679$, $SD = 0.092$), and was lower when both medium ($M = 0.626$, $SD = 0.099$) and small rewards ($M = 0.632$, $SD = 0.096$) were available. The monetary reward level did not further interact with incentive session, $F(2,60) = 2.13$, $p = 0.127$, $\eta^2_G = 002$. Further, there was no effect of incentive type on task performance, $F(1,30) = 0.99$, $p = 0.327$, $\eta^2_G = 0.009$. This suggests that, as expected, participant performance was sensitive to the monetary rewards and did not qualitatively differ across social and liquid feedback.

We next focused on the effects of feedback valence. Although there was no main effect $F(2,60) = 2.82$, $p = 0.067$, $\eta^2_G = 0.010$, feedback valence did interact with incentive type, $F(2,60) = 5.56$, $p = 0.006$, $\eta^2_G = 0.018$, suggesting that valence effects were distinct for the social feedback relative to the liquid feedback. However, feedback valence did not further interact with monetary reward, $F(4,120) = 0.53$, $p = 0.718$, $\eta^2_G = 0.001$, nor was the 3-way interaction significant, $F(4,120) = 2.28$, $p = 0.065$, $\eta^2_G = 0.005$. To decompose the feedback valence × incentive type interaction, we examined the feedback valence effect in each incentive type (i.e., social, liquid) separately. In the liquid feedback, we observed the expected effect of feedback valence, $F(2,60) = 5.16$, $p = 0.009$, $\eta^2_G = 0.027$, whereby juice trials had higher reward rate ($M = 0.663$, $SD = 0.100$) than saltwater trials [$M = 0.581$, $SD = 0.208$; $t(30) = 2.46$, $p = 0.020$, $d = 0.462$; **Figure 2**]. This pattern replicates the findings of the prior liquid feedback studies (Yee et al., 2016, 2019) and suggests that participants were able to additively combine liquid and monetary rewards to modulate task performance. In contrast, the social feedback condition did not produce any evidence of reliable integration effects, as feedback valence showed no influence on reward rate ($F[2,60] = 0.51$, $p = 0.601$, $\eta^2_G = 0.002$). These conclusions were supported by supplemental analyses examining the effects of incentive session on reaction time and accuracy data (see **Supplementary Material** for comprehensive descriptive summaries and analyses).

Affect Ratings

One question is whether there might be a dissociation between the motivational and affective impact of social and liquid incentives. As a means of addressing this issue, we examined

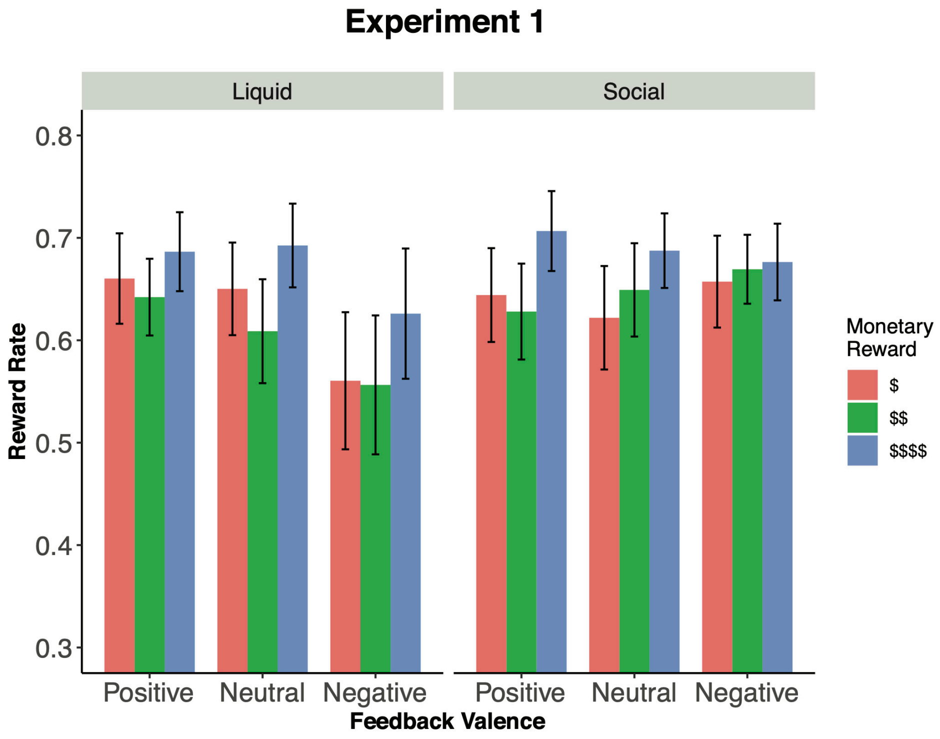

FIGURE 2 | Incentive integration effects by experimental manipulation (Experiment 1). The figure shows reward rate by monetary reward level and feedback (i.e., liquid, social). Participants showed a main effect of monetary reward and feedback during the liquid feedback session. However, there was only a main effect of monetary reward, but not feedback during the social feedback session. Error bars represent 95% confidence intervals around the mean.

the positive and negative affect ratings that participants self-reported following each incentive block for both the liquid and social incentives. Overall, there were no differences in affect ratings across the two incentive types, $F(1,30) = 2.40$, $p = 0.132$, $\eta^2_G = 0.007$; see **Supplementary Material** for a complete results on all ratings. Likewise, the effect of incentive type did not interact with feedback valence, $F(2,60) = 0.017$, $p = 0.983$, $\eta^2_G < 0.001$, or affect term (positive, negative), $F(1,30) = 1.10$, $p = 0.303$, $\eta^2_G = 0.002$. Consequently, we examined each incentive type separately, to determine the degree to which each type of feedback influenced affect ratings. In the liquid feedback condition, a feedback valence × affective term interaction was observed, $F(2,60) = 15.09$, $p < 0.001$, $\eta^2_G = 0.122$ (**Figure 3**). This was due to significantly higher ratings for the positive affect terms in the juice condition ($M = 2.75$, $SD = 0.91$) relative to saltwater ($M = 1.85$, $SD = 0.72$; $t[30] = 5.67$, $p < 0.001$, $d = 1.087$). Conversely, the opposite pattern was observed for the negative affect terms, such that participants rated higher levels of negative affect for saltwater ($M = 2.18$, $SD = 0.82$) relative to juice [$M = 1.40$, $SD = 0.62$; $t(30) = 5.37$, $p < 0.001$, $d = 1.065$].

Interestingly, a similar pattern was also observed in the social feedback condition, with a significant feedback valence × affective term interaction, $F(2,60) = 4.21$, $p = 0.020$, $\eta^2_G = 0.032$. There were higher ratings for the positive affect terms in the positive social feedback condition ($M = 2.33$, $SD = 0.96$) relative to the negative social feedback condition [$M = 1.92$, $SD = 0.73$, $t(30) = 2.45$, $p = 0.020$, $d = 0.471$]. Conversely, participants rated higher levels of negative affect for the negative social feedback condition ($M = 1.85$, $SD = 0.94$) relative to the positive social feedback condition [$M = 1.53$, $SD = 0.73$, $t(30) = 2.19$, $p = 0.036$, $d = 0.377$]. This finding suggests that the social feedback condition was successful in modulating participants' self-reported affect in alignment with the type of feedback valence received. On the other hand, the effects of feedback valence on affect were surprisingly weaker in the social feedback condition than in the liquid condition (i.e., the effect size (generalized eta-squared) of the feedback valence × affect term interaction was 0.122 in the liquid feedback session and 0.032 in the social feedback session). Thus, the affect ratings are somewhat consistent with the task performance data in suggesting a stronger affective/motivational influence of liquid feedback relative to social feedback.

Discussion

In this experiment, we directly compared the motivational impact of social and liquid incentives when each modality was used as performance feedback in an incentive integration paradigm. Critically, this paradigm enabled us to determine whether valenced performance feedback (positive, negative, neutral) and monetary incentive cues were integrated together across both feedback modalities (social, liquid) to modulate motivation levels engaged to perform a highly challenging cognitive task. Replicating prior findings (Yee et al., 2016, 2019), in the liquid feedback condition we found effects of both monetary and

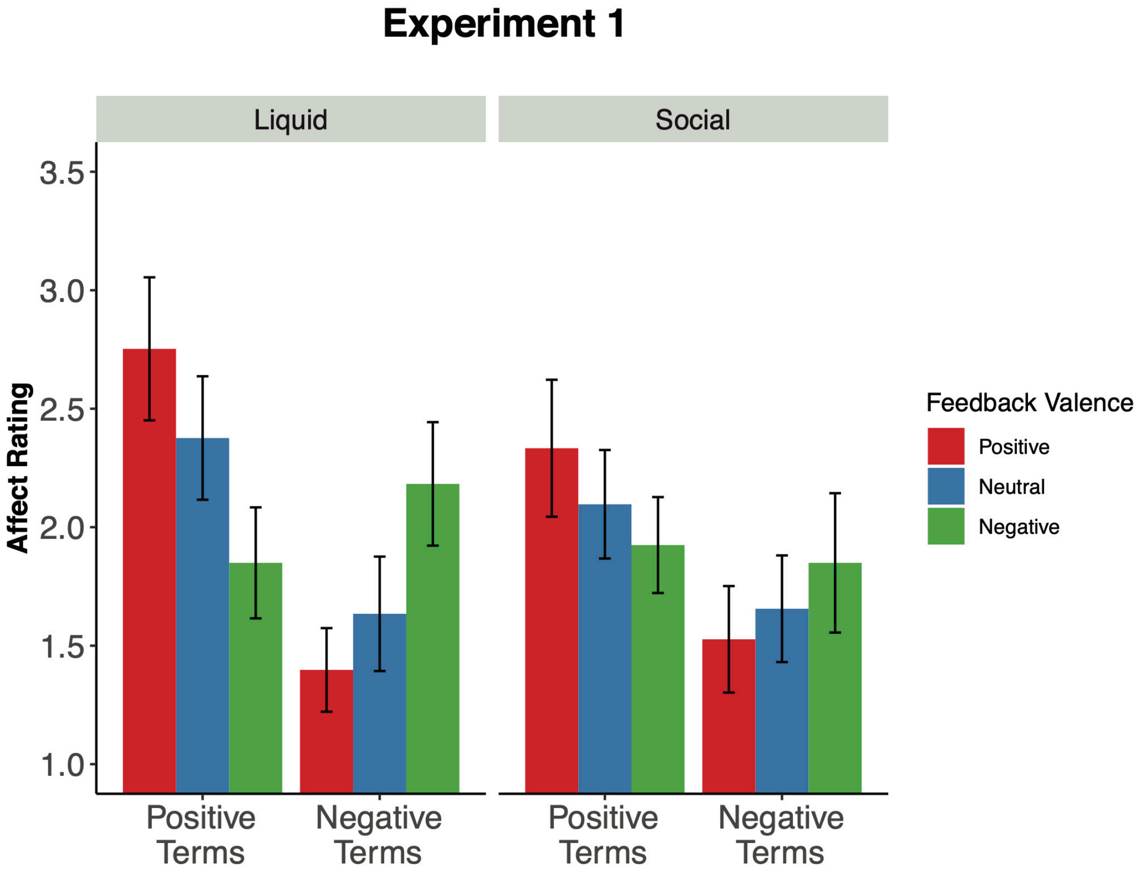

FIGURE 3 | Affect ratings by experimental manipulation (Experiment 1). This figure illustrates the mean affect rating for each incentive condition across both liquid and social feedback sessions. Participants rated the extent to which they were feeling each of the emotion words after each block of the cued task-switching paradigm using a five-point scale (e.g., 1-*not at all*, 5-*extremely*). Positive affect represents the average ratings across the following terms: "content," "inspired," and "excited." Negative affect represents the average ratings across the following terms: "ashamed," "irritable," and "upset." Error bars signify 95% confidence intervals around the mean.

liquid incentives on reward rate, suggesting that participants are able to additively combine the motivational value of these incentives to modulate task performance. In addition, for this condition, the post-block affect ratings showed robust effects of liquid feedback such that positively valenced words showed the highest ratings for juice relative to neutral, relative to saltwater (i.e., juice > neutral > saltwater), whereas negatively valenced words showed the opposite pattern (saltwater > neutral > juice), demonstrating that the liquid feedback manipulation was having a translatable effect to the participant's current affective state. Taken together, these results provide strong confirmation of prior work (Yee et al., 2016, 2019), demonstrating that monetary and liquid incentives can combine to modulate cognitive task performance through changes in experimentally-induced motivational states. Indeed, the affect ratings extend prior work by suggesting that not only does liquid feedback alter participants' motivational states during task performance, but that it also impacts their emotional state as well, at least to the degree that the self-reported affect terms are valid indicators of this state.

Conversely, social feedback does not appear to operate as strongly in this manner, or have a clear influence on cognitive task performance. Despite producing a numerically higher reward rate overall, we found no observable effect of social feedback on reward rate. Further, we found that the effects of social feedback on the post-block affect ratings were weaker than that observed in the liquid condition, though they followed the same pattern, with the highest ratings for the positively valenced affect terms coming in the positive social feedback condition (positive > negative), whereas the negatively valenced terms showed the opposite pattern (greatest in the negative social feedback condition). On the other hand, even though the effects of social feedback were weaker than liquid feedback, this observed pattern of results serves to validate that the manipulation was at least partially successful in having an impact on participants' psychological states (again under the assumption that the self-reported affect ratings are valid indicators of such states). Moreover, these results also suggest that there could be a potential dissociation between affect and motivation, such that social incentives do induce changes in participants' current affective state, but have no influence on their motivation to perform the task. Indeed, analyses of participants' self-reported ratings of motivation were consistent with this potential dissociation (see

Supplementary Material), in showing that there were no effects of social feedback valence on motivation despite participants' self-reported changes in affect across social feedback conditions. Nevertheless, it is also possible that impact of social feedback on both affect and motivation were reliably weaker than liquid feedback conditions, but this claim needs be investigated through additional studies. To provide convergent support, a second experiment was conducted comparing the effects of liquid and social feedback, with the same incentive integration paradigm.

EXPERIMENT 2

Experiment 1 demonstrated that primary liquid incentives are able to robustly modulate performance on a challenging cognitive task, whereas social incentives do not appear to have a translatable effect on participant motivation, as indexed by task performance. However, given the novelty of the social stimuli used in Experiment 1 (i.e., dynamic social messages), relative to the majority of the extant research on social incentives (i.e., static faces, written messages), it is unclear whether similar results would be obtained by using a more traditional means of operationalizing social incentives. To address this question, and increase continuity with the prior literature, in Experiment 2 static facial expressions were used as social feedback within the same incentive integration cued task-switching paradigm. Further, the limited sample size of Experiment 1 might have reduced our ability to detect the effects of social feedback on task performance, if such effects are not as strong as those previously observed effect for liquid feedback (Yee et al., 2016, 2019). Thus, Experiment 2 consisted of a considerably larger sample size, which enhanced our ability to detect the potentially smaller effect of social feedback on motivation. Consistent with the results of Experiment 1, we predicted that participants would be able to integrate liquid with monetary incentives, but not social and monetary, demonstrating a dissociation of primary incentive type in inducing motivational effects, and highlighting the complex and heterogenous effects of social incentives in motivating goal-directed behavior.

Materials and Methods

Participants

Eighty-three participants (62 females; 18–40 years; *M* = 28.35; *SD* = 6.87) were recruited from Washington University Psychology Department and Washington University School of Medicine Volunteers for Health subject pools. All participants provided written informed consent. Participants were given payment of $10/h in addition to task-based earnings contingent upon fast and accurate performance in the incentive blocks. Although the intent was to run this study only with monetary compensation, a small subset of participants were provided with course participation credit for their time, rather than the $10/h payment schedule. Nine participants were excluded: five participants for technical errors and four participants for failure to comply with the task instructions. The final sample consisted of 74 participants (56 females; ages 18–40, *M* = 28.27, *SD* = 6.90). All participants were native English speakers and reported no current or previous history of neurological trauma or seizures. The Washington University Human Research Protections Office approved all experimental procedures.

The effect sizes of monetary and liquid rewards in Experiment 1 were smaller than what was observed in prior work with this paradigm (Yee et al., 2016). However, using the effect sizes from Experiment 1, results from a power analysis suggest that a minimum of 65 participants would be necessary for 80% power to detect such effects, motivating a larger sample size in Experiment 2.

Task

Experiment 2 used the same incentivized task-switching paradigm as in Experiment 1; however, rather than using dynamic social feedback messages, participants were presented with static images of faces as valenced social feedback (positive-happy, neutral-neutral, negative-sad). The face images used as social feedback were derived from a subset of the NimStim database of multiracial facial expressions (Tottenham et al., 2009). This open source stimuli set was validated for the ability of untrained participants to reliably identify the emotion (i.e., happy, neutral, sad) of each face image[2]. The overall proportion correct was robust (*M* = 0.81; *SD* = 0.19) and demonstrated high agreement across stimuli between the rater labels and intended expressions (mean κκ= 0.79; *SD* = 0.17). We utilized 202 closed- and open-mouth faces out of the 672 images contained within the set, categorizing them into valences of happy, neutral, and sad. The average validity ratings for the happy, neutral, and sad faces in the NimStim set were 0.92, 0.86, and 0.72, respectively.

Procedure

The experimental session was identical in structure to the procedure described in Experiment 1, however, rather than completing each incentive condition (social feedback, liquid feedback) across two separate sessions, incentive type was counterbalanced across participants within the same session. Upon completing all task blocks, participants completed post-task questionnaires on which they rated how much they liked the incentive type (e.g., social or liquid feedback), how intense or arousing they found the stimuli; they also rated their overall levels of motivation, liking, and performance for each incentive type (e.g., $-positive social feedback, $$$$-saltwater) using a seven-point Likert scale. A complete analysis of this rating data is contained within the **Supplementary Material**.

Data Analysis

The data analysis approach was identical to that described in Experiment 1, utilizing repeated-measures ANOVA (followed by *post hoc* tests where appropriate), and reporting of effect-size with the generalized eta-squared measure (or Cohen's *d* for *t*-tests).

Results

Task Performance

As in Experiment 1, we used reward rate to quantify each participant's subjective motivation to implement cognitive

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[2] https://danlab7.wixsite.com/nimstim

control to earn the incentives offered in both the liquid and social feedback conditions. Across both incentive modalities, participants exceeded the expected reward rate (liquid: 73/74, social: 74/74), as determined by the criterion response time, suggesting that cognitive control was enhanced when participants were provided with increased motivational incentives during the task (i.e., the ability to receive rewards based on both fast and accurate task performance). However, when directly comparing the liquid and social feedback conditions, average reward rate was higher overall for social ($M = 0.718$, $SD = 0.103$) relative to liquid feedback [$M = 0.631$, $SD = 0.130$), $t(73) = 6.75$, $p < 0.001$, $d = 0.73$].

Consistent with the analyses conducted in Experiment 1, we used a full 3-factor ANOVA to provide comparisons between all of the task conditions (3 monetary reward levels × 3 feedback valences × 2 incentive types). In addition to the main effect of incentive type described above, there was also a main effect of monetary reward, $F(2,146) = 34.714$, $p < 0.001$, $\eta^2_G = 0.028$, indicating that reward rate was highest on trials with the highest monetary rewards available ($M = 0.721$, $SD = 0.109$), and was lower when medium ($M = 0.660$, $SD = 0.104$) and small rewards ($M = 0.651$, $SD = 0.118$), $ps < 0.001$, were available. Further, monetary reward level interacted with incentive type, $F(2,146) = 5.185$, $p = 0.007$, $\eta^2_G = 0.004$, suggesting that participant performance qualitatively differed across social and liquid feedback conditions. To decompose this interaction, we examined the effect of monetary reward for each incentive type separately. There was an effect of monetary reward for the liquid feedback condition, $F(2,146) = 22.53$, $p < 0.001$, $\eta^2_G = 0.036$, whereby reward rate was highest for high monetary reward trials ($M = 0.680$, $SD = 0.126$), relative to medium monetary reward trials ($M = 0.618$, $SD = 0.137$), and medium monetary reward trials relative to low monetary reward trials ($M = 0.594$, $SD = 0.169$), $ps \leq 0.035$ (i.e., \$ < \$\$ < \$\$\$\$). Likewise, there was also an effect of monetary reward for the social feedback condition, $F(2,146) = 16.20$, $p < 0.001$, $\eta^2_G = 0.022$, such that reward rate was highest for high monetary reward trials ($M = 0.745$, $SD = 0.113$), followed by both medium ($M = 0.702$, $SD = 0.104$) and low monetary reward trials ($M = 0.707$, $SD = 0.115$), $ps < 0.001$. However, in contrast to the liquid feedback condition, there was no difference between low and medium reward trials in the social feedback condition, $t(73) = 0.65$, $p = 0.518$, $d = 0.05$.

Next, we examined the effects of feedback valence. Although there was a main effect of feedback valence, $F(2,146) = 12.34$, $p < 0.001$, $\eta^2_G = 0.019$, it was qualified by an interaction with incentive type, $F(2,146) = 24.33$, $p < 0.001$, $\eta^2_G = 0.035$, which suggests that valence effects were distinct in the social relative to liquid feedback conditions. To decompose the feedback valence × incentive type interaction we examined the feedback valence effect in each incentive type (i.e., social, liquid) separately. There was an effect of valence for the liquid feedback condition, $F(2,146) = 24.42$, $p = 0.009$, $\eta^2_G = 0.027$, that again replicated prior findings (Yee et al., 2016, 2019): reward rate was highest for positively valenced trials (Juice; $M = 0.689$, $SD = 0.106$) and lowest for negatively valenced trials [Saltwater; $M = 0.562$, $SD = 0.212$, $t(73) = 5.42$, $p < 0.001$, $d = 0.71$]; moreover, relative to neutral trials (Neutral; $M = 0.641$, $SD = 0.154$), positively valenced trials were significantly higher and negatively valenced trials were significantly lower in reward rate, $ps \leq 0.002$ (**Figure 4**).

