ETIOLOGY, PATHOGENESIS, AND CONSEQUENCES OF MALADAPTIVE HABITS

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ETIOLOGY, PATHOGENESIS, AND CONSEQUENCES OF MALADAPTIVE HABITS

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Editorial: Etiology, Pathogenesis, and Consequences of Maladaptive Habits

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Keywords: habits, impulsivity, addiction, inhibitory control abilities, impulse control (pathology) disorders

Editorial on the Research Topic

Etiology, Pathogenesis, and Consequences of Maladaptive Habits

Maladaptive habits are behavioral patterns of inflexible behavior that reflect poor self-control and occur despite their harmful consequences. Those behaviors lead to undesirable outcomes in a broad range of a person's life domains. It is important to note that maladaptive habits, while prevalent, are not always a symptom of a disorder. Maladaptive habits develop in both psychiatric/neurological disorders and non-clinical samples; and reflect context-specific failure of self-control. There are many explanations concerning the etiology, pathogenesis, and consequences of maladaptive habits. Yet, more research is needed for understanding neurobiological and psychological mechanisms that support maladaptive habit formation and maintenance.

The study of maladaptive habits is particularly relevant since online tempting behaviors have never been so readily available and easy to engage in. Specifically, the current easy access to computers, tablets, and smartphones allows people to get repeated and continuous rewards by just pressing a button (e.g., "like," "buy," "bet," "match," "watch," "going," "match," etc.). Moreover, the high volume of cues (e.g., new message notifications, and thoughts about others' thrilling experiences) makes it increasingly hard to resist the temptation of engaging in such activities.

In the light of today's high-availability of ready-to-consume rewards, the aim of this Research Topic was to integrate contributions concerning the understanding, assessment, etiology, and consequences of different types of maladaptive habits. The collection includes ten articles addressing such topics.

Considering the assessment of impulsive behavior, this Research Topic includes a study presenting the adaptation of assessment tools such as the short version of UPPS-P to a Brazilian population (Pompeia et al.). In this paper, the authors found that the psychometric properties of the Brazilian Short Version of UPPS-P support the use of a single and general impulsivity score for this scale.

Two articles addressed the issues of impulsivity and maladaptive behaviors in non-clinical samples. Gicquel et al. discussed the role of environmental and human factors (some of them related to habits) pertaining to traffic accidents in youth, and proposed strategies for preventing them. Jelihovschi et al. examined the relationship between cognitive impulsivity and decision making in professionals and students from the management field. They found that cognitive impulsiveness, related to immediatism impair complex decision-making assessed by the Cognitive Reflection Test. Together, these two studies stress the relevance of considering tempting and impulsive behavior within non-clinical samples.

Within the frame of mental disorders, the consequence of impulsivity and maladaptive habits were presented and discussed in relation to suicidal behavior (Lima et al.), attention deficits and hyperactivity disorder (Coutinho et al.), hoarding behavior (Novara et al.; Vilaverde et al.), excessive smartphone use (Khoury et al.), and feeding and eating disorders (Strangio et al.). In

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Malloy-Diniz et al.

Maladaptive Habits

these articles, the authors present several patterns of hampered impulse control in individuals presenting mental health traits, suffering from mental disorders, including among their relatives. Taken together, these studies support the relationship between habits, impulsiveness, and inhibitory control deficits within a broad range of maladaptive outcomes.

Finally, the neurobiological perspective of understanding the etiology and maintenance of maladaptive habits has been adopted by a study examining the relationship between dopaminergic system and reward memory in addiction (Richter et al.). In this paper, the authors address the association between a genetic polymorphism related to the DRD2 expression (polymorphism C957T) and the memory for the reward stimulus related to addictive behavior.

Overall, the diversity of issues and knowledge fields that contributed to this topic provides unequivocal evidences that maladaptive habits are a pervasive pattern of behavior with undesirable outcomes in a large variety of settings. To a broader extent, this Research Topic offers a relevant framework for

further understanding the multifactorial basis of maladaptive habits and its relationship with adverse outcomes across the lifespan and life domains, in both clinical and non-clinical samples. We hence call for more research on this topic.