In contrast to the findings from Experiment 1, there was also an effect of valence in the social feedback condition, $F(2,146) = 3.46$, $p = 0.034$, $\eta^2_G = 0.004$. However, in the social feedback condition the valence effect was *actually opposite to the predicted pattern*, and the effect observed in the liquid feedback condition: reward rate was highest for negative social feedback ($M = 0.728$, $SD = 0.105$), relative to positive social feedback [$M = 0.707$, $SD = 0.113$, $t(73) = 2.88$, $p = 0.005$, $d = 0.18$]. Further, there was no difference in reward rate between positive and neutral ($M = 0.719$, $SD = 0.111$), or neutral and negative feedback trials, $ps \geq 0.190$. Feedback valence also interacted with monetary reward, $F(4,292) = 3.48$, $p = 0.008$, $\eta^2_G = 0.003$. The 3-way interaction was not statistically significant, $F(4,292) = 1.717$, $p = 0.146$, $\eta^2_G = 0.002$. These findings suggest that both primary incentive types (liquid, social) were able to modulate task performance. However, the social feedback effects were both qualitatively distinct and noticeably smaller in effect size from that observed in the liquid feedback condition ($d = 0.18$ social vs. $d = 0.71$ liquid), and moreover, opposite to what would be predicted from standard motivational valence account (i.e., negative > positive, rather than positive > negative).

Discussion

In Experiment 2, we directly compared the effects of social incentives using static faces, relative to liquid incentives. Replicating Experiment 1 and prior work (Yee et al., 2016, 2019), in the liquid feedback condition we found effects of both monetary and liquid incentives on reward rate, which indicates that the liquid feedback manipulation was having a translatable effect to participants' current motivational state. In contrast to the findings from Experiment 1, we also found an effect of social feedback on task performance; however, this effect was not as strong as the effect of liquid feedback and was also counterintuitive, in that it was *opposite to the expected pattern of results*, such that negative feedback elicited a slightly higher reward rate than positive social feedback. Taken together, these results provide strong confirmation of prior work (Yee et al., 2016, 2019), demonstrating that liquid incentives can modulate cognitive task performance through changes in experimentally-induced motivational states and highlight the lack of consistent integration effects for social feedback.

Further support for the distinct role of social feedback can be observed from the overall differences in task performance across both liquid and social conditions. Here, we observed higher overall reward rate (as well as higher accuracy; see **Supplementary Material**) in the social, relative to liquid, feedback condition. Although speculative, it is possible that the integration demands associated with the presence of two distinct incentives (monetary + liquid or social) increases the overall complexity of task demands (i.e., adding an additional cognitive load), which detracts from the ability to perform optimally in the heightened motivational context. If this is the case, then we would expect decreases in reward rate from positive to neutral to negative feedback valence scaled with the attainable

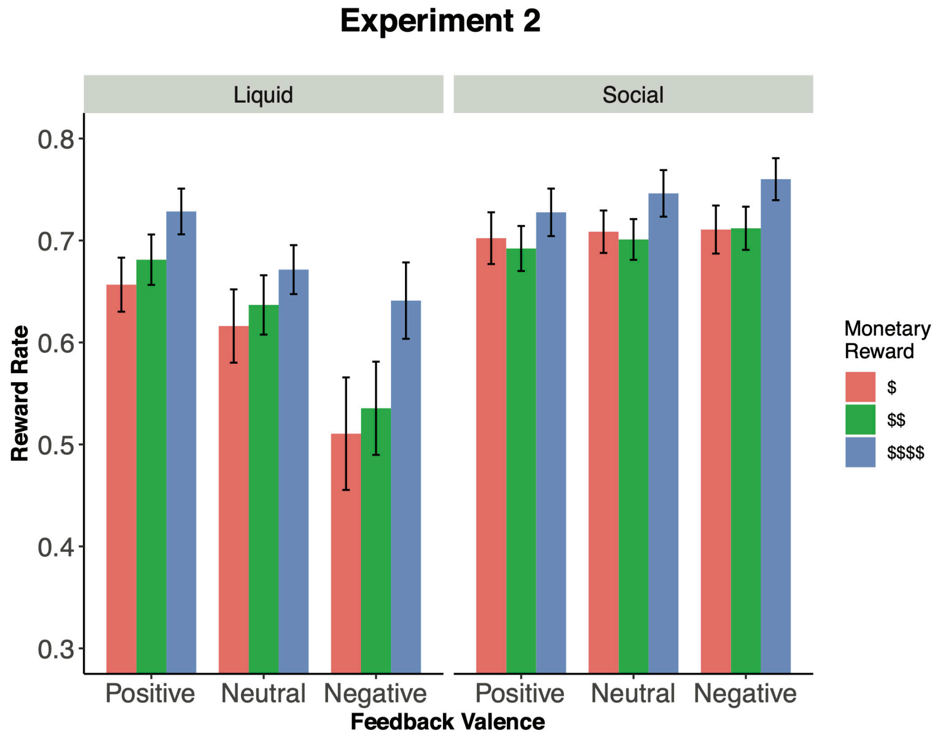

FIGURE 4 | Incentive integration effects by experimental manipulation (Experiment 2). This figure shows reward rate by monetary reward level and feedback (i.e., liquid, social). Participants showed a main effect of monetary reward and feedback during both the social and liquid feedback sessions. However, the effect of feedback was not as strong for social relative to liquid feedback. Error bars represent 95% confidence intervals around the mean.

monetary rewards. Though this is the exact pattern of results we observe in the liquid feedback condition, these effects are weaker in the social feedback condition. Thus, the results from the social feedback condition could indicate performance operating at ceiling levels, which could occur if the two incentives are actually not being directly integrated together in a valence-dependent manner, as appears to occur in the liquid feedback condition. Such an explanation could also potentially account for the qualitatively distinct valence effects observed in the social feedback condition. In particular, it is possible that such effects reflect an arousal rather than a true valence and integration effect, which is plausible given prior findings suggesting that negatively valenced facial expressions tend to be more arousing than positively valenced ones (Duval et al., 2013). Of course, these hypotheses would need to be supported by future work, which should benchmark liquid and social feedback conditions against incentive conditions that do not involve integration demands (e.g., a monetary incentive only condition).

GENERAL DISCUSSION

Across two experiments we found strong evidence supporting the role of liquid rewards as a robust motivationally-valenced incentive that can be integrated with monetary incentives to modulate cognitive task performance. This work extends our prior studies with the liquid feedback incentive integration paradigm (Yee et al., 2016, 2019) in two ways. First, we found that in addition to its motivational impact on behavioral performance in a challenging cognitive task, liquid feedback also influenced participants' self-reported affect in valence-specific ways, with appetitive liquid feedback increasing self-reported positive affect, and aversive liquid feedback increasing self-reported negative affect. Second, and most critically, the two studies converged in demonstrating that primary liquid incentives had a reliably stronger impact on task performance than did social incentives. This last point is critical, in that liquid and social incentives were directly compared with a paradigm specifically optimized to assess the motivational influence of non-monetary incentives, with a design that enabled the effect of these incentives to be measured in an incidental fashion, that is, in a manner less susceptible to demand characteristics or other confounding factors than other experimental approaches used in the literature.

Surprisingly, the findings with respect to social incentives across the two studies were counter to our initial predictions. In particular, we observed weak or null effects of social feedback on task performance in both studies. Moreover, we found preliminary evidence for a dissociation between affective and motivational responses to the social feedback, such that social incentives appear to impact participants' self-reported affective state, but not their motivation. Taken together, these results provide preliminary evidence of the dissociable of effects of primary reward type (i.e., liquid, social) in motivating cognitive behavior, whereby liquid incentives appear to induce both strong affective and motivational effects, whereas social incentives have a limited impact on behavior.

Despite the null or inconsistent effects of social feedback found in this study, it is important to consider the possibility that there are real motivational consequences of social incentives, but that our methods were not sufficiently sensitive to them, given the potential limitations associated with our current experimental paradigm and/or the social stimuli we used. For example, an alternative and potentially promising approach would be to test our social stimuli with a simpler task, rather than the highly challenging cued-task switching paradigm used in the current study, such as the Monetary Incentive Delay (MID) task (Knutson et al., 2003). Indeed, work using the MID has shown greater activity modulation in the right nucleus accumbens to social reward (smiling faces of differing intensities) relative to monetary reward, but the opposite pattern for behavioral results (i.e., higher hit rate for monetary relative to social incentives; Rademacher et al., 2014). Likewise, studies using simple approach or avoidance movements (i.e., arm extension or flexion) have found valenced effects to social stimuli (Nikitin and Freund, 2019). Thus, it is possible that we would have obtained a different pattern of results, if we had employed simpler tasks and/or behavioral response metrics.

Another possible interpretation of our findings is that even though the social stimuli were selected to increase ecological validity (e.g., using short videos clips and images of actual faces), they may have actually been ineffective in modulating motivational state. The stimuli, though selected to be meaningful and motivating (in both positive and negative directions), may have seemed artificial to the participants, and could have been easily ignored. Indeed, it is possible that participants switched strategies for the social feedback condition, relative to liquid feedback, and selectively attended to the monetary reward cues (e.g., $$, $$$$) to guide performance, effectively ignoring the messages provided by the feedback stimuli. If attention was more strongly directed to the monetary incentive cues in the social feedback condition, then we would have predicted stronger monetary effects relative to the liquid feedback condition. In fact, we observed the opposite pattern, in that monetary reward effects were also weaker in the social feedback conditions relative to liquid feedback.

Further, the stimuli may not have been personally meaningful, in that the feedback was presented by unfamiliar actors (section "Experiment 1") or unfamiliar faces (section "Experiment 2"), rather than by individuals known or influential to the participants. For example, presenting participants with social feedback provided by known and influential figures, such as friends or family members, could have been more effective, and more reflective of these experiences in daily life contexts. Indeed, recent work has shown that social closeness, as indexed by the degree to which participants rated how much they liked the person giving them social feedback, modulated activity in the ventral striatum in response to feedback, and also increased favorable impressions of the person after receiving positive social feedback from them (Hughes et al., 2018). Studies from daily life also support the idea that there is strong affective coupling between an individual and their close social partners (Mejía and Hooker, 2015), which could suggest that messages delivered by close others would have a stronger impact on affect and motivation than unknown actors. Further, other work also suggests that diverse incentive types (e.g., money, food, social) have similar motivational effects when they are equated in subjective value (Lehner et al., 2017). Thus, it is possible that our social stimuli might exhibit equivalent motivational effects to the liquid stimuli, if we were to carefully match each participant's incentive value across liquid and social domains prior to performing the incentive integration paradigm.

Nevertheless, it is worth noting that these critiques apply to almost all of the existing laboratory studies that have examined processes related to social reward and motivation. Most of these studies use fairly impoverished stimuli, like emoticons or sentences relaying social information, which also could be construed as being artificial and would seem to be even more easily ignored. Despite these potential shortcomings, prior studies utilizing these relatively impoverished stimuli have shown significant responses in the neural regions associated with reward processing (i.e., striatum, vmPFC), such as when the social stimuli are images of static faces (Cloutier et al., 2008; Spreckelmeyer et al., 2009), or feedback messages consisting only of written sentences or even just numerical ratings (Hughes et al., 2018; Izuma et al., 2008; Korn et al., 2012). Thus, it is possible that the social incentives utilized in this study may have elicited reward related neural activity.

A related concern associated with the prior literature is that there is little evidence of robust brain-behavior relationships in studies using social rewards to identify reward-related neural activity. Indeed, recent work has found differential patterns of behavior across incentive modalities, in that performance costs were only observed for social stimuli, while performance benefits were only observed for monetary rewards on a cognitive control task, despite shared activation patterns and magnitude of response across value-encoding regions of the brain to both monetary and social incentives (Park et al., 2018). These findings suggest that social incentives can engage the same brain regions that support the processing of a diverse range of rewarding stimuli to motivate behavior, even when the social stimuli aren't very life-like or particularly social in nature. Yet there is little support for the assumption that these types of social stimuli will motivate changes or enhancements in goal-directed behavior. Such findings highlight the distinct possibility that social motivational variables are actually less effective, or at least less consistent, than other types of incentive modalities in motivating behavior, even when they are accompanied by equivalent neural responses to reward.

In summary, our results do show that provided with social incentives, participants are able to improve their performance on a challenging cognitive task relative to a non-rewarded baseline condition. Nevertheless, despite popular theorizing that social incentives are potentially more motivating to humans than other primary incentives, our findings stand in contrast to this claim. In our incentive integration cued task-switching paradigm, social incentives show clearly weaker and qualitatively distinct influences on motivated cognitive control and associated task performance than do liquid incentives. Future work is needed to characterize the role that social incentives play in motivating goal-directed behaviors, and how, or if, different components of reward processing (i.e., wanting, liking) to social stimuli contribute to such behaviors. This type of research is essential for understanding how diverse incentive types are used to guide decision-making processes in everyday life and motivate the successful mobilization of cognitive control.

DATA AVAILABILITY STATEMENT

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found in the article/**Supplementary Material**.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Washington University Human Research Protections Office. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

JC, DY, HH, RT, and TB designed the research. JC, AN, and KS performed the research. JC, DY, HH, AN, KS, and TB analyzed the data. JC wrote the first draft of the manuscript. All authors edited the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2020.02212/full#supplementary-material

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Neural Basis of Increased Cognitive Control of Impulsivity During the Mid-Luteal Phase Relative to the Late Follicular Phase of the Menstrual Cycle

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Hormonal changes across the menstrual cycle have been shown to influence reward-related motivation and impulsive behaviors. Here, with the aim of examining the neural mechanisms underlying cognitive control of impulsivity, we compared event-related monetary delay discounting task behavior and concurrent functional magnetic resonance imaging (fMRI) revealed brain activity as well as resting state (rs)-fMRI activity, between women in the mid-luteal phase (LP) and women in the late follicular phase (FP). The behavioral data were analyzed and related to neural activation data. In the delay discounting task, women in the late FP were more responsive to short-term rewards (i.e., showed a greater discount rate) than women in the mid-LP, while also showing greater activity in the dorsal striatum (DS). Discount rate (transformed *k*) correlated with functional connectivity between the DS and dorsal lateral prefrontal cortex (dlPFC), consistent with previous findings indicating that DS-dlPFC circuitry may regulate impulsivity. Our rs-fMRI data further showed that the right dlPFC was significantly more active in the mid-LP than in late FP, and this effect was sensitive to absolute and relative estradiol levels during the mid-LP. DS-dlPFC functional connectivity magnitude correlated negatively with psychometric impulsivity scores during the late FP, consistent with our behavioral data and further indicating that relative estradiol levels may play an important role in augmenting cognitive control. These findings provide new insight into the treatment of conditions characterized by hyper-impulsivity, such as obsessive compulsive disorder, Parkinson disease, and attention deficit hyperactivity disorder. In conclusion, our results suggest that cyclical gonadal hormones affect cognitive control of impulsive behavior in a periodic manner, possibility via DS-dlPFC circuitry.

Keywords: cognitive control, impulsivity, menstrual phase, dlPFC, dorsal striatum

INTRODUCTION

It has been posited that observed influences of menstrual cycle phase in women on reward-related impulsivity reflect alterations in brain dopamine function and thus downstream effects of those alterations on dopamine efferent targets in the basal ganglia and frontal cortex (Xiao and Becker, 1994; Jackson et al., 2006). These circuits are critically involved in temporal and reward processing (McClure et al., 2004; Kim et al., 2012); they are organized by gonadal steroid hormones during early development and are modulated by these hormones in adults (Xiao and Becker, 1994; Jackson et al., 2006). When estradiol levels are highest during the late follicular phase (FP), women have been shown to be more responsive to rewarding substances, such as cocaine (Terner and De Wit, 2006), and reward-related activation in the mesolimbic system has been shown to be enhanced in the late FP, compared with that in the mid-luteal phase (LP) when progesterone levels peak (Dreher et al., 2007). Self-reported liking of smoked cocaine is greater during the late FP than the mid-LP (Sofuoglu et al., 1999; Evans and Foltin, 2006). Animal studies have also provided evidence of estrogenic modulation of reward-related impulsivity. For example, female rats exhibit their maximal cocaine self-administration levels shortly after estradiol peaks, and exogenous administration of estradiol enhances the acquisition of cocaine self-administration in ovariectomized female rats (Lynch et al., 2001; Jackson et al., 2006). These findings suggest that the proclivity of female mammals to wait for a higher reward is reduced in the late FP relative to the mid-LP.

In contrast, progesterone may play a role in reducing impulsive behavior by favoring more cognitive control. Progesterone is a female gonadal hormone that is often included in hormonal contraceptives and drugs used to maintain pregnancies (Jones et al., 2005). Exogenously delivered progesterone can alleviate stimulant abuse in animals (Anker et al., 2009; Zlebnik et al., 2014) and may support stimulant use cessation in humans (Evans and Foltin, 2006, 2010; Quinones-Jenab and Jenab, 2010; Fox et al., 2013; Carroll and Lynch, 2016; Swalve et al., 2016). Furthermore, progesterone, or its metabolite allopregnanolone, reduce stress and impulsive behavior as measured by the Stroop test in humans (Milivojevic et al., 2016). Neuroimaging studies have demonstrated that increases in progesterone levels from the late FP to the mid-LP result in changes in activity in several prefrontal cortex regions (Dreher et al., 2007; Van Wingen et al., 2008; Ossewaarde et al., 2011; Marečková et al., 2012). Thus, the relatively high progesterone and low estradiol levels during the mid-LP may affect the functioning of brain regions involved in cognitive control in a manner that results in reduced impulsivity.

The main estrogen receptor is highly expressed in the amygdala (Wharton et al., 2012), which sends glutamatergic efferents to the striatum, especially the dorsal striatum (DS), a crucial brain area in the reward system related to impulsivity (Yager et al., 2015). Cummings et al.'s results (2014) suggested that estradiol enhances dopamine release in the DS, but not ventral striatum (VS), in female rats. A recent study showed that women's responses to drug cues in the DS, specifically in the putamen, were modulated by menstrual phase (Franklin et al., 2019).

A large body of evidence indicates that the dorsolateral prefrontal cortex (dlPFC) plays an important role in cognitive control (Sheline et al., 2010; Cieslik et al., 2013). Moreover, the quality of communication between the DS and dlPFC may modulate cognitive control of impulsivity. A neural circuit linking the right caudate nucleus head and putamen with the dlPFC has been identified as a cognitive loop (Rotge et al., 2008). Commonly, patients with altered frontal-striatal function—such as in obsessive compulsive disorder (Heuvel et al., 2005), Parkinson disease (Williamsgray et al., 2007), and Huntington's chorea (Watkins et al., 2000)—exhibit executive functioning deficits. Reduced resting state (rs)-functional connectivity between the right caudate and dlPFC has been associated with cognitive control deficits in internet gaming disorder (Yuan et al., 2016). Remarkably, in a functional magnetic resonance imaging (fMRI) study examining rs-functional connectivity in women smokers, Wetherill et al. (2016) found that, compared to data obtained during the LP, when in the FP of their menstrual cycles women had lower rs-functional connectivity between cognitive control areas (dorsal/subgenual anterior cingulate cortex and medial orbitofrontal cortex) and a reward-related region (i.e., the VS) as well as less cognitive control over their smoking behavior.

Humans have a tendency for delay discounting, a phenomenon wherein the value of a delayed rewards are over-discounted relative to that of a reward that can be obtained immediately or sooner (Frederick et al., 2002; Green and Myerson, 2004). Delay discounting has been conceptualized as an index of impulsivity (Staubitz, Lloyd, and Reed). Theoretically, the more a person discounts the value due to its delay, the more impulsive their choice is considered. Patients with conditions that affect brain dopamine systems, namely Parkinson disease and obsessive compulsive disorder, have been shown to exhibit more pronounced delay discounting than healthy and neurotypical people (Guttman and Seeman, 1985; Volkow et al., 1993; Hesse et al., 2005). This intensified preference for selecting of smaller, sooner rewards over larger, later rewards in these populations has been termed a Now bias (Smith et al., 2014).

The aim of the present study was to investigate the neural mechanisms underlying the modulatory effects of menstrual cycle phase on cognitive control of impulsivity with an event-related monetary delay discounting behavioral task and a rs-fMRI study. We chose to compare behavioral and imaging results between the late FP, when there are high estradiol levels with low progesterone levels, and the mid-LP, when both estradiol and progesterone levels are relatively high (**Figure 1**). We hypothesized that, compared to women in the mid-LP, women in the late FP would show a greater Now bias in the delay discounting task concomitant with higher activity in the DS. Furthermore, we hypothesized that a brain regions related to cognitive control, including the dlPFC, would be more active during the mid-LP, leading to the behavioral acceptance of later, larger rewards. Finally, we hypothesized that DS-dlPFC functional connectivity may play an important role in regulating impulsivity. To test our hypotheses, choices in the delay discounting task (McClure et al., 2004), performed during fMRI scanning, were compared between women in the late FP and women in the mid-LP (task fMRI study). Because fMRI signal fluctuations at rest contain information about functional network architecture (Fox et al., 2005; Fox and Raichle, 2007; Biswal, 2012), we also compared rs-functional connectivity between these two groups (rs-fMRI study) and correlated the connectivity data to hormone level data.

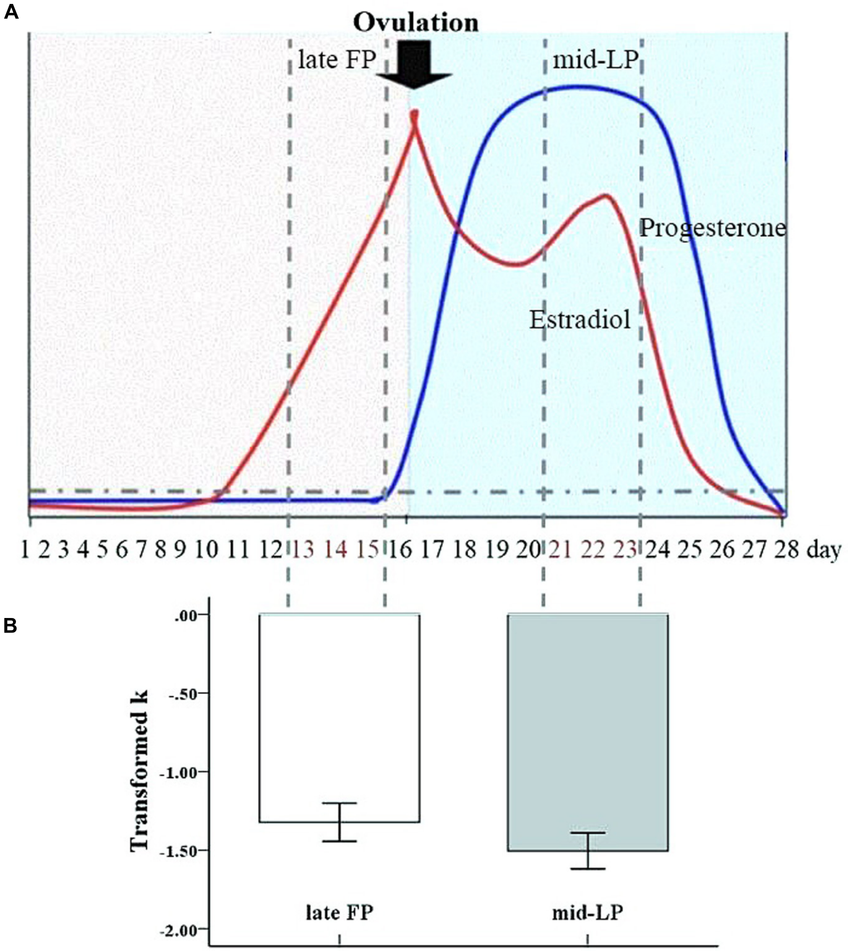

FIGURE 1 | Transformed discount rate (*k*) by menstrual phase. The mean transformed *k* value was significantly greater during the late FP than during the mid-LP (error bars indicate the standard error of the mean).

TASK fMRI STUDY

Methods

Participants

A cohort of 24 healthy, right-handed, female undergraduates (mean age [± standard deviation (SD)], 22.79 ± 1.44 years; range 20–25) were enrolled. The participants were recruited from a larger, common subject pool with certain inclusion/exclusion criteria, only individuals who were heterosexual, reported having a 28- to 30-day menstrual cycle, and did not take any form of hormones in the previous 3 months were included. Because the criteria for these other studies included heterosexuality as an inclusion criteria, the participants in the current study were exclusively heterosexual. However, it is important to note that this criteria was incidental (and otherwise irrelevant) for the research questions addressed in the current study. The participants were asked to come to the laboratory on two separate occasions (late FP and mid-LP) to complete an intertemporal choice task. The tasks were the same the two testing times, but we did not state this explicitly to the participants.

We used the backward counting method to predict each participant’s next menstrual onset, late FP (14–16 days prior to the predicted menstrual onset), and mid-LP (6–8 days prior to the predicted menstrual onset). This method has been successfully used to predict other effects of theoretical interest (Durante et al., 2011; Zhuang and Wang, 2014). If a woman’s next predicted menstrual onset was 8–14 days away, she was scheduled to complete the mid-LP testing first (*N* = 10); otherwise, she was scheduled to complete the late FP testing first (*N* = 14).

All participants had normal or corrected-to-normal vision. No participants reported a history of a psychiatric disorder or current use of a psychoactive medication. The protocol was reviewed and approved by the Ethics Committee of the local University and the study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants, and they were compensated 50 RMB per hour.

Behavioral Task and Procedure

Prior to scanning, the subjects were presented with a 9-rung ladder scale. They were instructed to place themselves on the ladder that ranged from 1 (lowest rung) to 9 (highest rung) based on where they stand compared to others in terms of family economic level and social status level, respectively (Adler et al., 1994).

The intertemporal binary choice paradigm (see **Supplementary Material**) was performed as described previously (McClure et al., 2004). In each pair of choices, the sooner option always had a lower reward value than the delayed option. The two options were separated by either 2 weeks or 1 month, with wait times ranging from the day of the experiment to 6 weeks later. Thus, the sooner option was sometimes available immediately and sometimes available after a delay (see **Figure 2**). The reward amount ranged from 31.25 to 250.00 RMB (USD equivalent, $5–40; conversion rate 1:6.25). In each experiment, the participant made 48 binary hypothetical choices, and the order of the choices was randomized within and across the participants.

The behavioral experiment was conducted entirely inside an fMRI scanner. The participants were instructed to make a series of choices between a smaller, sooner reward ($r1$ available at delay $t1$) and a later, larger reward ($r2$ available at delay $t2$; where $r1 < r2$ and $t1 < t2$). Each participant was instructed to indicate her preference as soon as the choice was displayed by pressing one of two buttons that corresponded with the location of the preferred option with her right hand. The smaller, sooner options were always presented on the left. Decisions were self-paced with a maximum allowed reaction time of 15 s. After each choice, a feedback screen was presented for 2 s to indicate the choice outcome (McClure et al., 2004). All responses were submitted well before the 15-s time limit. Each subject completed two 24-trial runs. Each trial was followed by a jitter interval (1500 ms, 50% of trials; 4000 ms, 25%; 6000 ms, 16.7%; and 12,000 ms, 8.3%). Prior to being presented with the choices, the participants were administered two control questions to familiarize themselves with the nature of the task. The entire experiment took ∼ 8 min. The stimuli were presented via the *in vivo Esys* system for fMRI (Gainesville, FL, United States).

Imaging Data Acquisition

Scanning was conducted on a 3-T Siemens scanner at the fMRI laboratory of East China Normal University in Shanghai. Functional images were acquired with a gradient echo-planar imaging sequence, 2000-ms repetition time (TR), 30-ms echo time (TE), 220-mm field of view (FOV), 3 mm × 3 mm × 3.5 mm

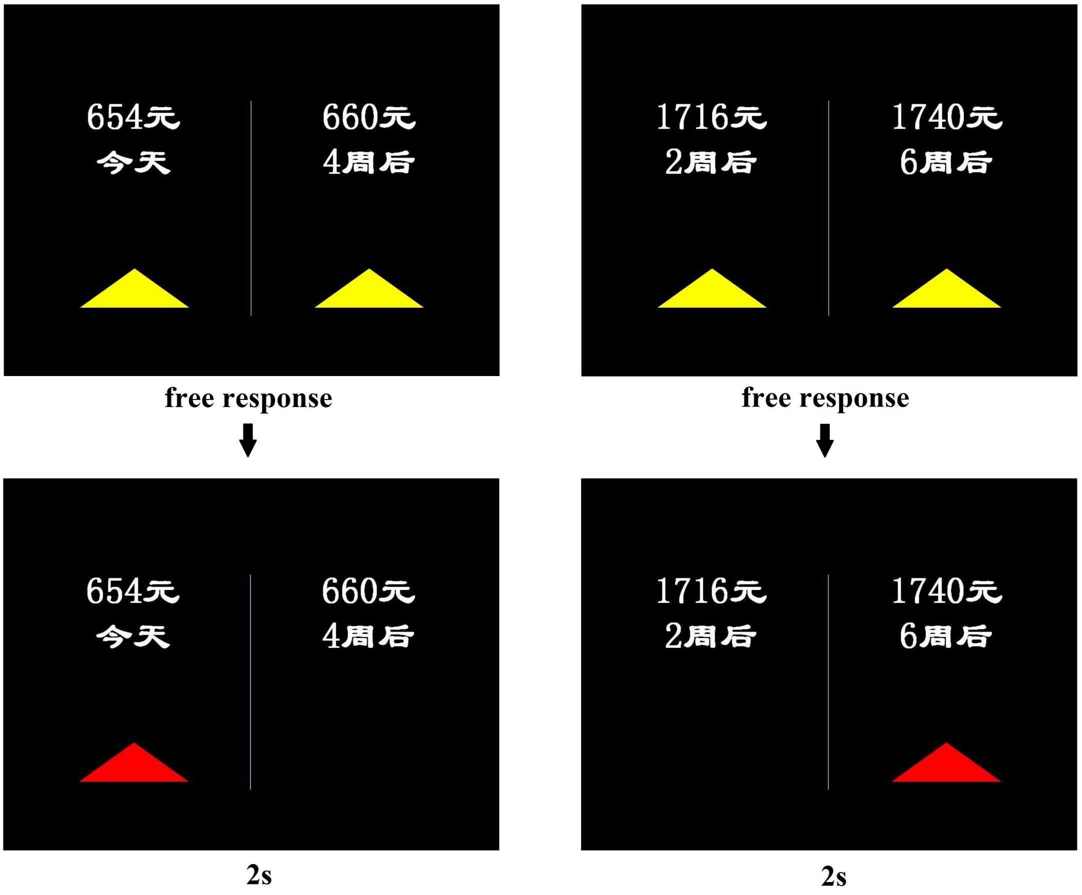

FIGURE 2 | Examples of sooner reward and delayed reward options. During fMRI scanning, in each trial, the participants viewed a choice screen (above), made a self-paced choice response, and subsequently viewed a choice outcome screen (below) for 2 s. The reward options were in Simplified Chinese and read "今天" (now), 2 周以后 (2 weeks later), 4周以后 (4 weeks later), 6周以后 (6 weeks later).

voxel size and 32 slices. 112 images per scan were acquired and a total was 224 across the two scans. The first five TRs acquired were discarded to allow for T1 equilibration. Prior to the fMRI scanning, a high-resolution structural image was acquired with a T1-weighted, multiplanar reconstruction sequence (TR = 1900 ms, TE = 3.42 ms, FOV = 256 mm, 1 mm × 1 mm × 1 mm voxel size, and 192 slices).

Behavioral Data Analysis

We employed a calculation method similar to that used by Kim et al. (2012), in which the behavioral data were fitted assuming a hyperbolic discount function. The discounted value function is given by

$$V(r, t) = \frac{r}{1 + kt}$$

where r is the reward amount available at delay t, and V is the subjective value of the offer. The discount rate (k) for each subject was estimated by assuming a logistic decision function and maximizing the log-likelihood of the observed choices. Best-fit model parameters were determined in Matlab[1] using a simplex search algorithm with 100 random initial parameter values. Subsequently, the k values were transformed logarithmically to permit parametric statistical analyses. For each participants, we calculated an immediate choice ratio (ICR; the number of sooner choices divided by the total number of choices). Because arcsine-square root transformed ICRs correlate well with the hyperbolic discounting rate variable k (Boettiger et al., 2009; Xu et al., 2009), we subjected the ICRs to arcsine-square root transformation.

Logarithmically transformed k values were compared between the late FP and mid-LP conditions with paired samples t-tests. We also conducted a correlation analysis between the transformed k and ICR values. The paired samples t-test was used to test for an order effect on the transformed k across the two menstrual phase conditions.

Imaging Data Analysis

The fMRI data were analyzed in Statistical Parametric Mapping 8 (SPM8, Wellcome Department of Cognitive Neurology, London, United Kingdom). We performed a slice-timing correction and, subsequently, aligned the data to correct for head movement. Images were smoothed with an 8-mm full-width at the half-maximum Gaussian kernel and then normalized to the Montreal Neurological Institute template and re-sampled at 3 mm × 3 mm × 3 mm resolution.

General linear modeling (GLM) was conducted in SPM8. For the first level GLM analysis, we used an event-related design to estimate neural responses to events of interest. Potentially confounding variables, such as trial-by-trial head movements and choice outcomes (i.e., motor responses), were included in the GLM as regressors of no interest. As suggested by the as soon as possible model (Kable and Glimcher, 2010), we expected participants to overweight the value of the soonest available reward regardless of whether it was offered immediately or after a delay. We pooled all smaller, sooner rewards (ignoring whether they were available immediately or at a delayed time) chosen by the participants in a pair together to form the sooner reward choice condition. The remaining larger, later rewards chosen by the participants were pooled together as the delayed choice condition. Each condition [sooner reward choice in the late FP (SFP), sooner reward choice in the mid-LP (SLP), delayed reward choice in the late FP (DFP), and delayed reward choice in the mid-LP (DLP)] were modeled as reaction times from the decision onset. In the first-level analysis, simple main effects were computed for each participant for each of the above mentioned conditions by applying a '1 0' contrast, where 1 represents one of these conditions, and 0 represents all other possibilities.

For the second (group) level analysis, we conducted random effect modeling (flexible factorial design) to analyze the first-level individual contrast images. The main effect of menstrual phase was calculated by comparing late FP trials versus mid-LP trials. The main effect of delay discounting was obtained by comparing sooner-reward choice trials versus delayed-reward choice trials. The interaction between menstrual phase and delay discounting was calculated to extract brain regions that showed higher or lower sensitivity to the sooner reward outcome over the delayed reward outcome among women in the late FP versus women in the mid-LP.

All data were initially thresholded at a value of $p < 0.001$ (uncorrected), and the results were reported at a cluster statistical threshold of a family-wise error (FWE)-corrected $p < 0.05$. Activations were localized with the anatomy toolbox in SPM8 (Eickhoff et al., 2005) using the MRIcron automated anatomical labeling template (Tzourio-Mazoyer et al., 2002).

Region of interest (ROI) analyses

Region of interest analyses were conducted to further refine our hypothesis. ROIs were selected based on our hypotheses and previous studies (Cummings et al., 2014; Franklin et al., 2019). Based on prior relevant work (Pine et al., 2010), the following Montreal Neurological Institute (MNI) coordinates for bilateral ROIs were defined: putamen, MNI coordinates 30 −3 −12 and −24 12 −9; caudate, MNI coordinates 21 24 −3 and −9 12 9; and dlPFC, MNI coordinates 42 18 27 and −45 33 18. We extracted an average beta value for each ROI in each condition (sooner reward choice and delayed reward choice in each menstrual phase) for each participant by selecting a 6-mm sphere around the coordinates using the MarsBaR ROI toolbox 0.44 in SPM8 (Brett et al., 2002). All beta values were submitted to a 2 (delay discounting: sooner vs. delayed reward choice) × 2 (menstrual phase: FP vs. LP) × 6 (the aforementioned ROIs) mixed measures analysis of variance (ANOVA). We also completed a 2 (delay discounting: sooner vs. delayed reward choice) × 2 (menstrual phase: FP vs. LP) mixed measures ANOVA for each ROI. Mean beta values are reported with SDs.

Functional connectivity analysis

To test our neural circuitry hypothesis, we conducted beta series correlation (BSC) analyses of the functional connectivity between the DS (putamen and caudate) and dlPFC within each condition (SFP, SLP, DFP, and DLP). First, based on the above-defined ROIs, each trial was modeled as a separate event of interest (Rissman et al., 2004) and the beta series associated with each

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[1] https://www.mathworks.com/

trial type within each ROI were extracted and sorted by study condition. Pair-wise BSC analyses were performed for the DS and the dlPFC. After calculating the correlation between activities in each ROI pair individually for each subject and for each condition across the time series, the correlation values obtained were subjected to Fisher transformation prior to being subjected to ANOVAs designed to detect which correlations varied across delay discounting choice and menstrual phase.

Correlations between DS-dlPFC functional connectivity and discount rate

We conducted correlation analyses between discount rate (transformed *k*) and functional connectivity (as indexed via BSCs) within each condition to investigate the effect of DS-dlPFC circuitry on impulsivity.

Results

Demographics

A total of 8 participants were excluded from further analysis, including 3 for excessive head motion (>2-mm displacement in the *x*, *y*, or *z* dimension, or >2° angular shift) during scanning, 2 because tracking of their next menstruation revealed that we did not have an accurate menstrual date, and 3 whose behavioral data did not conform to the model from the log-likelihood of observed choices. The 16 remaining participants (mean age 22.44 ± 1.31 years; range, 20–24) included 8 participants who were initially scanned during their late FP, and 8 who were initially scanned during their mid-LP. The mean scores of the 16 participants in the final analyses had mean family economic and social status level scores of 5.81 ± 0.40 and 5.44 ± 0.51, respectively. There was very high agreement among the participants on subjective socioeconomic status [intra-class correlation (1,15) = 0.788], which suggests that behavioral effects observed in the experiment cannot be attributed to a confounding effect of subjective value variations.

Behavior

A paired samples *t*-test did not show an effect of testing order (i.e., which phase women were in during first test) on transformed *k* values [$t_{2,14} = -0.97$, $p = 0.35$, $d = -0.52$]. Meanwhile, a paired samples *t*-test showed a significant difference in transformed *k* values between the late FP and mid-LP ($t_{1,15} = -2.14$, $p = 0.049 < 0.05$, $d = 0.\ 43$), with a significantly greater mean discount rate being observed in the late FP (−1.32 ± 0.49) than in the mid-LP (−1.51 ± 0.46) (**Figure 1**). Transformed *k* and ICR values were highly correlated within each menstrual phase (FP: $r = 0.94$, $p < 0.001$; LP: $r = 0.96$, $p < 0.001$) (see **Table 1**).

Whole Brain Analysis

We observed main effects of menstrual phase on activity in several visual areas, including greater activation during the mid-LP than during the late FP in the bilateral lingual gyrus, bilateral calcarine gyrus, left middle occipital gyrus, and left inferior occipital gyrus. No other meaningful brain areas were found in the opposite contrast. With respect to delay discounting, brain regions that were preferentially activated by the prospect of a sooner reward choice over a delayed reward choice (sooner > delayed) included the right putamen, the right thalamus, and the right supplementary motor area. In the reverse contrast (delayed > sooner), greater activation was identified in the left postcentral gyrus and left superior parietal lobule. Analysis of interactions between menstrual phase and delay discounting revealed more active regions in the left putamen, bilateral caudate, bilateral visual areas [Brodmann area (BA)17 and 18], left hippocampus, and left insula in the (late FP – mid-LP) - (sooner – delayed) comparison; there was no regions that were significantly more active in the reverse comparison (**Table 2**).

ROI Analyses

A 2 (delay discounting) × 2 (menstrual phase) × 6 (ROI) mixed measures ANOVA revealed a significant main effect of ROI ($F_{5,90} = 9.49$, $p < 0.001$, $\eta_p^2 = 0.35$) and a significant interaction of delay discounting and menstrual phase ($F_{1,90} = 8.97$, $p = 0.004$, $\eta_p^2 = 0.09$) (**Figure 3**; non-significant effect data are reported in the **Supplementary Material**). Regarding the ROI effect, *post hoc* analysis indicated that the beta value for the left dlPFC was significantly greater than the values obtained for all other ROIs ($p_s \leq 0.005$), while the beta value for the right dlPFC was significantly greater than the values obtained for the right putamen ($p = 0.003$) and right caudate ($p = 0.010$). Simple effects analysis of the delay discounting × menstrual phase interaction showed that when choosing the sooner rewards, beta values differed significantly between the late FP and mid-LP ($F_{1,90} = 6.61$, $p = 0.010$, $\eta_p^2 = 0.07$), with a greater mean beta value being observed in the late FP (0.98 ± 0.17) than in the mid-LP (0.58 ± 0.17). Specifically, for the left putamen, we found a significant main effect of menstrual phase ($F_{1,15} = 5.1$, $p = 0.040$, $\eta_p^2 = 0.25$), wherein women in the late FP (0.99 ± 1.22) had higher mean beta value than in the mid-LP (0.30 ± 0.77). There

TABLE 1 | Means and correlations of *k* and ICR values within menstrual phase datasets.

Statistical value	Late FP			Mid-LP		
	Mean (*n*)	**SD**	**Pearson correlation *r***	**Mean (*n*)**	**SD**	**Pearson correlation *r***
k	4.145 (16)	0.879		3.901 (16)	0.732	
ICR	0.544 (16)	0.208		0.478 (16)	0.180	
Transformed *k*	−1.323 (16)	0.488	0.938**	−1.506 (16)	0.458	0.964**
Transformed ICR	0.836 (16)	0.234		0.767 (16)	0.200	

*** Correlation is significant at the 0.01 level (2-tailed).*

TABLE 2 | Brain regions whose activity is altered in relation to menstrual phase or delay discounting.

Corrected *p*	***k***	**Regions of maxima peak**	**BA**	***T***	**H**	**MNI**		
						x	***y***	***z***
Interaction (late FP – mid-LP) - (sooner – delayed)								
<0.001	317	Caudate nucleus		5.77	R	21	24	9
		Putamen	11	4.33	L	−15	15	−6
		Caudate nucleus	25	4.15	L	−6	12	5
<0.001	255	Calcarine gyrus	18	4.94	L	−3	−84	12
		Middle occipital gyrus	18	4.52	L	−18	−102	5
		Superior occipital gyrus	17	4.42	L	−9	−102	9
		Lingual gyrus	18	4.28	R	12	−84	−9
		Cuneus	18	4.02	R	12	−99	12
0.005	126	Hippocampus	20	4.86	L	−33	−9	−16
		Inferior temporal gyrus	20	4.82	L	−45	−9	−27
		Insula	48	3.44	L	−36	−9	−6
0.017	94	Cerebellum	37	4.79	L	30	−39	−23
0.018	92	Putamen	48	3.61	L	−21	6	−6
0.035	77	Postcentral gyrus	48	4.22	L	−60	−15	23
		Precentral gyrus	6	3.83	L	−60	3	30
Main effect of menstrual cycle phase (mid-LP – late FP)								
<0.001	911	Lingual gyrus	18	6.16	L	−12	−96	−13
		Inferior occipital gyrus	19	5.25	L	−36	−90	−13
		Calcarine gyrus	18	5.13	L	0	−99	9
		Middle occipital gyrus	17	5.09	L	−12	−99	5
		Inferior temporal gyrus	37	4.30	L	−45	−61	−8
0.032	79	Cerebellum		4.94	L	−6	−78	−37
0.034	61	Precentral gyrus	6	5.05	L	−51	−3	51
Main effect of delay decision (sooner - delayed)								
<0.001	1233	Precentral gyrus	4	10.68	R	36	−21	54
		Supplementary motor area	6	5.77	R	6	0	47
		Superior parietal lobule	5	5.24	R	15	−51	65
<0.001	704	Cerebellum	37	8.04	L	−21	−45	−27
		Lingual gyrus	18	3.93	L	−18	−72	−6
<0.001	304	Rolandic operculum	48	5.64	R	48	−18	19
		Thalamus		5.12	R	18	−21	9
		Putamen	48	4.11	R	30	−12	2
Main effect of delay decision (delayed - sooner)								
<0.001	709	Postcentral gyrus	4	10.72	L	−42	−27	65
		Superior parietal lobule	7	4.82	L	−24	−42	72
0.027	62	Cerebellum	19	6.08	R	15	−51	−16

Results are reported at cluster significance after FWE correction at p < 0.05 for multiple comparisons; k = cluster size; L, left; R, right; H, hemisphere.

was a significant delay discounting × menstrual phase interaction for the right putamen ($F_{1,15}$ = 5.02, p = 0.040, η_p^2 = 0.25). Simple effect analysis showed that the mean beta value was significantly higher when women chose sooner rewards in the late FP (0.02 ± 1.12) than when they did so in the mid-LP (−0.76 ± 0.72; $F_{1,15}$ = 7.96, p = 0.010, η_p^2 = 0.35). No other effects were significant (**Figure 3**).