AUTHOR CONTRIBUTIONS

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

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Hoarding Symptoms Are Not Exclusive to Hoarders

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Hoarding disorder (HD) was originally conceptualized as a subcategory of obsessive compulsive disorder (OCD), and numerous studies have in fact focused exclusively on investigating the comorbidity between OCD and HD. Hoarding behavior can nevertheless also be found in other clinical populations and in particular in patients with eating disorders (ED), anxiety disorders (AD), major depression (MD), and psychotic disorders (PD). The current study was carried out with the aim of investigating, using a validated instrument such as the Saving Inventory-Revised (SI-R), the presence of HD symptoms in patients diagnosed with ED, AD, MD, and PD. Hoarding symptomatology was also assessed in groups of self-identified hoarders and healthy controls. The results revealed that 22.5% of the ED patients exceeded the cut-off for the diagnosis of HD, followed by 7.7% of the patients with MD, 7.4% of the patients with AD, and 5.9% of the patients with PD. The patients with ED had significantly higher SI-R scores than the other groups in the Acquisition and Difficulty Discarding scales while the AD, MD, and PD patients were characterized exclusively by Difficulty Discarding. These data suggest to clinicians that hoarding symptoms should be assessed in other types of patients and especially in those affected by Bulimia and Binge eating.

Keywords: hoarding, clinical population, Bulimia, Binge eating, Major Depression, Anxiety Disorders, Psychosis

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INTRODUCTION

Hoarding disorder (HD) has recently been included in Obsessive-compulsive spectrum disorders of DSM-5 as a distinct condition (Mataix-Cols et al., 2010; Pertusa et al., 2010). From the time studies were first carried out on the disorder (Frost and Gross, 1993; Frost and Hartl, 1996) HD has been defined and characterized by: (a) excessive acquisition of large quantities of useless objects; (b) difficulty in discarding possessions; (c) cluttering of living spaces so as to preclude the activities for which they were intended. It has been reported that after onset, HD generally follows a chronic course with prevalence ranging from 2.3% in younger age groups to 6.2% in older ones (Samuels et al., 2008) and spontaneous remissions are rare (Gilliam and Tolin, 2011). According to a study by Italian investigators, its prevalence reaches as high as 6% in the Italian population (Bulli et al., 2014). The prevalence of hoarding in the female gender is controversial: in a sample of self-identified hoarders (SIH), Frost et al. (2011) reported that 78% was made up of women while the percent of women and men in the general population was, respectively, 5.6 and 2.6%. No gender differences were found in the non-clinical Italian population (Bottesi and Novara, 2012; Bulli et al., 2014).

The problem of comorbidity has always characterized hoarding because of a poor diagnostic definition (until DSM-5) and the symptoms overlap with those observed in mood disorders, anxiety disorders (AD), eating disorders (ED), or Schizophrenia Spectrum. The perspective has

generally been unidirectional when other psychopathological characteristics have been evaluated in HD patients and in some cases bidirectional when HD characteristics have been investigated in patients diagnosed with other disorders. Absence of relevant comorbidity has been reported in 25 to 42% of hoarders (London Field Trial for HD; Grisham et al., 2005; Frost et al., 2011; Mataix-Cols et al., 2012; Hall et al., 2013).

Comorbidity with Depression and Anxiety

Since HD has been considered a subcategory of obsessive compulsive disorder (OCD), several studies have considered samples of hoarders exclusively with OCD comorbidity. Although according to some studies approximately 18-33% (Rasmussen and Eisen, 1989; Frost and Hartl, 1996) of OCD patients have hoarding comorbidity, 83% percent of hoarders do not meet the criteria of OCD (Frost et al., 2010). A stronger comorbidity with Mood Disorders [Major Depressive Disorder (MDD) 50-75%] and AD [Generalized Anxiety Disorder (GAD) 23-39%, Panic 15%, Agoraphobia 14%, Specific phobia 26-29%, and Social phobia 14-71%; Samuels et al., 2002; Lochner et al., 2005] has, moreover, been found in OCD patients with HD. The fact that depression is the most commonly co-occurring symptom in HD has also been confirmed by a recent study designed by Hall et al. (2013) who reported that 42% of the self-identified HD population had depression as measured by the Depression and Anxiety Stress Scale (DASS; Lovibond and Lovibond, 1995).

One of the few studies that considered diagnoses other than OCD is one by Tolin et al. (2011) who examined hospitalized patients presenting for treatment of anxiety problems. That study uncovered that 28% of the GAD patients had clinically significant hoarding symptoms followed by the patients diagnosed with OCD (16.6%) and those with Social Phobia (14.8%). These data have also been confirmed in a population diagnosed as hoarders in whom the prevalence of MD reached 50.7%, followed by GAD (24.4%), Social Phobia (23.5), and OCD (18%) (Frost et al., 2011).