Similarly, we found a significant delay discounting × menstrual phase interaction for the right caudate ($F_{1,15}$ = 6.86, p = 0.020, η_p^2 = 0.31). Simple effect analysis showed that the mean beta value was significantly higher when women chose the sooner rewards in the late FP (0.27 ± 0.77) than when they did so in the mid-LP (−0.19 ± 0.80; $F_{1,15}$ = 8.65, p = 0.010, η_p^2 = 0.37). We did not find any significant effects for the left caudate (**Figure 3**).

For the right dlPFC, there was a significant delay discounting × menstrual phase interaction ($F_{1,15}$ = 5.90, p = 0.030, η_p^2 = 0.28), but no significant effects were observed in the simple effects analysis. However, we did observe a tendency showing that the mean activation level in the DLP condition (1.67 ± 2.86) was higher than in the other conditions (SLP, 1.02 ± 2.28; SFP, 1.41 ± 1.91; DFP, 1.38 ± 2.34). No significant main effects (delay discounting, $F_{1,15}$ = 1.32, p = 0.270, η_p^2 = 0.81; menstrual phase $F_{1,15}$ = 0.53, p = 0.480, η_p^2 = 0.34) and no significant delay discounting × menstrual phase interaction

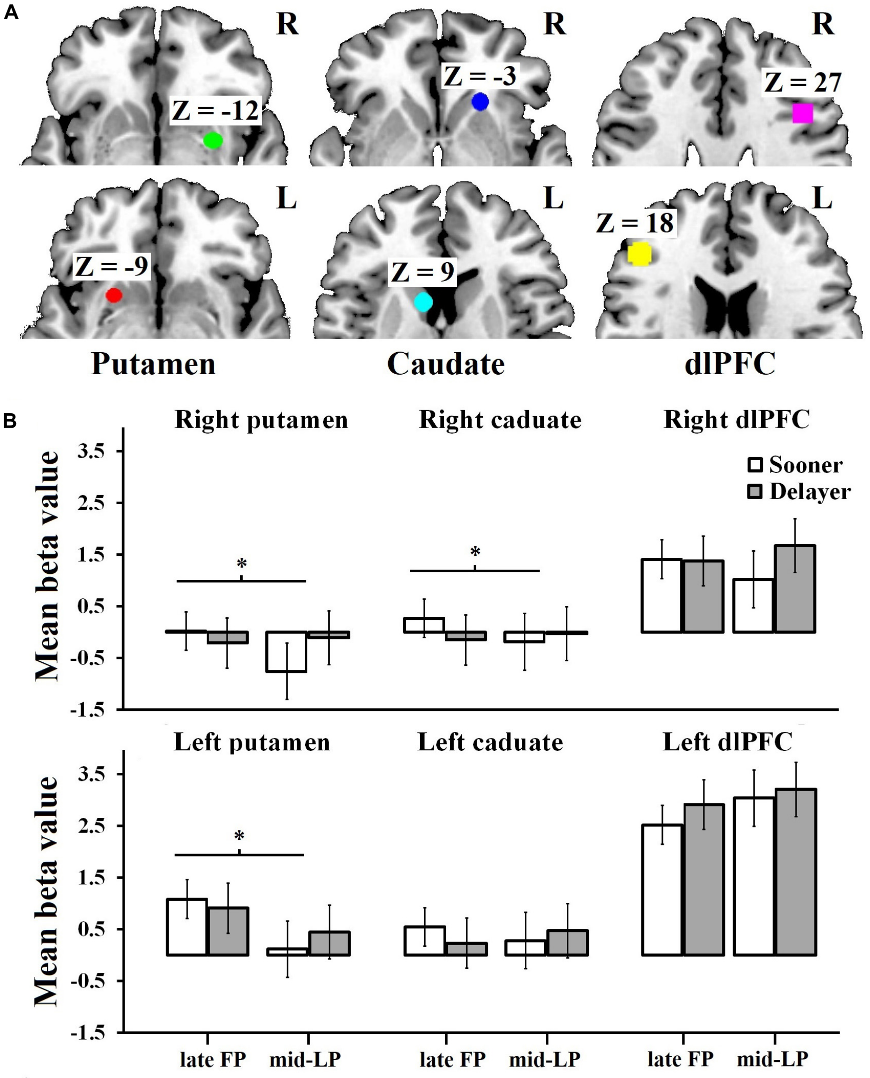

FIGURE 3 | Mean beta values for ROIs by condition. **(A)** The ROIs of the left putamen [–24, 12, –9], right putamen [30, –3, –12], left caudate [–9, 12, 9], right caudate [21, 24, –3], left dlPFC [–45, 33, 18], and right dlPFC [42, 18, 27]. **(B)** Activation of the left putamen was significantly higher during the late FP than during the mid-LP. Moreover, when choosing sooner rewards, the mean beta values of the right putamen and the right caudate were much greater during the late FP than during the mid-LP. A significant interaction was observed for the right dlPFC; simple effects analysis showed a tendency for right dlPFC activation to be higher in the DLP condition than in the DFP, SLP, and SFP conditions. *The effect is significant at the 0.05 level.

($F_{1,15}$ = 0.33, p = 0.570, η_p^2 = 0.02) were observed for the left dlPFC (**Figure 3**).

The results above indicated that the right DS was more active during the late FP than during the mid-LP when sooner rewards were chosen (i.e., SFP > SLP for right DS). In contrast, the dlPFC showed a tendency to be more active during the mid-LP than during the late FP when delayed rewards were chosen (i.e., DLP > DFP for the dlPFC).

Functional Connectivity Across Menstrual Phases

An ANOVA revealed a significant main effect of menstrual phase on the functional connectivity between the left putamen and left dlPFC ($F_{1,15}$ = 7.40, p = 0.020, η_p^2 = 0.33). The magnitude of this connectivity was significantly stronger in the mid-LP (0.22 ± 0.32) than in the late FP (0.00 ± 0.42). There were no other significant ROI functional connectivity effects.

Correlations Between DS-dlPFC Functional Connectivity and Discount Rate Across the Menstrual Phases

In the SFP condition, functional connectivity between the right caudate and the bilateral dlPFC correlated inversely with discount rate (right caudate-right dlPFC: r = −0.64, p = 0.010; right caudate-left dlPFC: r = −0.64, p = 0.010) (**Figure 4**). Conversely, in the SLP condition, functional connectivity between the right dlPFC and the right putamen correlated directly with discount rate (r = 0.50, p = 0.050).

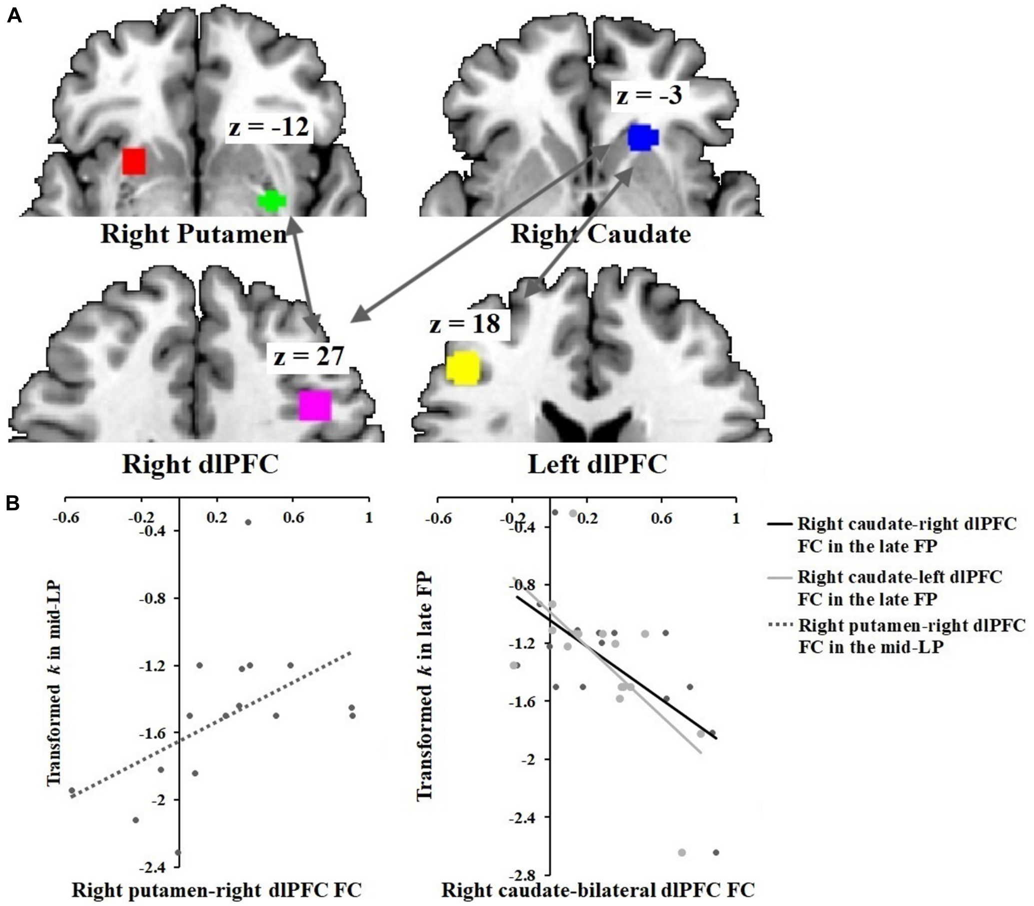

FIGURE 4 | Correlations between DS-dlPFC functional connectivity and discount rate across menstrual phases. **(A)** ROIs: right putamen [30, –3, –12], right caudate [21, 24, –3], right dlPFC [42, 18, 27] and left dlPFC [–45, 33, 18]. **(B)** Discount rate correlated positively with right putamen-right dlPFC functional connectivity in the SLP condition. Discount rate correlated negatively with right caudate-bilateral dlPFC functional connectivity in the SFP condition.

Discussion

Using the delay discounting task, which assesses intertemporal choice similar to the task used by McClure et al. (2004), we demonstrated that delay discounting behavior in women was affected by menstrual phase, such that the discount rate was significantly greater in the late FP than in the mid-LP, and this augmented discount rate was associated with enhanced activity in the DS. Specifically, greater activation was observed in the left putamen during the late FP than during the mid-LP. Moreover, women showed greater activation in the right DS (putamen and caudate) when choosing sooner rewards in the late FP than when do so in the mid-LP (i.e., SFP > SLP), indicating that the right DS is more responsive to immediate rewards during the late FP than during the mid-LP. These results are consistent with the prior findings showing that a heightened drug cue-responsivity in women is associated with enhanced activity in the DS, especially in the putamen (Cummings et al., 2014; Franklin et al., 2019). Indeed, behavioral impulsivity has been linked to dopamine levels in the putamen. For example, in adult men, higher trait impulsivity as measured by Barratt Impulsiveness Scale (BIS) scores correlated negatively with dopamine transporter availability in the putamen (Costa et al., 2013). Additionally, a lower dopamine synthesis capacity in the putamen, indexed by 6-[^{18} F]fluoro-L-*m*-tyrosine signal, was shown to be predictive of an elevated Now bias and a reduced willingness to accept low-interest rate delayed rewards (Smith et al., 2016).

The VS/nucleus accumbens have been strongly implicated in the seeking the sooner rewards in intertemporal choice paradigms (McClure et al., 2004; Kim et al., 2012), with nucleus accumbens activation in particular being related to reward magnitude sensitivity (Ballard and Knutson, 2009). Our not finding an effect of menstrual phase on these areas suggests that VS reward sensitivity may not be modulated by menstrual phase. Indeed, intertemporal choice in humans has been shown to vary with region-specific dopamine processing, with regionally distinct associations with sensitivity to delay (the putamen) and reward magnitude (the VS) (Ballard and Knutson, 2009; Smith et al., 2016). Studies have linked dopamine availability in the putamen with time perception, a cognitive process thought to contribute to discounting of delayed rewards (Wittmann and Paulus, 2008; Takahashi, 2011; Smith et al., 2016). For example, Parkinson disease patients, who have deficits in putamen dopamine signaling, show selective impairments in time duration comparison (Dormal et al., 2012). A pharmaco-fMRI study related the relationship between dopamine depletion and time perception specifically to activity in the putamen (Coull et al., 2012). Our finding the putamen was more active in the SFP condition than in the SLP condition suggests that naturally cycled ovarian steroid hormones may modulate an aspect of time perception in intertemporal choice, perhaps through steroid hormone modulation of dopamine levels. However, proving such a modulatory effect would require dopamine level data. Future research should compare dopamine levels across menstrual phases to help elucidate the influence of steroid hormones on intertemporal choices.

Although we observed a significant menstrual phase × delay discounting interaction influence on right dlPFC activity, simple effect analysis revealed only a trend toward higher activation in the DLP condition relative the other conditions. *Post hoc* analysis of ROIs indicated that beta values were significantly higher for the dlPFC than for the DS. Because the striatum and prefrontal cortex are intermodulated via frontostriatal networks (Yuan et al., 2016), impulsivity variance across menstrual phases may be determined, at least in part, by relative activity levels between the DS and dlPFC. Although the activity in the dlPFC was stable across menstrual phases, heightened DS activity during sooner reward selection in women late FP may lead to relatively less potent top-down cognitive control. Conversely, lesser DS activity during the mid-LP may enable more potent cognitive control. Thus, our results suggest that the activities of the DS and dlPFC relative to each other may determine the level of cognitive control over impulsivity, such that there is stronger cognitive control during the mid-LP than during the late FP.

The present results also support the notion that DS-dlPFC circuitry is involved in the regulation of impulsivity. Specifically, when participants chose sooner rewards during the late FP, right caudate-dlPFC functional connectivity correlated negatively with discount rate, indicating a linear relationship between the reduced right caudate-dlPFC connectivity and increased impulsivity (indexed by discount rate) during the late FP, consistent with rs-functional connectivity findings in participants with internet gaming disorder (Yuan et al., 2016) and cigarette-dependent women (Wetherill et al., 2016). Conversely, in the SLP condition, right putamen-right dlPFC functional connectivity correlated directly with discount rate. The hierarchical reinforcement learning theory (Holroyd and Yeung, 2012) has suggested the dlPFC and motor structures in the DS (mainly the putamen) execute options chosen by other brain regions. If so, the aforementioned correlation may reflect an effect of execution function.

Anatomically, the DS includes the dorsal regions of the putamen and caudate nucleus (Porter et al., 2014). Although these two subregions both receive nigrostriatal dopaminergic projections (Fallon and Moore, 1978) and are involved in motivated behavior via the prefrontal cortex, functionally, the caudate is important for reward-related cognition whereas the putamen is more involved in motor behaviors (Baskerville and Douglas, 2010). Thus, the opposing directionality found in our results may reflect different functions of the DS-dlPFC circuitry.

Our results suggest that DS-dlPFC functional connectivity may modulate impulsivity in intertemporal choices, with opposing directionality and differential involvement of brain regions depending upon menstrual phase.

This study had notable limitations. First, although we hypothesized that, brain regions related to cognitive control would be more active during the mid LP, we did not find a significant main effect of menstrual phase on the activation of brain regions related to cognitive control. This negative finding could be related to inherent characteristics of cognitive involvement in the task (McClure et al., 2004), which could confound the effect of menstrual phase. Second, menstrual phase was not confirmed by any biological tests such as hormonal assays, potentially reducing phase designation accuracy. Previously studies have found that estimates based on the backward counting method, as used here, are correct 80–90% of the time (Carroll, 2018). Indeed, several participants were excluded after follow-up revealed inaccurate estimates. Third, the delay discounting task is hypothetical. Although previous studies have shown no significant differences behaviorally or neurologically between hypothetical and real reward outcomes (Johnson and Bickel, 2002; Madden et al., 2004; Lagorio and Madden, 2005; Bickel et al., 2009; Kim et al., 2012), it is possible that an extraordinarily impulsive person might much more easily forego a tantalizing immediate reward for a delayed larger reward in a hypothetical situation than in a real situation (Reynolds et al., 2006; Rosati et al., 2007; Jimura et al., 2009; Smits et al., 2013; Carroll, 2018). Fourth, the sample size of the present study was small, which weakens the strength of our results. Finally, that the smaller, sooner options were always presented on the left during scanning would influence our results on hemispheric asymmetry.

Use of the bilateral dlPFC as a seed can be a valuable tool for exploring the function of cognitive control networks in rs-fMRI studies (Cieslik et al., 2013; Hwang et al., 2015; Tao et al., 2017). Thus, to further probe whether there is increased cognitive control functioning during the mid-LP, relative to the late FP, and the involvement of DS-dlPFC circuitry in impulsivity regulation, we conducted a rs-fMRI experiment in the following accompanying study with a inclusion of hormonal assay confirmed menstrual phases.

HORMONE AND rs-fMRI STUDY

Methods

Participants

A cohort of 53 healthy, right-handed, female undergraduate participants (mean age ± SD, 22.77 ± 2.35 years; range 19–28) were recruited from a larger, common subject pool with certain inclusion criteria, namely: heterosexual sexual orientation; 28- to 30-day menstrual cycle; and no use of any form of hormones in the previous 3 months. The reason that the participants in the current study were exclusively heterosexual was the same as in the task fMRI study above. Therefore, the heterosexuality as an inclusion criteria was incidental (and otherwise irrelevant) for the research questions addressed in the current study. The study cohort included 28 women in their late FP (mean age, 22.54 ± 2.18 years) and 25 women in their mid-LP (mean age, 23.04 ± 2.54 years). Each woman was subjected to rs-fMRI. Late FP and mid-LP were considered to be 14–16 days and 6–8 days prior to the next predicted menstrual onset, respectively, determined as in Study 1. The testing order was randomized across participants and phases.

All participants had normal or corrected-to-normal vision. No participants reported a history of a psychiatric disorder or current use of psychoactive medications. The protocol was reviewed and approved by the Ethics Committee of the local university, and the study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants, and they were compensated 50 RMB per hour.

Hormone Assays

A saliva sample was obtained from each participant immediately before scanning. To control for circadian influences on hormone levels, all experimental sessions were performed between 12:00 pm and 8:00 pm. Each participant drooled ∼2 mL of saliva passively into a collection tube, and each saliva sample was preserved in a refrigerator (−20°C). All samples were processed for estradiol and progesterone levels with DRG International ELISA kits and the ELISA results were measured with a Thermo Devices Multiskan MK3 by ThermoFisher Scientific Shanghai Company. One-way ANOVAs were conducted on each hormone separately to verify cycle phases with sample collection time as the covariate.

BIS-11

After finishing the saliva sample collection, participants completed the BIS-11 (Patton et al., 1995). The BIS-11 is a self-report questionnaire containing 30 items divided into three subscales: (i) attentional impulsiveness (e.g., "I am a careful thinker"); (ii) motor impulsiveness (e.g., "I do things without thinking"); and (iii) non-planning impulsiveness (e.g., "I am more interested in the present than the future"). Each item was scored from 1 (*strongly disagree*) to 4 (*strongly agree*), with higher scores indicating higher levels of impulsivity.

Image Acquisition

Previously, rs-functional connectivity has been used to analyze neural circuitry dynamics in normal populations (Choi et al., 2012) and in pathological states (Fox and Greicius, 2010). The rs-fMRI scanning was conducted in a 3-T Siemens scanner at our institution's fMRI facility. Functional images were acquired with a gradient echo-planar imaging sequence, 2000-ms TR, 30-ms TE, 384-mm FOV, 3 mm × 3 mm × 3.5 mm voxel size, and 33 slices. The images associated with the first ten repetitions were discarded to allow for T1 equilibration. Participants were instructed to relax with their eyes open during scanning, which lasted about 8 min. Prior to fMRI scanning, a high-resolution structural image was acquired with a T1-weighted, multiplanar reconstruction sequence (TR = 2530 ms, TE = 2.98 ms, FOV = 256 mm, 1 mm × 1 mm × 1 mm voxel size, and 192 slices).

Preprocessing

Preprocessing was performed in advanced DPARSF module V3.2 software. After correcting all volume slices for varying signal acquisition times, the images in each participant's series were realigned. Individual structural images were then co-registered to the mean functional image. The transformed structural images were segmented into gray matter, white matter, and cerebrospinal fluid (Ashburner et al., 2005). Friston's 24-parameter model was utilized to regress out head motion signal artifacts from the realigned data. White matter and cerebrospinal fluid signals were regressed out to reduce respiratory and cardiac effects. Spatial smoothing (4-mm full-width at half-maximum kernel) were applied to the functional images.

Independent Component Analysis (ICA)

GIFT (Group ICA of fMRI Toolbox) (Calhoun et al., 2001) was used to conduct group-level ICA. In the pre-processing step, datasets from each individual were mean corrected by subtracting the image mean per time point. Thereafter, for each participant, dataset dimensionality was reduced with principal component analysis using the default setting. Then, the data were group concatenated and subjected to two further principal component analysis data reduction steps. Next, the infomax algorithm was used to estimate 53 independent components from the reduced data. Finally, individual spatial maps were back-constructed from group-level component estimates with group ICA. The time courses and values of each map were scaled to represent percent signal change. No temporal filtering was applied to the data in GIFT.