While comorbid hoarding symptomatology in OCD populations is well established and has been amply demonstrated, it is not clear if it is linked to anxiety or depression given the scarcity of studies carried out until now. The current study, in fact, aimed to investigate hoarding symptomatology in groups of those patients.

Comorbidity with Eating Disorders

The association between HD and ED is controversial and understudied. When OCD hoarders were compared with OCD non-hoarders, the severity of symptoms seemed to depend on the female component of the sample which also included ED patients (Wheaton et al., 2008). Some of the first studies (Halmi et al., 2003) that examined hoarding in ED patients found that those subjects did not differ from OCD controls as far as presence of hoarding symptoms was concerned (16.5% vs. 13.8%, respectively). This finding was recently confirmed by an Italian study which reported that 15.5% of the ED patients studied exceeded the clinical cut-off level (Novara and Bottesi, 2013).

Fontenelle et al. (2004) reported, moreover, that 26.7% of the hoarders also had an ED (Bulimia in 13.3% of the cases and Binge eating in the rest), while Frost et al. (2011) found that only 1.4% of a population of hoarders had ED.

Until now a single item on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS; Goodman et al., 1989) specifically concerned with hoarding has been used to investigate hoarding symptomatology in ED patients. The current study, which assessed these patients using a more exhaustive, specific measure such as the Saving Inventory-Revised (SI-R), will make it possible to compare its findings with those that will be registered by future investigations based on standardized assessment instruments.

Comorbidity in Psychosis

The relationship between HD and psychosis has been studied less assiduously although it is considered one of the pathologies associated to *Hoarding* (Pertusa et al., 2010). Repetitive acquisition behaviors and excessive care of objects of little value have often been found in patients with schizophrenia and have been positively correlated especially to the male gender and the Caucasian race (Luchins et al., 1992). In a study carried out to quantify the presence and the variety of repetitive behaviors (including hoarding) in a sample of 400 chronic patients with schizophrenia, Tracy et al. (1996) reported that the percent of patients manifesting abnormal acquisition behavior was below 20%. No other study, to our knowledge, has specifically investigated HD characteristics in patients with schizophrenia.

The principal aim of the current study was to investigate the prevalence of HD symptoms in patients diagnosed with ED, Major Depression (MD), AD, and Psychosis (PD) as well as in groups of SIH and healthy controls using a validated, standardized assessment instrument such as the SI-R. Given literature findings, we expected to identify a greater frequency of depression symptoms in a group of SIH (SIH group) and the highest percentage of hoarding symptoms in the AD patients. The study also intended to examine the relationship between HD symptoms severity and disease duration.

MATERIALS AND METHODS

Participants

One hundred twenty-four patients with an established diagnosis were enrolled in the study. Forty-one (100% female) of these were consecutively hospitalized patients suffering from Bulimia or Binge eating (ED group = 10 had the former and 31 the latter); the others were consecutively presenting outpatients who were grouped as follows: 39 (56.4% female)had MD (MD group), 27(63% female) had AD (AD group = 17 with general anxiety disorder, 6 with panic disorder, 2 with adjustment disorders with anxiety, 1 with acute stress disorder, 1 with social AD), 17 (52.9% female) had psychotic disorders (PD group in the recovery phase = 12 were diagnosed with schizophrenia and 5 with schizoaffective disorder). All of the patients were diagnosed by expert clinicians following the Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition

Text Revision (DSM-IV-TR; American Psychiatric Association [APA]). Pharmacotherapy regarded 36,58% of ED group (SSRI or phenothiazine), 46,15% of MD group (SSRI), 35,29% of AD group (SSRI), and the 52,94% of PD group (clozapine or valproate sodium).

Exclusion criteria to the study were: mental retardation, head injury/neurologic diseases, and symptoms that could be signs of serious health conditions. Patients with comorbid personality disorders were not excluded (ED group: N=6; MD group: N=3; AD group: N=3; PD group: N=1). This study was approved by the Ethical Committees of the Department of General Psychology and by the clinical structure in which the participants were hospitalized and/or interviewed. The 49 (83.7% female) SIH who were enrolled were considered the SIH group; 48 (66.7% female) healthy individuals from the community at large were also enrolled (and considered the healthy control – HC-group).