Networks of interest were identified from the 53 components by spatial sorting. The executive control network (ECN) was identified by spatial sorting and statistical comparison to the resting state network 2 (RSN2) described by Mantini et al. (2007), which is strongly associated with goal-directed stimulus-response selection. RSN2 is comprised of areas within the bilateral intraparietal sulcus and at the intersections of the precentral and superior frontal sulcus, ventral precentral cortex, and middle frontal gyrus regions (Mantini et al., 2007). An RSN2 mask was constructed in WFU_PickAtlas 3.0 (Berry et al., 2015). Correlations between ECN components and RSN2 components were calculated and reported with the standard of $r \geq 0.30$ (Weis et al., 2017).

An independent sample *t*-test was carried out on the group level to estimate the effect of menstrual phase (late FP vs. mid-LP) on the beta weights of each identified component of the ECN in SPM8. Initially, the data were thresholded at $p < 0.001$ (uncorrected); the results are reported at a cluster statistical threshold of $p < 0.05$ (FWE-corrected). Activations were localized based on the MRIcron automated anatomical labeling template (Tzourio-Mazoyer et al., 2002).

Correlations Between Hormone Levels and Activity in Brain Regions

After preprocessing, the amplitude of low-frequency fluctuations of the BOLD signal (ALFF), which is thought to be related to regional spontaneous neural activity, was used to identify differences in regional resting cerebral function between menstrual phases (Cordes et al., 2001). After bandpass filtering (0.01–0.08 Hz), white matter and cerebrospinal fluid signals were removed. Following linear detrending, voxel-wise time series were transformed to the frequency domain by fast Fourier transformation to obtain power spectra. The ALFF measure at each voxel represents the square root of the power across a low-frequency range. The ALFF of each voxel was z-transformed for each subject to standardize the data to allow inter-subject comparisons. Multiple regressions of estradiol, progesterone, and relative estradiol [calculated as (estradiol - progesterone)/progesterone], and relative progesterone [calculated as (progesterone - estradiol)/estradiol] levels on z-transformed ALFF data were conducted for each menstrual phase to verify hormone-correlated brain activity.

Correlations Between Behavioral Impulsivity and DS-dlPFC Functional Connectivity

The relationship between the impulsivity and DS-dlPFC functional connectivity was investigated by correlation analyses. We defined ROIs (bilateral putamen/caudate and dlPFC) and analyzed the functional connectivity between these ROIs from each participant's preprocessed data using the coordinates and methods described for the task fMRI study above. Regression analyses were conducted on DS-dlPFC functional connectivity data relative to each BIS-11 subscale score for each menstrual phase.

Results

Demographics

Two participants were excluded for excessive movement during scanning (≥2-mm maximum displacement in the *x*, *y*, or *z* dimension; or ≥2° angular motion). Two participants were excluded due to incorrect menstrual date estimation discovered upon tracking the next menstrual cycle. Of the 49 remaining participants (mean age, 22.86 ± 2.29 years; range, 19–28), 25 were scanned during their late FP (mean age, 22.52 years ± 2.38), and 24 were scanned during their mid-LP (mean age, 23.21 ± 2.19). Age did not differ significantly between the two menstrual phase groups ($t_{2,47} = 1.05$, $p = 0.30$, $d = 0.31$).

Hormone Assays

Hormone concentrations for each menstrual phase group are reported in **Table 3**. A one-way ANOVA with collection time as a covariate confirmed significantly higher progesterone levels in the mid LP group than in the late FP group ($F_{1,46} = 4.16$, $p = 0.047$, $\eta_p^2 = 0.08$). Meanwhile, estradiol levels were similar between these two groups ($t_{2,49} = 0.17$, $p = 0.68$, $\eta_p^2 = 0.004$).

TABLE 3 | Mean (± SD) estradiol and progesterone levels.

Hormone	Menstrual phase	
	Late FP	Mid-LP
Estradiol, pg/ml	4.52 ± 2.50	6.27 ± 3.66
Progesterone, pg/ml	28.10 ± 33.39	170.33 ± 130.38

ECN

An independent sample *t*-test revealed a significant difference between the late FP and the mid-LP groups for component 50 activity. Higher activity was observed in the right dlPFC (superior frontal gyrus, BA 8, $p = 0.050$, FWE-corrected, $k = 20$) during the mid-LP than during the late FP (**Table 4** and **Figure 5**). No other significant differenced were found between the menstrual phases for the activities of any other ECN components.

Correlations Between Hormone Levels and Brain Region Activity in Whole-Brain Analysis

During the late FP, no significant correlations were found between absolute levels of estradiol or progesterone and the observed ALFF in brain regions. There was a significant positive correlation between the relative progesterone level and the ALFF in areas within the right hippocampus, thalamus, precuneus, and left angular gyrus. During the mid-LP, there was a significant positive correlation between absolute estradiol level and ALFF of brain areas within the bilateral dlPFC and superior medial prefrontal cortex. Relative estradiol level correlated with the ALFF of brain regions in the right dlPFC and left postcentral gyrus as well. Relative progesterone level correlated with the ALFF of brain areas within the right superior temporal and middle temporal cortices (**Table 5**).

ROI Based rs-Functional Connectivity Correlations With BIS-11

A significant negative correlation was found between BIS-11 attentional impulsivity subscale scores and rs-functional connectivity between the right caudate and right dlPFC ($r = -0.47$, $p = 0.020$) during the late FP (**Figure 6**). No significant correlations were found during the mid-LP.

Discussion

Hormone assays confirmed the menstrual phases (late FP, mid-LP) predicted by the backward counting method. In the rs-fMRI study, the right dlPFC (superior frontal gyrus) was significantly more active during the mid-LP than during the late FP, consistent with our hypothesis of there being greater cognitive control functioning in the mid-LP than in the late FP.

The magnitude of right caudate-right dlPFC rs-functional connectivity correlated negatively with BIS-11 attentional impulsivity subscale scores during the late FP, consistent with the above reported findings in our delay discounting task-based

TABLE 4 | Brain regions whose activity is altered in relation to menstrual phase in the ECN.

Corrected *p*	*k*	Regions of maxima peak	BA	*T*	H	MNI		
						x	*y*	*z*
Mid-LP – late FP								
0.05	20	Superior Frontal Gyrus	8	5.28	R	27	15	57

Results are reported at Cluster significant after FWE correction at p < 0.05 for multiple comparisons; k = cluster size, MNI, Montreal Neurological Institute. L, left; R, right; H, hemisphere; BA, Broca's area.

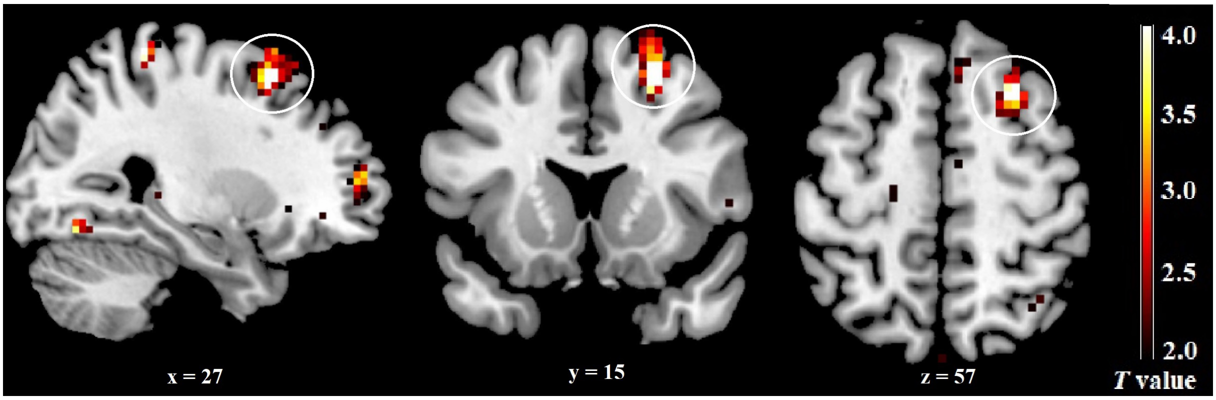

FIGURE 5 | Differences in the ECN across menstrual phases. The right dlPFC was significantly more activated during the mid-LP than during the late FP.

TABLE 5 | Correlations between hormone levels and brain activity.

Corrected *p*	*k*	Regions with maxima peaks	BA	*T*	H	MNI		
						x	*y*	*z*
Positive correlations of relative PROG with brain regions in the late FP								
0.015	29	Hippocampus	29	8.85	R	12	−39	9
		Thalamus		6.54	R	15	−30	9
		Precuneus	27	4.23	R	21	−39	3
0.045	23	Angular	39	6.63	L	−45	−54	27
Positive correlations of E2 with brain regions in the mid-LP								
<0.001	109	Superior frontal gyrus	11	7.58	R	21	72	0
		Middle frontal gyrus	46	5.66	R	45	57	12
		Medial superior frontal gyrus	10	5.66	R	15	72	9
<0.001	54	Middle frontal gyrus	46	6.12	L	−48	51	−3
Positive correlations of relative E2 with brain regions in the mid-LP								
0.019	27	Postcentral gyrus	43	6.43	L	−60	−15	36
0.034	24	Superior frontal gyrus	6	5.61	R	24	−9	66
Positive correlations of relative PROG with brain regions in the mid-LP								
<0.001	22	Superior temporal gyrus	22	5.17	R	72	−30	9
		Middle temporal gyrus	22	5.00	R	72	−39	3

Results are reported at Cluster significant after FWE correction at $p < 0.05$ for multiple comparisons; k = cluster size; L, left; R, right; H, hemisphere.

experiment in study 1. No positive correlations between rs-functional connectivity and impulsivity were observed.

Our finding of positive correlations of dlPFC activity with absolute or relative estradiol levels during the mid-LP suggests that augmented cognitive control function during the mid-LP may be accounted for by the relative levels of estradiol to progesterone, wherein both hormones are elevated. Previous work has shown that a change in the Now bias in intertemporal choices correlates inversely with changes in estradiol levels, decreasing from the low estradiol period of the menstrual phase (estradiol nadir is during menstruation) to the late FP (estradiol levels increase gradually in the early FP then increase rapidly until peaking in the late FP) (Smith et al., 2014). The present results further suggest that it may be the relative level of estradiol that modulates cognitive control of impulsivity during the mid-LP. Consistent with this possibility, the induction of several adaptive behaviors associated with gonadal hormones in intact animals have been shown to require concurrent changes in circulating levels of estradiol and progesterone (Tennent et al., 1980). It is possible that the lack of significant correlations between estradiol levels and activities of brain regions during the late FP in this study were due to there being a quite narrow range in hormone level variabilities (Smith et al., 2014).

On the other hand, our correlation analysis indicated that brain regions related to social cognition, especially in relation to theory of mind (Gallagher and Frith, 2003), are particularly sensitive to the relative levels of progesterone during the mid-LP. Higher progesterone levels in humans have been reported to be associated with greater motivation for affiliation (Schultheiss et al., 2004); whereas, cooperative tendencies have been shown to correlate negatively with estimated estradiol levels (Anderl et al., 2015). From an evolutionary perspective, it is noteworthy that the mid-LP is the

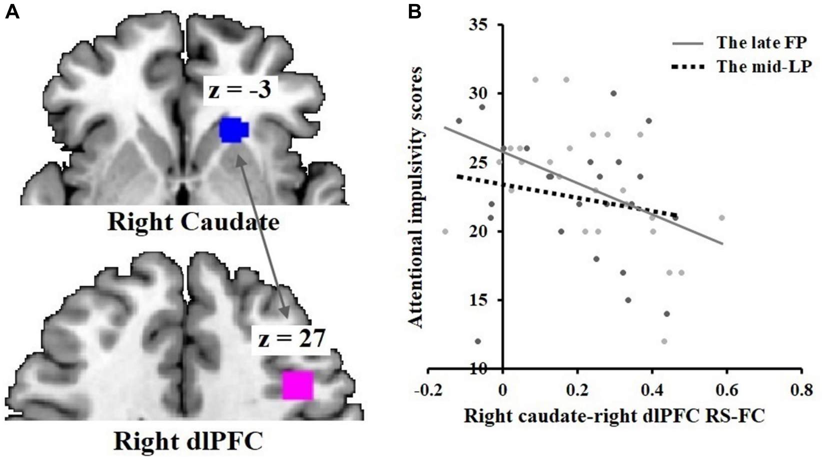

FIGURE 6 | Negative correlation between attentional impulsivity and DS-dlPFC functional connectivity in the late FP. **(A)** Rs-functional connectivity between the right caudate [21, 24, –3] and right dlPFC [42, 18, 27]. **(B)** Negative correlation of attentional impulsivity with right caudate-right dlPFC rs-functional connectivity in the late FP; no such effect was observed in the mid-LP.

phase when women's progesterone levels are highest and women's reproductive systems are preparing for possible pregnancy (Maner and Miller, 2014). Thus, the activation of brain regions related to social cognition and theory of mind may provide advantages for pregnant women.

GENERAL DISCUSSION

In the presently reported task-based fMRI and rs-fMRI studies, we demonstrated that circulating gonadal steroid hormones in women affected cognitive control of impulsivity, such that women had greater cognitive control on impulsivity during the mid-LP than during the late FP. Neurophysiologically, the DS and dlPFC are the main brain regions involved in cognitive control of impulsivity via the DS-dlPFC neural circuit. Specifically, right dlPFC activity was significantly stronger relative to the activity of DS during the mid-LP than during the late FP, and right dlPFC activity was sensitive to relative estradiol levels during the mid-LP. This cognitive advantage during the mid-LP may have evolutionary roots. As mentioned above, from an evolutionary perspective, the immediate goal of women in their mid-LP would be protection of their potential baby. The present finding of relative progesterone levels correlating positively with brain regions involved in social cognition provides direct evidence for this proposed goal. Thus, according to hierarchical reinforcement learning theory (Holroyd and Yeung, 2012), women keeping a higher level of cognitive control function would be adaptive for facilitating the realization of these goals by fulfilling a variety of women's specific social goals during their mid-LP.

On the other hand, the DS was significantly more responsive to reward stimuli in the late FP, the phase associated with weak cognitive control, than it was during the mid LP. This change in neural responsiveness could also serve the evolutionary goal of mating. Evidence has shown that menstrual phase influences women's cognitive control in relation to male faces but not in relation to female faces in a manner that appears to reflect their potential fertility during the late FP (Roberts et al., 2009). Indeed, a number of studies have shown increased impulsive behavior in relation to mating motivation in the late FP relative to the mid-LP. For example, women have been shown to exhibit enhanced impulsivity favoring the selection of sexier clothing and accessories near ovulation (Durante et al., 2008, 2011; Zhuang and Wang, 2014), especially under the priming condition of mating motivation (Zhuang and Wang, 2014). Also, women have been found to be more mobile and socially active in contexts related to mating motivation (Fessler and Navarrete, 2003; Miller et al., 2007).

LIMITATIONS, IMPLICATIONS, AND FUTURE RESEARCHES

The current findings indicate that ovarian hormones impact impulsive behaviors and that relative estradiol and progesterone levels may modulate the relationship between cognitive control and impulsivity. These results and their underlying neural basis have important implications for understanding the neural mechanisms that mediate impulsive control in a variety of contexts, including drug abuse (Cummings et al., 2014), postpartum psychosis, which is associated with drastic hormonal changes and a loss of inhibition (Ahokas et al., 2000), and borderline personality disorder, which has been associated with a variance in aggressive and impulsive behaviors over different menstrual phases (Dougherty et al., 1999). Our findings may provide novel directions for the treatment of these disorders and others, including attention deficit hyperactivity disorder, Parkinson disease, and obsessive-compulsive disorder. For example, manipulating the hormonal milieu may be helpful for alleviating these disorders and diseases. Treatment during the mid-LP may be particularly effective and important for attenuating hyperimpulsivity.

The present findings should be considered in the context of two notable limitations. Firstly, the sample size in the task-based fMRI study was relatively small, which may have weakened the power of and level of significance in our results. Secondly, the hormone and rs-fMRI study did not include direct assessments of dopamine levels across the menstrual phases, which limits our ability to make conclusions regarding a direct relationship between dopaminergic pathway activity and the observed difference in impulsive behavior between menstrual phases. Determination of dopamine levels at different points within the menstrual cycle in future research would help to provide a more detailed understanding of the influence of female gonadal hormones on impulsive behaviors.

In conclusion, natural menstrual cycle phase affected cognitive control of impulsivity. Women were more apt to postpone receiving rewards during the mid-LP than during the late FP. Our fMRI findings support the possibility that menstrual phase-associated behavioral changes may be consequent to hormonally induced alterations in the dlPFC and DS and the communication between these brain regions.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Committee on Human Research Protection, East China Normal University. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

J-YZ conceived and designed the experiments. J-XW, QL, and MF performed the experiments. J-XW analyzed the data. J-YZ wrote the manuscript. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnhum.2020.568399/full#supplementary-material

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Expectancy to Eat Modulates Cognitive Control and Attention Toward Irrelevant Food and Non-food Images in Healthy Starving Individuals. A Behavioral Study

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It is thought that just as hunger itself, the expectancy to eat impacts attention and cognitive control toward food stimuli, but this theory has not been extensively explored at a behavioral level. In order to study the effect of expectancy to eat on attentional and cognitive control mechanisms, 63 healthy fasting participants were presented with an affective priming spatial compatibility Simon task that included both food and object (non-food) distracters. The participants ($N = 63$) were randomly assigned to two groups: an "immediate expectancy" group made up of participants who expected to eat immediately after the task ($N = 31$; females = 21; age = 26.8 ± 9.6) and a "delayed expectancy" cohort made up of individuals who expected to eat a few hours later ($N = 32$; females = 21; age = 25.0 ± 8.0). Slower reaction times (RTs) toward the food and non-food distracters and a more pronounced effect on the RTs in the incompatible condition [i.e., the Simon effect (SE)] were noted in both groups. The effect of the food and non-food distracters on the RTs was more pronounced in the immediate with respect to the delayed expectancy group. The magnitude of the SE for the food and the non-food distracters was also greater in the immediate with respect to the delayed expectancy group. These results seem to indicate that when the expectancy to eat is short, the RTs are delayed, and the SE is more pronounced when food and non-food distracters are presented. Instead, when the expectancy to eat is more distant, the distracters have less of an effect on the RTs and the correspondence effect is smaller. Our results suggest that the expectancy to eat can modulate both attention orienting and cognitive control mechanisms in healthy fasting individuals when distracting details are competing with information processing during goal directed behavior.

Keywords: expectancy, cognitive control, visual attention, Simon task, food, reward sensitivity

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INTRODUCTION

Although food can be considered a primary reward (Berridge, 1996), it is nevertheless essential for our survival. It is widely recognized that food deprivation increases the reinforcement value of a food reward (Raynor and Epstein, 2003; Epstein and Leddy, 2006), suggesting that an individual's metabolic state can modulate subjective motivation and the desire to eat. As food salience seems to be regulated by energy balance and hedonic hunger interaction, these mechanisms may affect how we process environmental cues (Benarroch, 2010; Berthoud, 2011).

Given their salience for survival under specific metabolic conditions, food stimuli may trigger motivational approach processes including allocation of attentional resources (i.e., food-related attentional-bias) and cognitive control toward food stimuli (Nijs et al., 2010; Testa et al., 2020). Both attentional bias and cognitive control in the presence of food-related stimuli have been shown to be intensified in healthy individuals by a variety of conditions, including food and sleep deprivation and mood modulation (Mogg et al., 1998; Stockburger et al., 2009; Forestell et al., 2012; Loeber et al., 2013; Sänger, 2019). Other factors that have been shown to modulate the magnitude of food-related attentional bias and cognitive control toward food (i.e., response inhibition and interference control) seem to be conditioned by an individual's characteristics, including personality traits (e.g., attentional impulsivity) (Hou et al., 2011; Jasinska et al., 2012), eating styles such as eating in response to external food cues (i.e., external eating), and weight status (Castellanos et al., 2009; Werthmann et al., 2011; Yokum et al., 2011; Hendrikse et al., 2015; Carbine et al., 2018; Testa et al., 2020).

Neuroimaging research in healthy participants has shown that food stimuli are processed in the brain by an extended network encompassing primary sensory areas depending on the sensory modality (e.g., visual, olfactory) regions involved in reward processing such as the insula and the orbitofrontal cortex (OFC) and areas involved in control of attention and cognition such as the lateral prefrontal cortical regions (see for systematic meta-analysis: van der Laan et al., 2011; Huerta et al., 2014). Food-deprived individuals show enhanced activity in reward-related brain areas (LaBar et al., 2001; Porubská et al., 2006; Führer et al., 2008; Siep et al., 2009), while satiated participants show enhanced activity of the lateral prefrontal areas [e.g., the dorsolateral prefrontal cortex (DLPFC)] in Gautier et al. (2001), Smeets et al. (2006), Thomas et al. (2015). DLPFC activation has also been associated with higher levels of self-control over food choices, suggesting that it is involved in controlling food intake (Hare et al., 2009; Hollmann et al., 2012).

Another factor that seems to affect food-related processing in the brain is the anticipation of receiving an immediate food reward. It has been posited that the expectancy to receive a food-related gratification increases the activation of those brain regions, such as the OFC, the dopaminergic midbrain, the amygdala, and the striatum that are involved in reward processing (O'Doherty et al., 2002). It has nevertheless been reported that in monkeys the expectancy of receiving a reward after a particular response is associated with activity in the DLPFC (Watanabe, 1996). These data suggest that expectation of a reward modulates brain areas involved in cognitive control and reward processing, possibly facilitating goal-directed behaviors concordant with the incentive value of the contingent reward expected (Berridge, 1996; Watanabe, 1996).

Malik et al. (2011) set out to investigate the immediate as well as delayed effects of the expectancy to eat on human information processing of food and non-food images. The fasting participants participating in their study were instructed to look at images of food and scenery during two different functional magnetic resonance (fMRI) sessions. In one session, the participants were informed that they could expect to eat immediately after the session (the immediate expectancy condition); in the other, they were informed that they could expect to eat a few hours later (the delayed expectancy condition). The results showed that the food images compared with scenery images yielded bilateral activation in the visual areas as well as in the left insula and amygdala in both food expectancy conditions. In the delayed expectancy one, however, the left DLPFC, the hippocampus, and the putamen were additionally activated, while in the immediate expectancy condition, the right OFC activity was enhanced. These data suggest that temporal information regarding immediate or delayed eating affects the salience of food-related stimuli in starving individuals, modulating the activity of the brain areas involved in reward processing and cognitive control.