Instruments

The Italian version of the SI-R (Frost et al., 2004; Novara et al., 2013), a 23-item self-report questionnaire which quantifies compulsive hoarding, was used to assess hoarding in all of the groups studied. The respondents were asked to rate the items on the inventory's three sub-scales - Clutter, Difficulty Discarding/Saving, and Acquisition – with reference to situations taking place over the previous week's time using a 5-point Likert scale (0 = never, 1 = rarely, 2 = sometimes/occasionally, 3 = Frequently/Often, 4 = Very often). In addition to a total score, it is also possible (for both the original and the Italian versions) to compute sub-scores for each of the sub-scales; these were found to show good internal consistency and test-retest reliability. Scores exceeding 40 indicate the presence of clinically significant HD. The following cut-offs scores were identified for the original English version: Clutter: raw scores \geq 15; Difficulty discarding: raw scores ≥ 13 ; Acquisition: raw scores ≥ 13 (Frost et al., 2004).

The *Beck Anxiety Inventory* (BAI; Beck et al., 1988; Italian version Sica et al., 2006), which is a 21-item multiple-choice self-report inventory, was used to measure the severity of anxiety in the participants. The items inquire about common symptoms recently experienced by the respondent; the inventory has been found to have a good internal consistency and test-retest reliability. Good psychometric properties have also been confirmed for the Italian version.

The *Beck Depression Inventory – II* (BDI-II; Beck et al., 1996; Italian version Ghisi et al., 2006), which is a 21-item multiple-choice self-report inventory and one of the most widely used psychometric tests, was utilized to evaluate depression in the participants. The instrument identifies the presence and severity of affective, cognitive, motivational, psychomotor, and vegetative symptoms of depression in accordance with the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria. The original version of the BDI-II was found to have good internal consistency (both in students and in patients), good test-retest reliability at 1 week, and good convergent and discriminant validity. The Italian version of the BDI-II was also found to have good psychometric properties.

Procedure

The overall recruitment was carried out between 2013 and 2015 by experienced operators; no incentive was offered for participation. The individuals with ED were consecutively hospitalized patients; the individuals with MD, AD, and PD were outpatients recruited at the mental health units specialized in the treatment of those psychopathologies. The SIH were respondents to advertisements on university bulletin boards and Internet sites seeking volunteers for a research study examining HD features in the Italian population. The large pool of individuals (N = 515)who voluntarily agreed to complete a battery of questionnaires were informed about the aims of the research and were asked to sign consent statements. Those volunteers who got a score higher than the 90° percentile on the total SI-R score (raw score \geq 36) were enrolled in the SIH group. The healthy subjects included in the HC group were likewise individuals who responded to advertisements seeking volunteers for psychological studies.

All the patients in the ED, AD, MD, and PD groups and the individuals in the SIH and HC groups received a complete explanation of the study's aim and what their participation entailed. All signed informed consent statements to participate in the study. The participants were asked to complete a form providing their socio-demographic details. They were then asked to fill out the three inventories which were administered in a counterbalanced order to avoid any order effects.

Statistical Analyses

Pearson's chi square and univariate analysis of variance (ANOVA) were used to compare groups with regard to socio-demographic variables and the BAI, BDI-II, and SI-R scores; the Bonferroni *post hoc* procedure was used to further explore mean differences between groups.

In order to further assess group and gender differences on the SI-R scores, a series of 2 (group) \times 2 (gender) ANOVAs was conducted.

Cronbach's alphas were computed for each group's total and subscale SI-R scores in order to assess the internal consistency of the questionnaire. The internal consistency values were thus rated: $\alpha \geq 0.90 =$ "optimal"; $0.90 > \alpha \geq 0.80 =$ "excellent"; $0.80 > \alpha \geq 0.70 =$ "good"; $0.70 > \alpha \geq 0.60 =$ "sufficient"; $\alpha < 0.60 =$ "insufficient."

Pearson's correlations were conducted separately for the ED, MD, AD, and PD groups in order to explore the association between disease duration, age, and total SI-R scores.

RESULTS

Means, standard deviations (SD) ranges and Bonferroni *post hoc* comparisons with reference to age, education, disorder duration, and BAI and BDI-II scores are outlined in **Table 1**.

The BAI (Beck et al., 1988; Italian version Sica et al., 2006) uncovered no differences between groups as far as physiological anxiety symptoms were concerned ($F_{5,215} = 2.05$, p = 0.07). There were instead significant differences between groups in depression symptom scores on the BDI-II (Beck et al., 1996; Italian version Ghisi et al., 2006) ($F_{5,215} = 24.01$, p = < 0.001).

TABLE 1 | Means standard deviations (SD) ranges and post hoc comparisons of age, education, duration of the disorder, BAI and BDI-II scores across the groups studied.