In a study investigating starving individuals, it was found that the expectancy to receive a food reward influenced the early orientation of attention toward food pictures (i.e., there was a gaze direction bias) (Hardman et al., 2014). Generally speaking, however, there is a paucity of studies investigating how the expectancy to eat affects orienting attention attentional bias and cognitive control.

A novel affective version of the Simon task using food and non-food distracters was recently developed to investigate their effects on cognitive control and attention orienting in starving normal-weight and severe obese individuals (Testa et al., 2020). A study using the new Simon task reported that with respect to a condition without distracters (i.e., neutral condition), distracting images interfere with orienting of attention (i.e., attentional bias) delaying the overall response speed and cognitive control by slowing down reaction times (RTs) when incongruent spatial information competed for response selection (i.e., cognitive control bias). In addition, severely obese individual showed a larger cognitive control bias for food images compared to controls, and a linear relationship was found between subjective hunger perception and the RTs registered during the spatial incongruent condition in the presence of the food images in both the normal weight and severely obese participants (Testa et al., 2020).

The original Simon task, which was devised to study the response selection phase of information processing, typically involves participants who are asked to respond to a task-relevant stimulus (a color or an image) as quickly as possible by pressing the same color coded button that may be on the right or left. Another task-irrelevant feature is also presented. Researchers have found that RTs are faster when the task-relevant stimulus and the response position correspond, meaning they are on the same side (i.e., the corresponding condition) than when they are not (i.e., the non-corresponding condition). This correspondence (faster responses for spatial correspondence, slower responses for non-spatial correspondence) has been called the Simon effect (SE) (Simon and Rudell, 1967; Nicoletti and Umiltà, 1994; Lu and Proctor, 1995). It has been posited that the SE is determined by a conflict between two pathways: the fast direct automatic pathway activating the response spatially corresponding with the stimulus location and the slow indirect controlled pathway activating the appropriate response depending on task demands (Cohen et al., 1990; Tagliabue et al., 2000; Ridderinkhof, 2002).

As the newly developed affective Simon task seemed suitable to study food-related attentional bias and its interference with cognitive control mechanisms, we used it to evaluate how immediate or delayed expectancy to eat can modulate RTs and interference control in fasting individuals. The healthy volunteers who were enrolled were asked to fast, and on the scheduled day, they were randomly assigned to one of two groups. Those assigned to the first group were advised that they would be given something to eat immediately after the experimental session; those assigned to the second one was advised that they would be given something to eat a few hours later. During this Simon task, food and non-food images are able to interfere or bias at two different levels of information processing: at the time attention is being oriented and during response selection. With regard to the former, the cues are expected to affect the time required to orient attention toward task relevant information, delaying overall RTs when distracting (in particular, photos of food) images are presented. With regard to the second, they are expected to affect cognitive control functions when conflicting spatial information is presented.

In the light of these considerations and the knowledge presently available on mechanisms modulating or biasing orienting attention and/or cognitive control when motivationally salient but task-irrelevant images are presented together with task-relevant stimuli, we designed an experiment and formulated different hypotheses. First, we expect to replicate findings of our previous work by Testa et al. (2020) showing the effect of food/non-food distracters on orienting attention (i.e., delayed RTs compared to the neutral condition) and a food specific effect on cognitive control (i.e., larger SE with food distracter) in starving individuals.

Second, we hypothesis that food and non-food images have a more pronounced effect on RTs (i.e., delaying them) in the immediate expectancy group with respect to the delayed one which would suggest a modulation of expectancy on orienting attention bias. Third, we expect that task-irrelevant distracters have a more pronounced interference on cognitive control (i.e., the magnitude of the SE) in participants expecting to eat shortly with respect to those expecting to wait; this would suggest a modulation of expectancy of cognitive control during response selection. The effect of expectancy over cognitive control could be food-specific or more general in presence of task-irrelevant distractors (both food and non-food).

MATERIALS AND METHODS

Study Participants

The sample size could not be calculated *a priori* due to insufficient information during the planning of the study; thus, a convenient sample of 64 right-handed healthy individuals was chosen. The participants were mainly graduate and post-graduate students from the Universities of Padova and Bergamo who volunteered to participate (**Table 1**: participants' socio-demographic and anthropometric variables). A clinical interview was conducted to assess the history or the presence of neurological and/or psychiatric condition. The study's exclusion criteria were neurological diseases, psychiatric disorders, and being younger than 18 or older than 65. All the participants received a full explanation of the experimental procedure we were using and were asked to sign a consent form. The study was performed in accordance with the Helsinki Declaration (Editors, 2004) and approved by the local Ethical Committee (Padova-University Hospital ethical committee Prot. N.: 3067/AO13).

Procedure

All the participants were instructed to fast for 6 h prior to the experimental session which, in all cases, was scheduled at the same time of the day (12–2 p.m.). Adherence to this instruction was tested asking to them the time of their last meal and if they had eaten something other before coming to the laboratory. Each participant filled out a series of questionnaires (listed below) and subjective ranking of hunger/satiety/desire to eat at the beginning of the session and was then randomly assigned to one of two groups. These self-report measures were adopted to exclude the confounding effect of group differences in impulsivity, eating-related attitudes, and subjective perception of hunger/satiety/desire to eat. Those in Group 1 were informed that they would eat immediately after the task (i.e., immediate expectancy group); those in Group 2 were informed that they would eat 2 h later (i.e., delayed expectancy group).

Material

Affective Simon Task (See Figure 1)

The experimental setting was a dimly lit room. Each participant was seated in front of (58 cm away from) a 15-inch CRT computer screen. The task consisted of 480 experimental trials presented in four blocks, each consisting in 120 trials. A practice block of 42 trials preceded the beginning of the real session. The participant was reminded by a message appearing on the screen before he/she read the instructions for the task and at the beginning of each block of trials that that he/she would be able to eat immediately (if he/she was in Group 1) or 2 h later (if he/she was in Group 2).

Each trial started with a central black fixation cross subtending 0.5° of visual angle, displayed on a light gray background. The fixation cross was surrounded by a black square perimeter with the side subtending 3° of visual angle. After a variable interval, ranging from 2000 to 3500 ms, the target stimuli were presented at an eccentricity of 4.5° of visual angle on the left or right of the fixation cross for 147 ms. The target stimuli were 4 × 4 red-and-black or green-and-black checkerboards subtending 1.48° of visual angle. A 4 × 4 black-and-white checkerboard was presented together with the target as contralateral filler. A central distracter (a cross) was also displayed inside the square for 2000 ms. The distracters consisted of images of food, objects, or a black cross projected on a white background (neutral condition). The duration of the inter-trial intervals ranged from 1000 to 2000 ms. Ten food and 10 non-food images (objects) were selected from a validated dataset (Blechert et al., 2014)[1].

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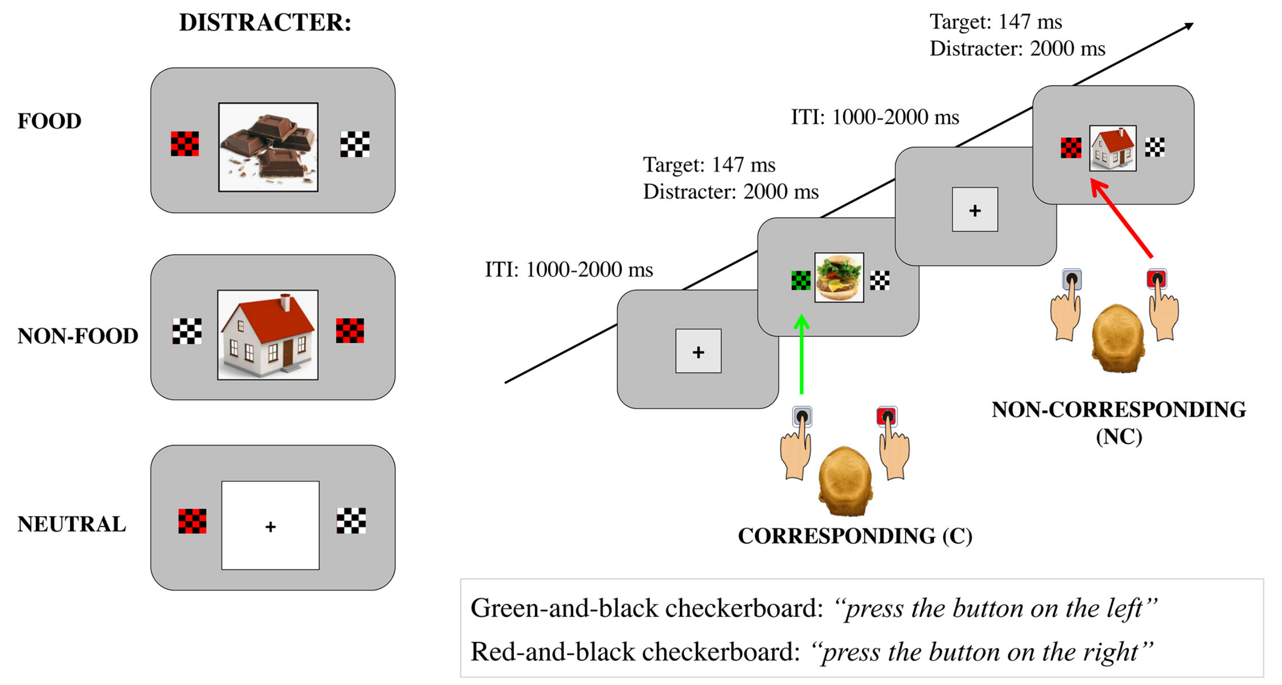
[1] Image numbers were: 18, 32, 45, 46, 54, 107, 110, 145, 167, 176, 1008, 1025 1033, 1036, 1044, 1060, 1096, 1081, 1117, 1137.

TABLE 1 | Mean (standard deviation) values of the socio-demographic and anthropometric variables of the entire group and of the two sub-groups (immediate and delayed expectancy).

	Male/female	Age (years)	Education (years)	Height (cm)	Weight (kg)	BMI (kg/m^2)
All the participants (*N* = 63)	21/42	25.9 (8.8)	13.9 (2,6)	169 (8.00)	61.2 (10.1)	21.2 (2.5)
Immediate Group (*N* = 31)	10/21	26.8 (9.6)	13.7 (2.7)	170 (8.00)	60.0 (8.8)	20.7 (2.0)
Delayed Group (*N* = 32)	11/21	25.0 (8.0)	14.2 (2.4)	169 (9.00)	62.4 (11.2)	21.7 (2.8)

The t-tests for independent groups did not uncover any differences between them.



Green-and-black checkerboard: *"press the button on the left"*

Red-and-black checkerboard: *"press the button on the right"*

FIGURE 1 | A schematic drawing of the trials using a Simon task and examples of both corresponding (C) and non-corresponding (NC) conditions (on the right) and the three types of distractors presented during the task: a food item, an object, and a neutral distractor (on the left).

The participants were instructed to keep their eyes on the screen and to respond to the task-relevant stimulus as quickly and accurately as possible. Half of the participants were instructed to press the left button (the letter "Z" of the keyboard) with their left index finger if the target was the red-and-black checkerboard, and the right button (the letter "M") with their right index finger if it was the green-and-black one, independently of its spatial position.

These instructions were inverted for the other half of the participants. The three types of distracters (a piece of food, a non-food object, and a cross on a neutral white background which we considered a neutral condition) were presented in half of the cases with corresponding color/location responses and in the other half with non-corresponding color/location responses. The RTs and the accuracy of the responses of each participant for each trial were registered. Individual RTs and accuracy (i.e., probability of correct response) in the different task conditions were screened for outliers, given a cutting point of 2 standard deviations (SD) from the mean response value (conservative threshold). The data of one participant whose percentage of correct responses was lower than two SD of the mean accuracy rate were not included in our analyses.

To control for a speed accuracy trade-off, the mean RTs adjusted for response accuracy [adjRTs = RTs/p (correct response)] were calculated. Data are reported as means ± SD.

Self-Report Measures

The Yale Food Addiction Scale (Innamorati et al., 2015) was used to investigate additive eating patterns, the Binge Eating Scale (BES; Gormally et al., 1982) was used to investigate the presence of binge eating behavior, the Power of Food Scale (PFS; Lowe et al., 2009) was used to investigate the attraction to food, the Dutch Eating Behavior questionnaire (DEBQ; van Strien et al., 1986) was used to assess emotional, external, and restrained eating patterns, and the Eating Attitude Test 26 Item (EAT-26; Garner et al., 1982) was used to investigate eating disorders. The Barratt Impulsiveness Scale (BIS-11; Fossati et al., 2001) and the Behavioral Inhibition System/Behavioral Activation System (BIS/BAS; Carver and White, 1994) were used to measure two motivational systems.

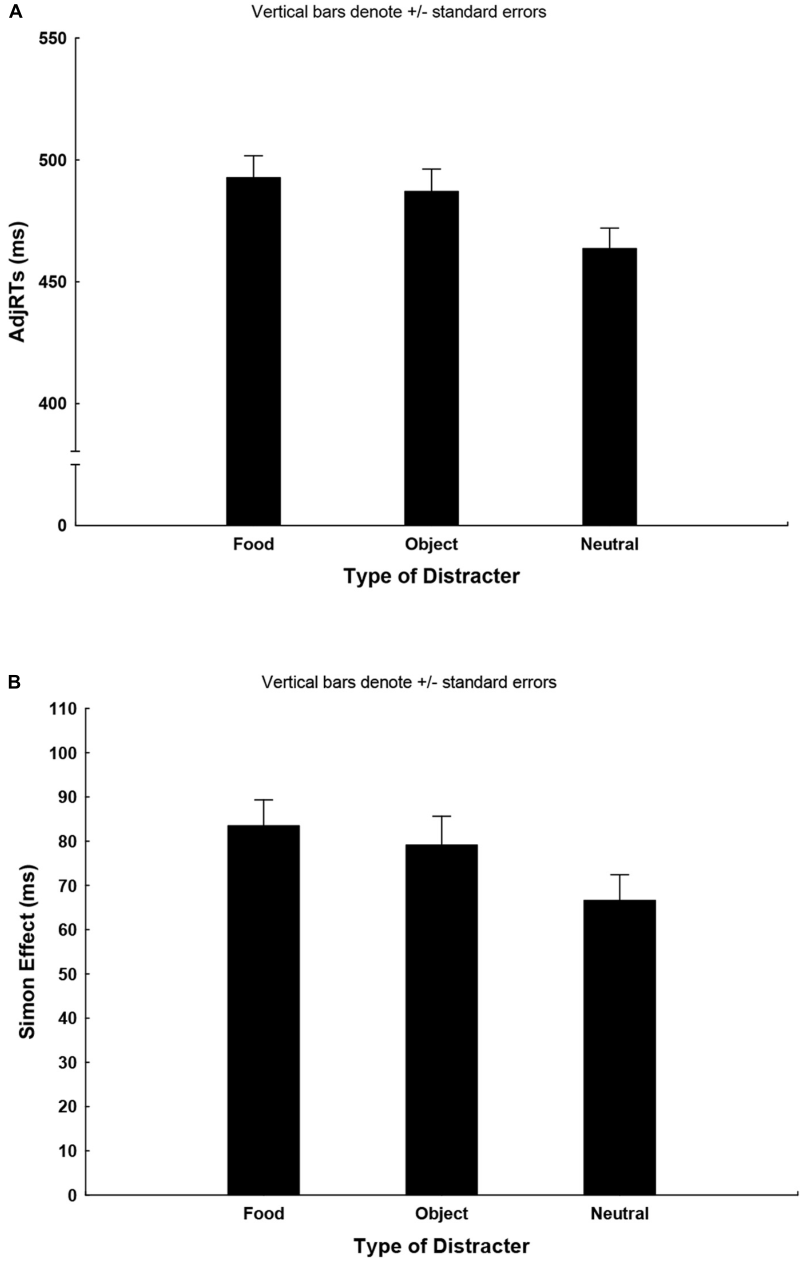


FIGURE 2 | (A) The graph shows the mean adjRTs for the three distracters (i.e., the food, the non-food, and the neutral images) of all the participants. The ANOVA uncovered the main effect the type of distracters, revealing that both food and non-food distracters slow down RTs compared with the neutral condition. **(B)** The graph shows magnitude of the Simon effect for the three distracters (i.e., the food, the non-food, and the neutral images). The ANOVA on adjRTs uncovered the interaction between correspondence and the type of distracters, and planned contrast on the magnitude of the Simon effect reveal that only food distracters increase the magnitude of the Simon effect compared to the neutral condition ($p < 0.009$).

The participants' subjective levels of hunger, satiety, and desire to eat were rated using Likert scales ranging from −5 (max) to 5 (min).

Data Analysis

A series of *t*-tests for an independent group were first performed to exclude differences in the participants' socio-demographic and anthropometric variables (i.e., age, years of education, height, weight, and body mass index = kg/m^2).

To test and corroborate previous findings on the effect of food and non-food distractors over orienting attention (i.e., adjRTs) and cognitive control (i.e., magnitude of SE), in starving individuals, we first run 2 × 3 repeated measures ANOVAs with correspondence (C vs NC) and the type of distracter (food, object, and neutral) as within participants independent variable factors.

Then, to test the effect of expectancy over the orienting attention and cognitive controls biases induced by food or non-food distracters, RTs in the C and the NC trials for the food and object distracters were separated from those for the neutral condition (i.e., C_food – C_neutral; NC_food – NC_neutral; C_object – C_neutral; NC_object – NC_neutral), and second $2 \times 2 \times 2$ repeated measures ANOVA was run with the group as between individual variable (immediate vs delayed), and the correspondence (C, NC) and the type of distracters (food and object) as participants individual variables.

The effect size was expressed as the partial eta squared and interpreted according to Richardson (2011) (<0.06 low; 0.06–0.14 moderate; >0.14 high).

RESULTS

The *t*-tests used to analyze the participants' socio-demographic and anthropometric variables did not uncover any differences in the ages, years of education, height, weight, or body mass index variables of the two groups (**Table 1**). *T*-tests applied on self-report measures of subjective hunger/satiety/desire to eat, eating attitudes and traits of impulsivity did not show any significant difference between the two groups (see **Supplementary Tables S1–S3** for a detailed description of the results).

The ANOVA on adjRTs showed the significant main effect of the type of distracter: $F(2,122) = 46.1$; $p = 0.000001$; $\eta_p^2 = 0.43$, with slower RTs for both the food and non-food distracters compared to the neutral condition (food: 492 ± 74 ms mean ± SD; object: 487 ± 77 ms; neutral: 463 ± 70 ms; Bonferroni food vs neutral, $p < 0.00001$; object vs neutral, $p < 0.00001$; **Figure 2A**) and the main effect of correspondence: $F(1,61) = 219.7$, $p = 0.00001$; $\eta_p^2 = 0.78$, showing longer RTs in the NC condition (C: 443 ± 73 ms; NC: 519 ± 76 ms). This result reveals an attentional orienting bias of distracters images (both food and objects) on RTs. An interaction between correspondence and type of distracter: $F(2,122) = 5.0$, $p = 0.008$; $\eta_p^2 = 0.07$ was also detected, with *post hoc* showing longer RTs for the NC with respect to the C trials for all types of distracters. Planned contrast on the SE highlighted a larger magnitude of the SE only for food distracters with respect to the neutral condition (food: 83 ± 46 ms; neutral: 67 ± 46 ms; $p < 0.009$; **Figure 2B**), depicting a food-specific cognitive control bias in our starving participants.

The analysis to the test the effect of expectancy uncovered a significant main effect of group: $F(1,61) = 9.6$, $p = 0.003$; $\eta_p^2 = 0.13$, confirming the larger orienting attention bias due to distracter images in the "immediate expectancy" group (food-neutral: 38 ± 33 ms; object-neutral: 32 ± 33 ms) with respect to the "delayed expectancy" group (food-neutral: 20 ± 31 ms; object-neutral: 14 ± 34 ms; **Figure 3A**). Interestingly, together with the main effect of correspondence: $F(1,61) = 13.0$, $p = 0.0006$; $\eta_p^2 = 0.17$, revealing a larger effect of food and non-food distracters on the NC condition (33 ± 38 ms) with respect to the C one (21 ± 33 ms), a significant group × correspondence interaction was also detected: $F(1,61) = 5.04$, $p = 0.03$; $\eta_p^2 = 0.08$. *Post hoc* analysis on this later effect revealed a significant difference between C and NC conditions in the immediate expectancy group (NC = 47 ± 36 ms, C = 23 ± 30 ms; $p < 0.001$), but not in the delayed group (NC = 19 ± 36 ms, C = 14 ± 28 ms; $p <$ ns). In addition, the effect of distracters in the NC condition was larger in the immediate expectancy group with respect to that in the delayed group (NC immediate group: 47 ± 36 ms, NC immediate group: 19 ± 36 ms; *post hoc* $p < 0.001$). This result suggests that the bias on cognitive control induced by food and non-food distracters was larger in the immediate with respect to the delayed expectancy group (**Figure 3B**).

DISCUSSION

The current study set out to evaluate the effect of the expectancy to eat on orienting attention and cognitive control in the presence of distracting food or non-food images. A modified version of the Simon task was administered to healthy fasting participants who were divided into two groups: those who were told they would be given something to eat immediately after the session and those who were told they would be given something to eat a few hours later.

Results corroborate our hypothesis, showing that immediate/delayed expectancy modulates both orienting attention and cognitive control bias, and these effects seem not to be food specific.

According to our first hypothesis, the participants' overall RTs were slower during the trials presenting both food and non-food distracters, confirming an orienting attention bias toward task-irrelevant distracting stimuli in starving participants. This is consistent with the findings of our previous work adopting the same task (Testa et al., 2020), and can presumably be explained by the interference of task-irrelevant centralized food and non-food images on those mechanisms involved in visually orienting attention toward lateralized task-relevant information.