	ED	MD	AD	PD	SIH	нс	Bonferroni
	(N = 41)	(N = 39)	(N = 27)	(N = 17)	(N = 49)	(N = 48)	post hoc
Age (yr)	20.59	49.95	45.19	52.24	25.02	36.27	MD=AD=PD=HC>ED
	(4.34)	(15.25)	(15.85)	(11.51)	(9.26)	(15.23)	MD = AD = PD = HC > SIH
	16–35	18–78	19–74	34-70	20-50	23-60	
Education (yr)	11.46	11.28	12.89	10.29	11.94	14.13	ED=MD=PD <hc< td=""></hc<>
	(3.52)	(3.22)	(3.52)	(3.18)	(3.07)	(3.49)	
	8–25	5–18	7–20	5–14	8–18	8–21	
Duration of thedisorder (yr)	4.00	10.11	10.67	17.65	-	-	ED <pd md="AD=PD</td"></pd>
	(2.83)	(10.43)	(10.13)	(11.39)			
	1-10	1-40	0–40	1–40			
BAI	8.30	7.19	9.92	3.87 (4.62)	10.74	8.87	-
	(9.29)	(7.63)	(11.90)		(7.55)	(6.75)	
	0-42	0–33	0-53	0–16	0-29	0–29	
BDI-II	20.77	23.77	16.63	22.35	29.61	9.18	ED=AD <sih< td=""></sih<>
	(12.77)	(9.97)	(10.55)	(11.28)	(6.45)	(7.67)	MD=PD=SIH>HC
	0-43	6–45	0–38	8–48	16-45	0–31	

ED, eating disorders; MD, major depression; AD, anxiety disorders; PD, psychotic disorders; SIH, self-identified hoarders; HC, healthy controls; BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory -II.

Bonferroni *post hoc* comparisons revealed that the healthy controls had significantly lower scores with respect to the other groups (all ps < 0.05). While the SIH group had higher scores than the ED (p > 0.001) and AD (p > 0.001) groups, no other differences between groups were found. Mean group SI-R scores are outlined in **Table 2**.

Bonferroni *post hoc* comparisons revealed that the SIH group had significantly higher Clutter scale scores with respect to the other groups (all ps < 0.001); the scores of the other groups were comparable (all ps > 0.05). A similar pattern was likewise found in the Difficulty Discarding scale as the SIH group had significantly higher scores than all the other groups (all ps < 0.001), the scores of the other groups were comparable (all ps > 0.05). Finally, with regard to the Acquisition scale, the SIH

group had higher scores with respect to all the other groups (all ps < 0.001). The ED group had scores that were higher than the MD and HC groups (p = 0.006 and p = 0.003, respectively); there were no differences between the ED, AD, and PD groups (all ps > 0.05). Finally, the SIH group had significantly higher total SI-R scores (than all the other groups all ps < 0.001); the scores of all the other groups were comparable (all ps > 0.05).

Results emerged from the 2 (group) \times 2 (gender) ANOVAs revealed a significant main effect of gender in regard to the Difficulty Discarding scale ($F_{1,219} = 6.33$; p = 0.01): in particular, males (M = 11.57; SD = 6.35) scored higher than females (M = 10.41; SD = 6.06). Furthermore, a significant group \times gender interaction ($F_{4,219} = 2.70$; p = 0.03) emerged: specifically, in the PD group males obtained significantly higher

TABLE 2 | Means, standard deviations (SD), ranges and Bonferroni post hoc comparisons for the Saving Inventory-Revised (SI-R) Total and subscales scores obtained by the 6 groups.

	ED group (<i>N</i> = 41)	MD group (N = 39)	AD group (<i>N</i> = 27)	PD group (<i>N</i> = 17)	SIH group (N = 49)	HC group (N = 48)	F _{5,215}	р	Bonferroni post hoc
Clutter	5.85	5.67	5.81	7.18	15.61	6.40	23.92	<0.001	ED=MD=AD=PD=HC <sih< td=""></sih<>
	(6.04)	(5.76)	(5.59)	(5.56)	(5.02)	(4.72)			
	(0-22)	(0-22)	(0-22)	(0-17)	(8-33)	(0-20)			
Difficulty discarding	9.55	7.61	9.33	9.82	17.45	8.65	23.20	< 0.001	ED=MD=AD=PD=HC <sih< td=""></sih<>
	(6.26)	(5.10)	(4.75)	(6.34)	(4.01)	(4.30)			
	(0-21)	(0-25)	(3-18)	(1-26)	(9-28)	(2-17)			
Acquisition	10.76	6.95	7.37	7.71	15.06	6.98	20.76	< 0.001	ED,MD,AD,PD,HC <sih< td=""></sih<>
	(6.50)	(4.61)	(4.43)	(4.22)	(3.99)	(3.94)			MD=HC <ed< td=""></ed<>
	(0-26)	(1-20)	(3-22)	(2-17)	(7-26)	(0-19)			ED=AD=PD
Total	25.87	20.23	22.52	24.71	48.12	22.02	33.17	< 0.001	ED=MD=AD=PD=HC <sih< td=""></sih<>
	(15.87	(13.22)	(13.05)	(12.85)	(8.52)	(10.61)			
) (3-63)	(2-62)	(6-60)	(9-44)	(38-67)	(4-53)			

ED, eating disorders; MD, major depression; AD, anxiety disorders; PD, psychotic disorders; SIH, self-identified hoarders; HC, healthy controls.

scores than females (p = 0.02), whether no gender differences emerged within the other groups (all ps > 0.05) A significant main effect of gender emerged also in regard to the total SI-R score ($F_{1,219} = 5.03$; p = 0.03); also in this case, males (M = 30.26; SD = 17.41) scored higher than females (M = 27.71; SD = 15.61).

Internal consistency values for the SI-R ran from sufficient ($\alpha = 0.67$). To optimal ($\alpha = 0.95$) for all the groups assessed.

On the basis of the wide range of score obtained by the different groups, it was decided to analyze the questionnaires from a categorical point of view.

Symptom Severity in the Study Groups

The percentages of participants with scores on the SI-R (total and subscales) above the cut-off levels are shown in **Table 3**.

Study findings highlighted significant differences between groups with regard to the percentage of individuals scoring above the cut-off level on the SI-R total score ($\chi_5^2 = 101.88$, p < 0.001) as well as on the Clutter ($\chi_5^2 = 42.05 \ p < 0.001$), Difficulty Discarding ($\chi_5^2 = 76.38$, p < 0.001), and Acquisition $(\chi_5^2 = 67.45, p < 0.001)$ scale scores. Just as in other studies examining groups of patients diagnosed with hoarding, those individuals included in the SIH group studied here had higher percentages of scores above the cut-off levels on all the scales with respect to the other groups. The percentages of individuals in the ED and MD groups with scores above the cut-off levels on the Clutter scale were quite similar (12.2 and 12.8%, respectively); those percentages were higher than those in the other groups (ranging from 4.2 and 11.8%). The percentages of individuals in the ED and PD groups with scores above the cut-off levels on the Difficulty Discarding scale were quite similar (30 and 35.3%, respectively) and were higher than those observed in the other groups (range: 17.9-25.9%). Finally, the percentage of ED patients who had scores above the cut-off levels on the Acquisition scale was higher (31.7%) than that in the other groups (percentages ranging from 7.4 to 17.6%), but lower than that in the HD group (73.5%).

There were no differences between groups with regard to the percentages of individuals who had scores above the BAI cut-off levels ($\chi_5^2 = 5.25$, p = 0.39); only 15.3% of the entire sample had clinically significant scores on this measure. There were instead significant differences with regard to the BDI-II ($\chi_5^2 = 69.74$, p < 0.001). A higher percentage (91.8%) of the

individuals included in the SIH group had scores above the cutoff level with respect to the other groups (percentages ranging from 8.3 to 53.8%).

Associations between Age, Duration of the Disorder, and Hoarding Symptoms

Correlational analyses did not uncover any associations between age or disease duration and the total SI-R score in any of the groups (ED: r = 0.08/12; MD: r = 0.20/-0.16; AD: r = -0.13/0.34; PD: r = 0.09/.19; SIH: r = 0.04).

DISCUSSION

None of the MD, AD, PD, or ED patients had sought assistance for problems linked to hoarding. Contrary to our hypothesis, 22.5% of the patients diagnosed with Bulimia and Binge eating exceeded the clinical cut-off levels for hoarding symptomatology; 7.7% of the MD, 7.4% of the AD, and 5.9% of the PD also did so. The fact that the study only considered patients with Bulimia and Binge eating and that a specific assessment measure was used to evaluate hoarding may explain the high percentage of hoarding symptoms found with respect to other studies whose data (Halmi et al., 2003) were based on a single item on the Y-BOCS (Goodman et al., 1989) specifically concerned with hoarding. Our ED group was moreover composed entirely of hospitalized patients and this could further explain the high percentage found with respect to the other groups. In light of these results, the higher prevalence reported for HD symptoms in ED might seems not to depend on a higher prevalence of females with a generally severe clinical condition requiring inpatient treatment.