One of the most relevant models for the attention system suggests that orienting attention in space is characterized by three partially independent mental operations: (1) engaging, (2) disengaging, and (3) moving (Posner and Petersen, 1990). The results of our trials indicate that distracting images during the visual orientation stage of an affective Simon task may cause an initial engagement of selective attention toward their position, even if it is irrelevant to the task. The participants needed to disengage their attention resources from the central image and move them toward the lateralized stimuli in order to focus on the task-relevant position. This additional, probably time-consuming process may explain why the RTs for the food and non-food distracters were longer than those for the neutral one.

The second hypothesis of a food-specific effect over cognitive control in starving individual was corroborated by the larger SE registered for the food (but not for the non-food) images with respect to the neutral condition. The interference of food on the response selection is possibly linked to the effect of hunger on cognitive control processes. Similarly, a correlation between the magnitude of the SE in the presence of food-distractors and the participants' subjective hunger perception was previously detected in starving individuals (Testa et al., 2020).

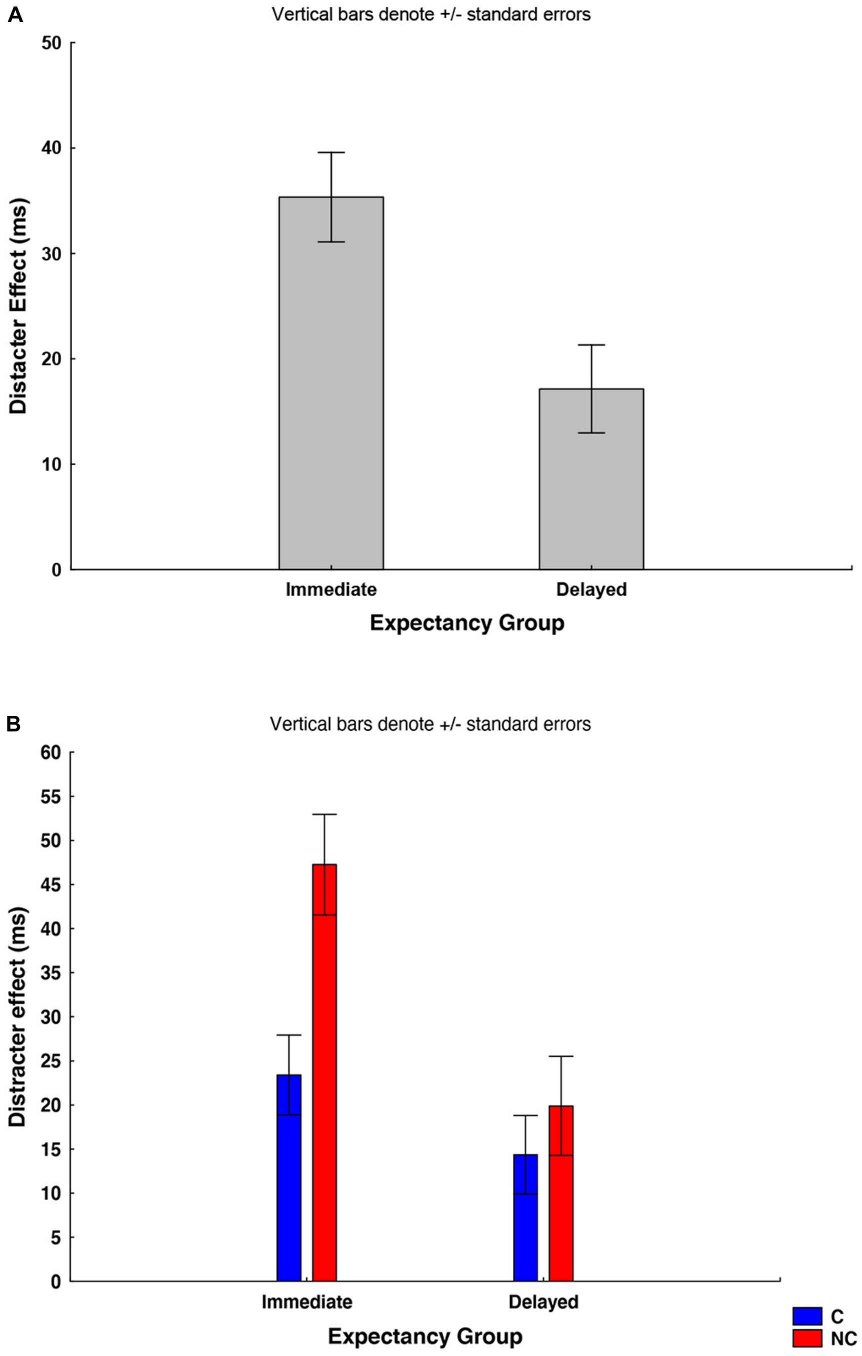


FIGURE 3 | (A) The graph shows the "distracter effect" (i.e., the differences in the RTs collected during the food and non-food distracting trials and those collected for the neutral condition). The ANOVA analyzing the two groups (immediate and delayed expectancy) separately uncovered the effect of group, highlighting a significantly higher attention bias produced by the food and non-food images in the immediate expectancy group with respect to the delayed one. **(B)** An interaction between group and correspondence was also found, revealing a significant difference between C (blue bars) and NC trials (red bars) in the immediate expectancy group, but not in the delayed one. *Post hoc p*s < 0.05.

Hunger may have increased the motivational salience of stimuli coming from the external environment affecting the time necessary to process them or to disengage attentional resources. A non-task relevant engagement of cognitive resources especially for food-related stimuli may have enhanced the ipsilateral activation response to the stimulus position, making additional cognitive control resources necessary to select the correct response. A mechanism of this kind would corroborate the findings of behavioral studies carried out in hungry individuals suggesting that hunger has a direct effect on the salience of food cues as it modulates inhibitory control over food-related response selection (Loeber et al., 2012, 2013).

Regarding the effect of expectancy over orienting attention, results indicated a larger distracting effect in the immediate expectancy group compared to the delayed one, which seems not to be specific for food-related stimuli. Thus, the finding suggests that expectancy modulates the efficiency of at least one of the operations involved in orienting attention toward a task-relevant lateralized feature, probably affecting mechanism related to disengagement of attention form irrelevant distracting image. It is possible that selective attention network's predisposition to potentially salient environmental stimuli is enhanced by the immediate expectancy to eat, a hypothesis that is certainly plausible in evolutionary terms in starving individuals. The effect is probably attenuated in the delayed expectancy group by the larger amounts of attentional resources allocated to task demands in the individuals who must refrain from thinking about food and repress their desire to eat for a longer time. In fact, the distracting effect was smaller. With respect to cognitive control, the interaction between expectancy and correspondence suggests that an immediate expectancy to eat enhances the distracting effect of both food and non-food images on spatial correspondence.

Taken together, these results suggest that the effect of expectancy affects both orienting attention and response selection in an independent but similar manner. Research focusing on cognition (Kornblum et al., 1990; Hommel and Prinz, 1997) describes different sources of conflict depending on the locus of interference, suggesting that there is a distinction between processing stimulus-stimulus (S-S) and stimulus-response (S-R) conflicts. For example, while in Stroop and Flanker tasks, conflict is between different features of the stimuli (i.e., an S-S conflict) competing for the selection of the correct response at a perceptual level, in a Simon task, there is a conflict between stimulus and response locations (i.e., S-R conflict). In this latter case, the spatial position of the stimulus is thought to automatically activate the responding hand ipsilateral to the stimulus position. In this light, expectancy seems to affect both stages of information processing, that is during orienting of attention as well as response selection. In the first case, distracters interfere with the selection of task-relevant information (i.e., the S-S conflict), while in the latter, they probably enhance the automatic activation of the response primed by the irrelevant stimulus position at a premotor level (i.e., S-R conflict).

We have the impression that in our study the expectancy to eat in an immediate as opposed to a delayed future further increased the predisposition of the orienting attention system to be automatically captured by potentially salient cues from the external environment. The delayed or postponed expectancy to eat may have, instead, attenuated the effect of irrelevant distracting images on the orienting attention system, probably via top-down influences from higher order brain areas linked to the control of selective attention (Posner and Petersen, 1990). A similar effect also seems to occur at the response selection stage during which the irrelevant position of the stimulus is thought to prime the hand ipsilateral to the stimulus, in which case the distracting effect of food and non-food images seems to be enhanced by an immediate expectancy and reduced by a delayed one.

The effect of expectancy on orienting attention and cognitive control over response selection could be linked to the measure of time the individual is expecting to wait before receiving a reward, in our case, food. Studies examining inter-temporal decision-making suggest that the tendency to settle for a smaller, immediate reward instead of a larger, delayed one is associated with higher impulsivity (Frederick et al., 2002; Sellitto et al., 2011) and with the activity of those brain areas controlling reward-related behavior, in particular, the OFC, the nucleus accumbens, the ventral tegmental area, the striatum, and the amygdala (Sellitto et al., 2010). The preference for a delayed, larger reward is, instead, associated with cognitive control and the activity of those areas implicated in executive control, in particular, the DLPFC (Figner et al., 2010), and is altered in obese individual (Schiff et al., 2016). These considerations seem to fit quite nicely with our findings. Regardless of individual differences in reward processing or cognitive control, the delayed expectancy to eat seemed to reduce the immediate expectation of receiving a reward, increase allocation of cognitive resources, and reduce impulsive behavior. An immediate expectancy to eat seemed, instead, to increase impulsivity and the need for rapid gratification. Similarly, episodic future thinking (i.e., a vivid mental simulation of future experiences) has been shown to reduce the preference for immediate rewards during a temporal discounting task (Peters and Büchel, 2010). In fact, when episodic future thinking concerns food-related thoughts, it has been found to reduce food intake and snacking in both healthy individuals (Dassen et al., 2016) and in obese patients (Daniel et al., 2013). Another study showed that episodic future thinking techniques reduced impulsive choices and alcohol consumption in alcohol-addicted individuals (Snider et al., 2016). By the same token, our data suggest that a mental projection of a delayed expectancy to eat could reduce impulsivity. Future studies investigating clinical populations characterized by impulsivity (e.g., individuals involved in substance abuse; behavioral addiction; binge eating disorders) may contribute to identifying a new treatment approach to enhance cognitive control toward addiction-related cues.

Malik et al.'s (2011) fMRI imaging study demonstrated a specific activation of the DLPFC for the food with respect to the scenery images in the delayed expectancy to eat condition. Thus, when the participants knew that they would not be eating for an extended period of time, they showed cognitive control in response to food cues. Although we were unable to directly explore brain activity during our own study, food stimuli did not appear to interfere with cognitive control in the participants belonging to the delayed expectancy group in whom we were expecting to detect maximal DLPFC activation. Unlike Malik et al.'s (2011) findings, ours demonstrate that the effect of expectancy on RTs was not food specific, but the differences in the paradigms adopted by the two studies may have rendered them incomparable. The modified Simon task we adopted used food and non-food images as task-irrelevant distracters, and our participants were instructed to focus their attention on the color of the lateralized target in order to carry out the task at hand. In Malik et al.'s (2011) study, participants were involved in a cue-reactivity task requiring only a passive view of the images. The difference in the relevance of the images in the two studies may reflect a different type of activation of the reward system, as has been suggested by another fMRI study (Siep et al., 2009). Another study using eye tracking methodology in fasting individuals likewise reported that expectancy to eat did not produce a specific effect on early orientation of attention toward food cues (Hardman et al., 2014). The findings that are presently available seem to indicate that the expectancy to eat has an effect on general mechanisms of selective attention and cognitive control and does not directly impact food reward systems involved in orienting attention.

These findings must be evaluated in the light of limitations. First, all of the participants were tested in fasting state which may have enhanced food salience leading to a similar interference from food stimuli on cognitive control in both expectancy groups. Examining these mechanisms also in satiated individuals would have permitted us to investigate how the desire to eat and food craving rather than hunger come into play in this interaction. Second, participants adherence to the 6 h of fasting before task execution was not objectively monitored (e.g., isolating them before starting the experiment), which is usually recommended in studies that manipulate hunger and satiety. Third, despite the fact that no group differences were found in the participants' characteristics according to the questionnaires that were utilized, the study design did not permit us to evaluate the effect of expectancy in highly impulsive individuals. Future studies examining healthy participants with high and low impulsivity traits will be able to explore the interaction of the impulsivity trait with expectancy in modulating orienting attention and cognitive control.

Finally, our data are based entirely on behavioral findings; utilizing both neuroimaging techniques and cognitive control tasks would have permitted us to explore neural activity in different expectancy conditions more directly.

CONCLUSION

In conclusion, the current study suggests that temporal expectation (immediate vs delayed) of a reward, in this case food in fasting individuals modulates both orienting attention and cognitive control mechanisms when irrelevant but salient stimuli are present in the environment. The expectancy of receiving a food reward in the immediate future increased the distracting effect and reduced the control of selective attention in the presence of stimuli competing with information processing. Furthermore, the expectancy of receiving a food reward in an immediate future reduced cognitive control in the presence of a spatial interference for response selection, hence increasing impulsivity. On the other hand, the expectancy of receiving a food reward in a more distant future produced, instead, a reduction of the distracting effect and enhanced cognitive control over response selection, leading to lower impulsivity.

These results shed new light on the effects of expectancy on cognitive processing in healthy individuals, and they suggest that selective attention and cognitive control may be manipulated also in clinical populations characterized by high levels of impulsivity, such as obese patients and participants with addictive disorders.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee of the Padua University Hospital. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

SS conceptualized the study. SS and GT recruited participants and collected, analyzed, and interpreted the data. SS and GT wrote the manuscript, with the support, the suggestions, and the correction of PA, MR, and DM. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

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BRIEF RESEARCH REPORT
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The Role of Motivation and Anxiety on Error Awareness in Younger and Older Adults

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Aging is associated with several changes in cognitive functions, as well as in motivational and affective processes, which in turn interact with cognitive functions. The present study aimed to investigate error awareness (EA), which declines with aging, in relation to motivation and anxiety. Adopting an experimental task, we firstly tested the hypothesis that EA could be enhanced through reward motivation. Secondly, we explored the relation between state and trait anxiety and EA, investigating the hypothesis of an association between EA and anxiety, and between anxiety and the potential benefit of motivation on EA. Thirty healthy younger (age range: 19–35 years; mean age 25.4 ± 5.1; 10 M) and 30 healthy older adults (age range: 61–83 years; mean age 69.7 ± 5.5; 12 M) took part in the study and performed both the classic Error Awareness Task (EAT) and one experimental task, called the Motivational EAT. In this new task, motivational incentives were delivered after aware correct responses and aware errors. For every participant, standard measures of state and trait anxiety and cognitive functions were collected. Confirming the presence of a significant age-related EA decline, results did not reveal any influence of reward motivation on EA, nor any relation between EA and anxiety. However, both younger and older adults had longer response times (RTs) and made more errors during the Motivational EAT, with the more anxious participants showing the greater RT slowing. Findings suggest that reward motivation might not be always beneficial for cognitive performance, as well as that anxiety does not relate to EA capacity. Results also recommend further investigation, as well as the assessment of EA in patients with either motivational deficits like apathy, and/or with anxiety disorders.

Keywords: motivation, anxiety, error awareness, aging, reward

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INTRODUCTION

A growing body of evidence suggests that performance monitoring and error awareness (EA) are negatively impacted by the aging process (1–9). As Harty et al. (1) highlighted, "this phenomenon is particularly concerning in light of the associations between impaired awareness of cognitive functioning and engagement in risky behavior, increased care-giver burden, poor motivation for treatment and poor general prognosis," and would therefore benefit from further investigation.

While the neural underpinning of this phenomenon has been the focus of few recent studies (1, 5, 7, 8), only one work (2) explored the possibility to counteract age-related EA decline. In detail, Harty et al. (2) suggested that anodal transcranial direct current stimulation (tDCS) over the right lateral prefrontal cortex brings to an improvement of EA in older adults. However, sometimes tDCS can be difficult to employ with older adults, because they may not fulfill all the inclusion criteria for the use of non-invasive brain stimulation [see (10)].

According to the Value-Based Cognitive Control framework (11–13), the presence of motivational incentives, like rewards, has the capacity to increase the motivational value of cognitive control, and to consequently bring to a cognitive performance enhancement. Despite the precise neural mechanism behind motivation-cognition interaction is still not clear, is now well established that dopamine plays a key in performance enhancement [(13); see also (14)], either by its tonic release in the prefrontal cortex (PFC), which might facilitate cognitive stability, or by its phasic release in the striatum, which may facilitate cognitive flexibility (13).

Beneficial effects of reward motivation on cognitive performance have been reported in both younger and older adults [for a recent review, see (15); see also (16–21)], with relevant advancement in aging research, increasingly aimed to understand the mechanisms behind age-related cognitive decline, and consequently to find effective strategies to counteract it.

However, to the best of our knowledge, nobody has yet investigated the effect of reward motivation on EA and, more importantly, in reducing the EA age-related decline.

Hence the first aim of the present study was to test the hypothesis of a positive effect of reward motivation on EA and, more specifically, on the age-related EA decline. To test this hypothesis, we designed an experimental EA task, the Motivational Error Awareness Task (EAT), introducing performance contingent feedback and positive motivational incentives (virtual monetary reward), and we tested both younger and older adults. By comparing their performance at this new task with the one at the Classical EAT [reported in our previous work, see (4)] we predicted to find a significant EA enhancement, as well as a reduction of the age-related EA decline, in the Motivational EAT.

The present work was also guided by a second aim, which was the investigation of the role of anxiety on EA and on the age-related EA decline. This second aim was inspired by several sources of evidence and theoretical frameworks indicating the existence of a relation between anxiety, cognitive performance, and aging.

For what concerns the relation between anxiety and cognitive performance, as recently summarized by Hoshino and Tanno (22), several studies demonstrate that trait anxiety can influence various cognitive processes, from early perceptual detection stages to higher-order processes, such as cognitive control. More specifically, according to both the Attentional Control Theory (ACT) by Eysenk et al. [(23); see also (24)] and the Dual Mechanisms of Control framework (DMC) (25, 26), elevated levels of trait anxiety decrease the functional efficiency of executive control, and more specifically of the proactive control mode (25, 26). Cognitive control is actually achieved through two distinct modes: proactive, which involves active maintenance of rules and goals, and reactive, which involves allocating attention to rules and goals on an as-needed basis, once a problem (such as the occurrence of a conflict, or an error) has arisen (25).

According to Braver (26), while non-anxious individuals are able to alternate flexibly between reactive and proactive control modes in accordance with changing task demands, the distraction caused by worries would make anxious individuals less efficient in implementing proactive control, and therefore more dependent on a compensatory increase of reactive control, especially when salient events, such as errors, occur [see also the *Compensatory Error Monitoring Hypothesis* by (27)].

Based on this first set of evidence and theoretical frameworks, we could therefore predict that higher levels of trait anxiety might be associated with higher error rates, as result of decreased levels of proactive control, but also with higher levels of EA, as result of a compensatory enhancement of reactive control. This prediction however, to the best of our knowledge, has not yet found a demonstration. Actually, to the best of our knowledge, so far only one study has explored the relation between anxiety and EA, without finding any significant association between the two (3). Harty et al. (3), however, employed the Hospital Anxiety and Depression Scale (HADS) (28), which asks participants to evaluate how they felt in the past week, and therefore does not assess trait anxiety.

Hence, we decided to further test the hypothesis of a positive association between trait anxiety and EA employing a different measure, such as the State-Trait Anxiety Inventory—STAI (29).

Furthermore, based on the literature suggesting a possible relation between anxiety and the age-related decline in cognitive performance (30–32) we also wanted to investigate if anxiety was in some way associated with the age-related decline on EA. In this case, given the fact that the direction and the temporal dynamics of the relation between the age-related cognitive decline and anxiety are not clear yet, we did not have a specific prediction.

Finally, as a third exploratory aim, we also wanted to investigate if anxiety would be related to the potential effect that the motivational manipulation employed in the present study might have had on EA. Actually, some recent studies suggest that motivation is an important variable in explaining the relation between trait anxiety and cognitive performance, because high trait-anxious individuals would be more apprehensive about their performance (33), and therefore more motivated to invest further cognitive effort when performing a task (22, 34). Our last prediction was therefore to find a positive association between trait anxiety and the potential beneficial effect of motivation on EA.

METHODS

Participants

Sixty healthy participants were recruited[1]: 30 younger adults (age range: 19–35 years; mean age 25.4 ± 5.1; 10 M) and 30

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[1] Participants in the present study were the same as in Masina et al. (4) with the exception of two elderly participants.

TABLE 1 | Mean scores obtained at the standard psychological and cognitive tests, and years of education, of both groups. Standard deviations are in parenthesis.

	Younger adults	Older adults
MoCA	28.1 (1.6)	25.9 (2.5)
STAI-S (Classical EAT)	34.2 (7.9)	32.6 (6.2)
STAI-S (Motivational EAT)	32.2 (4.8)	32.3 (6.0)
STAI-T	40.7 (9.7)	36.0 (8.7)
TIB	106.8 (4.7)	111.2 (8.6)
CRIq	92.7 (6.3)	105.3 (25.3)
Short term memory (mean score)	16.2 (4.2)	10.8 (2.5)
TMT B-A	39.0 (15.9)	63.1 (42.7)
Years of education	15.1 (2.7)	11.3 (5.5)

older adults (age range: 61–83 years; mean age 69.7 ± 5.5; 12 M). Inclusion criteria were: an age between 18–35 (younger adults) and 60–85 (older adults) years; the availability to take part in a two-session experiment; a normal or corrected-to-normal vision; the ability to sign the informed consent. Exclusion criteria were: present or past neurological or psychiatric diseases; use of neurological or psychiatric medications; a score at the Montreal Cognitive Assessment (MoCA) (35) under the Italian cut-off [i.e., 15.5 (36, 37)] (see **Table 1**). Participants received no compensation for taking part in the study. Written informed consent was obtained from all participants. The study was conducted in accordance with the Helsinki Declaration on human rights and was approved by the Ethics Committee of the School of Psychology at the University of Padua.