As far as the patients with MD (7.7%) and PD (5.9%) were concerned, no comparison can be made with data in the literature as no studies have been carried out on these populations, and assessment of hoarding, in any case and as has already been mentioned, has always been evaluated using a non-specific instrument (Tracy et al., 1996). The total percent of hoarders in our AD sample was inferior to that reported in the literature (Tolin et al., 2011), and this might be explained by differences in disease severity at the time of the initial diagnosis. Our sample was, for example, entirely made up of non-hospitalized patients while Tolin et al. (2011) study included only hospitalized ones.

TABLE 3 | Number and (percentages) of individuals in the six groups assessed scoring above the cut-off levels.

	ED group	MD group	AD group	PD group	SIH group	HC group
	(N = 41)	(N = 39)	(N = 27)	(N = 17)	(N = 49)	(N = 48)
Total SI-R	9 (22.5)	3 (7.7)	2 (7.4)	1 (5.9)	39(79.6)	2 (4.2)
Clutter	5 (12.2)	5 (12.8)	2 (7.4)	2 (11.8)	24 (49)	2 (4.2)
Difficulty discarding	12 (30)	7 (17.9)	7 (25.9)	6 (35.3)	45 (91.8)	9 (18.8)
Acquisition	13 (31.7)	5 (12.8)	2 (7.4)	3 (17.6)	36 (73.5)	5 (10.4)
BAI	4 (9.8)	4 (10.8)	5 (18.5)	1 (6.3)	11 (23.4)	8 (17)
BDI II	20 (51.3)	21 (53.8)	10 (37)	8 (47.1)	45 (91.8)	4 (8.3)

ED, eating disorders; MD, major depression; AD, anxiety disorders; PD, psychotic disorders; HD, hoarding disorder; HC, healthy controls.

When single subscales were considered, approximately 30% of the ED patients exceeded the clinical cut-off level with regard to both the Difficulty Discarding and Acquisition scales while Difficulty Discarding was the most representative symptomatology in the other groups of patients (35.3% for PD; 25.9% for AD; 17.9% for MD). The different clinical diagnosis considered (ED, PD, AD, MD) were thus characterized by single elements of the HD symptomatology: patients with Bulimia and Binge Eating had more Acquisition and Difficulty Discarding problems, while the PD, AD, and MD had only more Difficulty Discarding problems.

When the groups were compared utilizing the SI-R as a continuous variable, only the ED patients had significantly higher scores on the Acquisition scale with respect to the depression group; the findings for the rest of the clinical groups and the control patients, with the exception of the SIH, were comparable. These data confirm precedent studies with regard to construct independence and the diagnosis of HD defined by its characteristics of Clutter, Acquisition and Difficulty Discarding, (Frost and Hartl, 1996) but they also underline the importance of investigating specific features of hoarding in specific groups: Acquisition and Difficulty Discarding should be assessed, in particular, patients with Bulimia and Binge Eating, while Difficulty Discarding should be evaluated in patients with AD, MD, and PD.

As expected, depression was the most common comorbid condition in the SIH group; 91.8% of our sample exceeded the clinical cut-off level for depression and the BDI score registered by that group was similar to that in the depressed group. That percentage was found to be higher than ones registered by precedent studies examining individuals with HD selected from the general population (Frost et al., 2011) even if the individuals with SIH evaluated by our study had in fact SI-R scores that were overlapping with those of other HD (Frost et al., 2004) subjects. This may have been due to a characteristic of the Italian population that has not yet been extensively studied or to a self-selection bias on the part of the SIH who were enrolled in the study; we cannot, in fact, exclude the presence of other clinical symptoms in that group of participants.

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No association was found between hoarding severity, disease duration and age in the clinical groups. According to our findings, when hoarding is a comorbid condition with other pathologies, it does not seem to worsen when age increases. It is possible that the symptoms are stable and ego-syntonic and need to be investigated more extensively during the initial assessment phase.