Experimental Task Procedure

To test the hypothesis of a positive effect of reward motivation in EA, the performance at two different versions of the Error Awareness Task (EAT) (38) was compared.

In one version of the task, which will be hereby called the "Classical EAT" (4), a serial stream of single color words was presented at the center of the screen. Participants were asked to respond with a single-speeded press ("3" on the keyboard) when the word and its color font were congruent (go trials). In addition, they were trained to withhold the response when the word and its color font were incongruent (Stroop no-go trials), or when the word was presented twice in a row (repeat no-go trials). Following the offset of the word, the sentence "Hai commesso un errore?" [in English: "Did you make a mistake?"] prompted participants to monitor their performance online. In case participants realized they had made a mistake, they were required to press an error button (space bar), in order to signal it (see **Figure 1A**). The data concerning the Classical EAT performance of the overlapping participants have been reported in our previous study (4).

The second version of the task was designed for this specific study and was called the "Motivation EAT." It was identical to the Classical EAT, except for the presence of feedbacks and virtual rewards. Specifically, we decided to use both performance-dependent (positive or negative) feedback and virtual monetary incentives (high and low reward) in order to motivate our participants to perform at their best and, moreover, to motivate them to be aware of their own performance, and therefore their errors. For this reason, we did not directly reward/give a feedback after a stimulus response per se, but we delivered reward and feedback only after the response to the question "Did you make a mistake?" (see **Figure 1A**).

More in detail, in case of correct responses to stimuli and correct responses to the question "did you make a mistake," the feedback "Corretto!" ["Correct!"] was presented, as well as a virtual reward of € 0.50. On the contrary, in case participants did not respond in the correct way to the question "did you make a mistake?," the feedback "Sbagliato!" ["Incorrect!"] appeared, but no losses were applied. If participants made a mistake (wrong response to the stimulus) and responded "yes" to the question "did you make a mistake?," showing therefore error awareness, they received a virtual reward of € 0.10. Four conditions where therefore possible, as summarized in **Figure 1B**.

After receiving a reward, the information about the updated total wins appeared at the bottom of the screen. At the end of the experiment, each participant received information about the total wins.

The purpose of associating correct task responses with higher reward, and EA with lower reward, was to motivate participants to enhance performance monitoring without increasing error rate. At the same time, the choice to use only positive incentives and to give only negative feedback (and not negative incentives/punishment) after incorrect responses, was made because of the older adults' selective sensitivity to gains, and reduced sensitivity to losses [see (39)].

In both versions of the task, 675 stimuli were presented, in three blocks of 225 trials (200 go trials and 25 no-go trials, of which 12 Stroop no-go trials and 13 repeat no-go trials; see **Figure 1A**). The tasks were administered in two separate sessions and in a counterbalanced order.

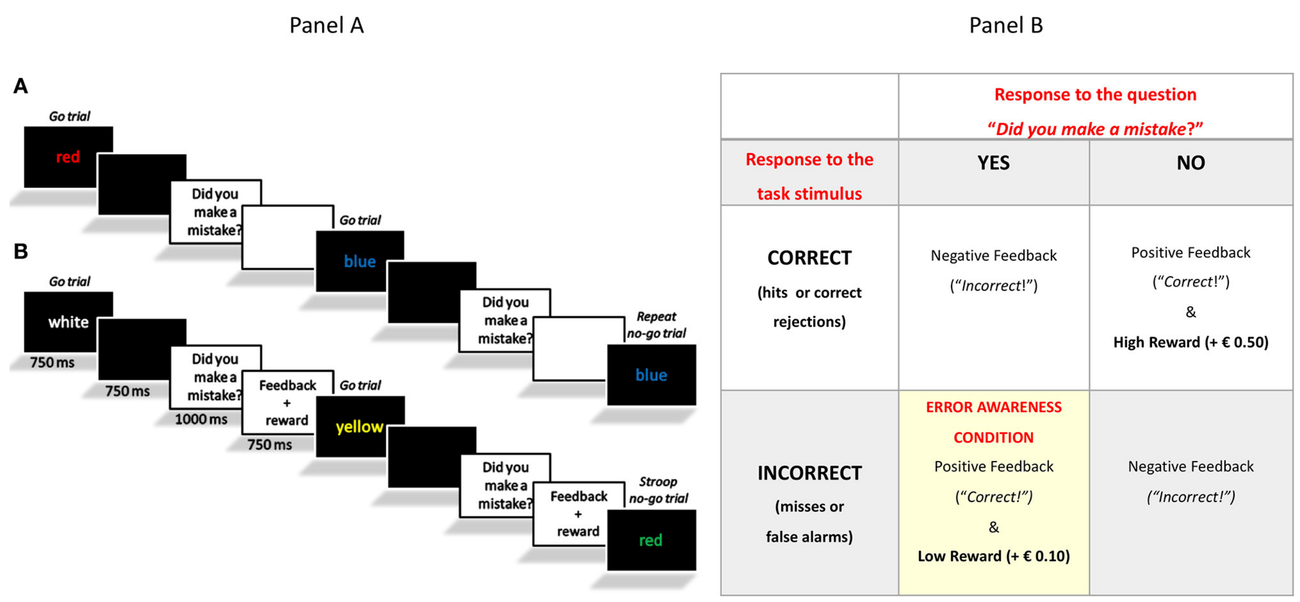
The experiments were run by E-Prime software (version 2.0 Psychology Software Tools, Pittsburgh, PA) installed on a personal computer equipped with a 15″ monitor.

Dependent variables considered as indices of performance were the correct response times (RTs) >100 ms, the accuracy rate at both go and no-go stimuli, and EA, calculated as the percentage of correctly signaled commission errors on the total number of commission errors (40).

Psychological Assessment

Both younger and older participants were asked to take part in a standard "paper and pencil" testing phase, where state and trait anxiety were collected. Specifically, at the end of each of the two sessions, participants completed the State-Trait Anxiety Inventory—State (29), while at the end of the second experimental session only, they also completed the State-Trait Anxiety Inventory—Trait (29).

Furthermore, we also employed the following standard cognitive tests: Verbal Short-Term Memory Test [immediate and delayed recall; both from ENB 2 (41)], in order to assess short-term memory; Trail Making Test A and B [from ENB 2 (41)],



	Response to the question "*Did you make a mistake?*"	
Response to the task stimulus	YES	NO
CORRECT (hits or correct rejections)	Negative Feedback ("*Incorrect!*")	Positive Feedback ("*Correct!*") & High Reward (+ € 0.50)
INCORRECT (misses or false alarms)	ERROR AWARENESS CONDITION Positive Feedback ("*Correct!*") & Low Reward (+ € 0.10)	Negative Feedback ("*Incorrect!*")

FIGURE 1 | (Panel a) Schematic representation of the experimental tasks. In Sessions 1 and 2, the Classical EAT **(A)** and Motivational EAT **(B)** were counterbalanced across participants. Only in the Motivational EAT participants received a feedback after a response and a reward after a correct response or a signaled error. **(Panel b)** Schematic representation of the rewarding scheme adopted in the Motivational EAT.

in order to assess general speed and task switching; Test di Intelligenza Breve—TIB [(42)—Italian equivalent of the National Adult Reading Test (43)], in order to estimate IQ; Cognitive Reserve Index questionnaire (CRIq) (44), in order to estimate cognitive reserve.

Data Analysis

One participant in the older group was excluded from analyses because of technical difficulties during the task, leading to a total sample of 59. The normality of the distribution of each variable of interest was assessed using Kolmogorov-Smirnoff test. Results indicated that both EA and the scores at the standardized psychological and cognitive tests were not normally distributed, while RTs and Accuracy rates resulted to be normally distributed in both tasks (minimum $p > 0.20$ at the Kolmogorov-Smirnoff test).

Therefore, within-group differences in the EA, measured in the two experimental conditions (Classical EAT vs. Motivational EAT) were assessed using Wilcoxon signed-rank test, while between group differences in terms of EA, as well as in terms of state and trait anxiety and cognitive functions were assessed using Mann–Whitney U-test. Based on Bonferroni correction for multiple comparisons, the significant p-value for these non-parametric tests was set equal to 0.004 (rounding down 0.05/12).

Between and within group differences in terms of RTs and accuracy were assessed by conducting two mixed ANOVAs, considering as within-subjects factor the *Task* (Classical EAT vs. Motivational EAT) and as between-subjects factor the *Group* (younger vs. older adults). Partial eta squared ($\eta_p{}^2$) was used as measure of effect size. Bonferroni correction was employed in case *post-hoc* comparisons were performed.

Correlations between EA, measured during the Classical EAT, and scores obtained at the standardized anxiety and cognitive tests, including the MoCA, were assessed using two-tailed Spearman's rank correlation coefficient. Information about age and education was also included in the correlation analysis. Correlations were conducted considering the total sample ($N = 59$). However, of the older adults group, three participants did not complete the STAI state scale, while one participant did not complete the TMT. Hence, in the analyses that considered these two tasks, N was respectively equal to 56 and 58. Based on Bonferroni correction, significant p-value for the correlations was set equal to 0.005 (0.05/10).

RESULTS

Table 1 reports the scores obtained at the standard psychological and cognitive tasks, together with information about education. EA, mean correct RTs and accuracy rates, as a function of task and group, are reported in **Table 2A**.

Results confirmed the presence of lower EA levels in older adults, when compared with the younger ones, in both tasks (Classical EAT: $U = 63.5$, $p < 0.0001$; Motivational EAT: $U = 160$, $p < 0.0001$). No significant results emerged in terms of EA when assessing the differences between the two tasks in both groups.

Older adults, when compared with the younger ones, had a significantly lower performance at the MoCA test ($U = 194.5$, $p < 0.0001$) and at the Short-term memory[2] test ($U = 130.5$, $p < 0.0001$). No significant differences were revealed between younger and older adults in terms of state and trait anxiety and in the other cognitive tests employed (TMT B-A, TIB, and CRIq).

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[2] Average between immediate and delayed recall scores.

TABLE 2A | Mean correct RTs (milliseconds), accuracy rates (%), and EA (%), as a function of task and group. Standard deviations are in parenthesis.

Group	**Classical EAT**			**Motivational EAT**		
	RTs	**Accuracy**	**EA**	**RTs**	**Accuracy**	**EA**
Younger adults	483.5 (59.7)	94.5 (2.3)	88.5 (7.7)	499.5 (76.7)	94.1 (2.8)	80.7 (13.9)
Older adults	630.4 (91.9)	95.5 (2.0)	57.6 (2.1)	654.26 (90.6)	94.8 (1.8)	56.7 (2.4)

TABLE 2B | Correlations between EA (Classical EAT), age, education and the scores at the standard cognitive and psychological tests.

	Age	**Education**	**MoCA**	**STAI-S**	**STAI-T**	**TIB**	**CRIq**	**Short term memory**	**TMT B-A**
EA	Rho = −0.67* p< 0.001	Rho = 0.36 $p = 0.006$	Rho = 0.47* p< 0.001	Rho = −0.02 $p = 0.89$	Rho = 0.1 $p = 0.47$	Rho = −0.13 $p = 0.33$	Rho = −0.04 $p = 0.77$	Rho = 0.43* $p = 0.001$	Rho = −0.41* $p = 0.001$

**refers to a $p < 0.005$.*

Results of the ANOVA on RTs confirmed the age-related decline in response speed, with significantly longer RTs in older adults, when compared with the younger ones, independently of the task $[F_{(1,57)} = 57.21$; $p < 0.0001$; $\eta_p^2 = 0.98]$. Moreover, results also showed a significant difference when comparing the two tasks, with longer RTs during the Motivational EAT with respect to the Classical EAT, independently of the group $[F_{(1,57)} = 9.23$; $p < 0.005$; $\eta_p^2 = 0.13]$. Finally, a significant difference between the two tasks also emerged in terms of accuracy $[F_{(1,57)} = 5.19$; $p < 0.05$; $\eta_p^2 = 0.08]$, with lower accuracy rates at the Motivational EAT, if compared with the Classical EAT, independently of the group.

Results of the correlation analysis (**Table 2B**) revealed that EA, assessed with the Classical EAT, was significantly related with both age (Rho = −0.671; $p < 0.0001$) and MoCA scores (Rho = 0.472; $p < 0.0001$). A positive significant association was also revealed between EA and short-term memory test score (Rho = 0.434; $p < 0.005$), while a negative significant association was present between EA and TMT B-A score (Rho = −0.411; $p < 0.005$).

No significant correlations emerged between EA and either state or trait anxiety (see **Table 2B**).

Based on the results obtained when comparing the Classical EAT and the Motivational EAT, namely the increase of both RTs and error rates, we decided to perform an additional a posteriori correlation analysis, to investigate possible associations between the RT and accuracy between-task differences, on the one side, and the scores obtained at the standard tests, on the other side.

Results showed that only one correlation met conventional statistical significance levels ($p < 0.05$), and precisely the one between state anxiety, measured in the Motivational EAT session, and the RT difference between the two tasks (Rho = 0.30; $p < 0.05$), with greater slowing in participants with higher state anxiety levels (**Figure 2**).

Because this result would not survive after applying multiple comparisons correction, we will consider and discuss this last result only for hypothesis generation for follow-up studies.

DISCUSSION

The first aim of the present study was to test the hypothesis of a positive effect of reward motivation on EA and, moreover, on age-related EA decline. Our prediction was that the presence of motivational incentives would have improved the EA levels and reduced the age-related EA decline.

As a second aim, the present study also explored possible associations between anxiety, especially trait, and EA. Our prediction was to find a positive association between the two. As a third exploratory aim, we investigate the possible interaction between anxiety, motivation and EA.

Results will be therefore discussed according to these three aims.

Reward motivation and EA

Differently from our prediction, EA did not improve when motivational incentives were associated to correctly detected errors, neither in younger nor in older adults. Moreover, the association of higher incentives with correct responses did not improve accuracy either, but on the contrary had a negative effect on it and on RTs, with both younger and older adults showing a higher error rate and slower responses during the Motivational EAT.

A first possible explanation for the lack of a reward effect is represented by the low difficulty of our tasks. First of all, the high accuracy rates that both younger and older adults showed on the Classical EAT indicate that our baseline experimental paradigm might have been not challenging enough for the purposes of the present study. Introducing motivational incentives in a more challenging task may have elucidated further effects of reward on accuracy.

Another possible explanation is that reward stimuli, being presented in the inter-trial intervals, distracted participants. This hypothesis would be in line with a series of previous works, which suggested that reward signals can automatically influence visual attention beyond, and sometimes against, the strategic control of goal-directed attention (45–47). This phenomenon is also explained in the well-established "distraction theory" (48, 49),

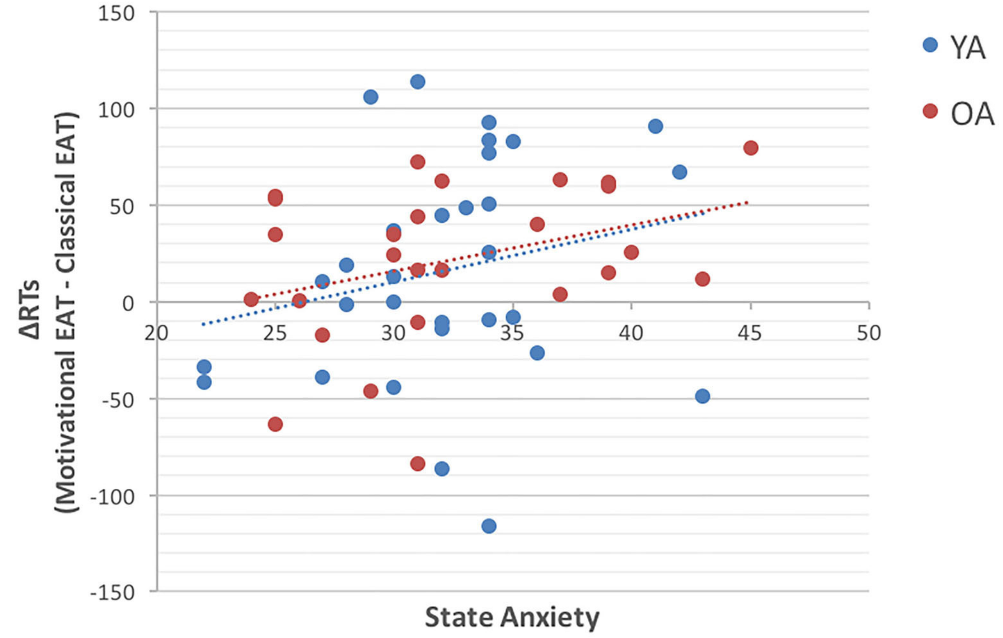

FIGURE 2 | The scatterplot represents the correlation between State Anxiety (on the X axis) and the ΔRT (on the Y axis) obtained by comparing the two experimental tasks. Precisely, ΔRT = (RTs in Motivational EAT – RTs in the Classical EAT). The blue dots represent younger adults (YA), while red dots represent older adults (OA). Results suggest that participants with higher state anxiety are the ones who show longer RTs in presence of reward.

according to which the presence of rewards could represent a distracting environment and may draw the performers' attention away from skill execution, causing the "choking under pressure" phenomenon (50).

Finally, the reward manipulation could have not be effective in enhancing task performance because of an inappropriate reward delivery timing. Actually, it has been shown that the effects of reward on cognitive performance also depend on when the information about the reward is presented. Specifically, while a pre-stimulus reward-cue seems to have positive effects on cognitive performance, a reward presented together with the stimulus can have detrimental effects on visual attention (51).

Anxiety and EA

Results of the present study did not reveal the presence of any correlation between state or trait anxiety and EA. On the contrary, significant correlations emerged only between EA and age, and between EA and scores obtained at the standard cognitive tests. Specifically, we report a significant positive association between EA and both the MoCA and short-term memory test performance, such as individuals with better general cognitive performance and with a more efficient short-term memory, are also more aware of their mistakes. We also found a negative association between EA levels and the task switching capacity, estimated through the TMT B-A. This further confirm the association with EA and high order cognitive abilities. We did not find any association between anxiety (state and trait) and any of the scores obtained at the other cognitive tests employed.

Furthermore, while we found a significant difference in terms of EA between younger and older adults, coherently with the literature (1–3, 5–9) and we found predictable age-group differences in general cognitive performance (i.e., MoCA) and short-term memory, we did not find any significant difference between the two groups in terms of state or trait anxiety.

Therefore, this second set of results suggests that state or trait anxiety might not have a role in modulating EA, and that age-related EA decline should be considered as a consequence of a more general age-related cognitive decline, without any association with state or trait anxiety.

Possible Interaction Between Motivation, Anxiety and Cognitive Performance

Results of the exploratory analysis, conducted in order to better understand the unpredicted higher RTs and error rates during the Motivational EAT, indicated that individuals who showed the longer RTs during the Motivational EAT were also the ones with higher level of state anxiety.

This result, although it has to be considered with caution, would be in line with the above-mentioned Compensatory Error Monitoring hypothesis (27), which suggests that anxious individuals need to make a greater effort in order to maintain task-related goals and a good level of performance. Interestingly, this theory also suggests that this greater amount of effort would be necessary to compensate for the distracting effect of worry, and would translate in a reactive control mode, which is more time consuming and could therefore explain the longer RTs.

We could therefore speculate that if our reward manipulation actually acted also as a distractor for our participants, this was particularly true for the ones with higher state anxiety.

At the same time, the possibility to obtain a reward could have been itself a reason to worry, causing therefore greater slowing in individuals who tend to be more anxious.

Limitations and Future Directions

Some limitations should be noted when considering our results.

First of all, the experimental task designed for the present study did not allow us to clearly disentangle the effect of reward stimuli on motivation from the one that it probably had on attention resources. As previously explained, the post-response reward presentation could have actually distracted our participants, leading to longer RTs and higher error rates. To overcome this limitation, future study might want to test a different timing of the motivational manipulation, presenting for example a pre-stimulus reward-cue, or directly employing a block design, comparing counterbalanced reward and non-reward task blocks.

Secondly, as previously mentioned, both our tasks might have been not challenging enough for the purposes of the present study. A more difficult task, or a task tailored on an individual baseline performance, may have elucidated further effects and could represent a future effort in order to further investigate if motivation might have a potential beneficial effect on EA. To this aim, the introduction of a standard test of reward sensitivity, like the BIS/BAS scale (52), as well as the recruitment of a larger sample, would be helpful as well.

An interesting and extremely valuable future direction, in our opinion, would be also represented by the study of EA in clinical samples, such as patients with either motivational deficits like apathy, and/or with anxiety disorders. Assessing EA both alone and in relation to the presence of motivational incentives in these populations could actually represent an ideal condition, which would allow to better understand the interaction between EA, motivation and anxiety, with great benefit from both a theoretical and a clinical point of view.

CONCLUSIONS

To the best of our knowledge, this work represents the first study investigating the effect of reward motivation on EA as well as the relation between EA and trait anxiety, in both younger and older adults. Taken together, results of the present study confirm the presence of an age-related EA decline and suggests its strict relation with the general cognitive status as well as with the short-term memory capacity. Results also show the absence of a significant relation between state and trait anxiety and EA, as well as the lack of effect of reward motivation on EA.

We therefore hope that this study will inspire many others, which, by overcoming the above-mentioned limitations, should be aimed to add new evidence in this research field, in order to clearly establish if and how EA can be enhanced through reward motivation. Moreover, we hope that this study will be considered also for its practical implications, such as the need to find effective strategies to enhance EA as well as the importance of assessing EA in the clinical practice. In our opinion, because a deficient EA would have detrimental effects on any rehabilitation outcomes, EA assessment should be present together with both cognitive and psychological tests in every clinical assessment, especially if the patient is an older adult, and particularly before any rehabilitation and treatment procedure begins. The introduction of an EA assessment in the clinical practice would in this way improve the effectiveness of any interventional approach, and therefore represent an important development in psychiatry, as well in clinical psychology and neuropsychology.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of the School of Psychology at the University of Padua. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

ED, FM, and DM: study's conceptualization. ED and FM: data collection and analysis. ED, FM, AV, and DM: data interpretation, writing up, and revision of the manuscript. All authors have approved the final manuscript.

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