One of the study's principal limitations concerns the persons in the SIH group. As they did not complete other questionnaires investigating general or specific psychopathologies such as OCD, it is impossible to exclude other concomitant pathologies. The prevalence of hoarding found in our group, which was equal to 7.57% (39/515), was nevertheless consistent with percentages in the general population registered by other studies (2-6 %; Samuels et al., 2008; Bulli et al., 2014). Given the limitations of self-report inventories, we are convinced that only an appraisal of a patient's habitation or a personal interview with the patient him/herself or a relative can confirm a diagnosis of hoarding, a disorder which is frequently underestimated by clinicians. Furthermore, the higher prevalence of females than males in all the groups, despite apparently not affecting our results, might limit the generalizability of present findings. Another obstacle to generalizability might regard the medication regimen of participants; for example, some evidence suggests that hoarding behavior in Schizophrenia might depend on antipsychotic treatment (Pertusa and Fonseca, 2014).

These data suggest that hoarding symptoms should also be investigated in other types of patients and especially in those affected with Bulimia, Binge eating, AD, MD as well as in subjects with psychosis in remission. Future studies should consider also the role of emotional regulation in the development and maintenance of hoarding symptoms in clinical populations, since it has resulted as a mediating variable in ED (Raines et al., 2015) as well as in HD (Shaw et al., 2015).

AUTHOR CONTRIBUTIONS

CN: Conducted experiments and wrote the manuscript. GB: Contributed to the statistical analysis. SD: Contributed to the recruitment of patients. ES had an organizational role.

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The Effect of Abuse History on Adolescent Patients with Feeding and Eating Disorders Treated through Psychodynamic Therapy: Comorbidities and Outcome

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Objectives: The first aim of our study was to compare the characteristics and comorbidities of patients with eating disorders between those who suffered from a childhood abuse and those who did not. Our second aim was to analyze the differences in the outcome of the psychodynamic therapy between abused and not abused patients.

Methods: Twenty-six adolescent patients with eating disorders were assessed. Adolescent were evaluated by a single expert psychiatrist by checklists and questionnaires: EDI 3, SCL 90, BIS11, Dissociative Experiences Scale, Global Assessment of Functioning, SCID II, and CTQ-Self control (SF). According to the results of CTQ-SF (cut-off \geq 8), patients were divided into two groups: those who had experienced a history of abuse and those who had not. They underwent a psychodynamic psychotherapy and were assessed again after 12 months.

Results: Eleven patients (42.3%) had a history of abuse according to CTQ score. No significant differences were found in abused and not abused patients in their demographic, clinical, and comorbid characteristics (sex, age, type of eating disorder, comorbid impulse control, personality, and addictive disorders). Abused patients showed a significantly higher score in many scale. The psychotherapeutic intervention in patients with a history of abuse resulted only in a significant decrease in symptom checklist-90 (SCL-90) psychoticism dimension (p < 0.05), whereas in patients with no history of abuse a significant decrease was found for SCL-90 somatization, obsessive—compulsive and phobic anxiety dimensions, the SCL-90 Global Severity Index, the Eating Disorder Inventory-3 interceptive deficits, and the dissociative experience scale.

Conclusion: Regarding the first aim of our study, we proved that history of abuse is not significantly related to patient comorbidities. Regarding our second aim, history of abuse was related to patient improvement only for psychotic symptoms; whereas patients who had not experienced an abuse improved in a variety of symptoms. Thus, abuse history can be considered as a negative prognostic factor for patients with eating disorders

undergoing dynamic psychotherapy. However, this psychotherapy may have a role in preventing early psychotic disorders in patients with and without an history of abuse.

Keywords: psychodynamic therapy, adolescents, abuse, addiction disorder, impulse control disorder, feeding and eating disorders

INTRODUCTION

Eating disorders consist of impairment in body image perception and extreme behaviors, such as rejection or desire for food, which debilitate patients in terms of both physical and psychological health.

According to the DSM-5, the complete diagnostic class of eating disorders is named "Feeding and Eating Disorders" and lists: anorexia and bulimia, pica (eating inedible substances), rumination disorder (regurgitation of ingested substances), avoidant/restrictive food intake disorder (lack of interest in the sufficient food intake), and binge eating disorder (1).

In DSM-5, the age of eating disorder onset has been lowered, with a more severe prognosis and the need for a differentiated and complex treatment, which should be specific to developmental disorders of children and adolescents (2). Previous studies have showed a number of similarities between food addiction and other addictive behaviors including activation of specific brain regions and neurotransmitter systems, disrupted neuronal circuitry, and behavioral indicators of addiction, such as continued use despite negative consequences (3). Impulsivity and emotional dysregulation (ED) have a fundamental role in food addiction, as well as both of them play salient roles in drug use disorders (4).

Moreover adolescence is the period of onset of personality disorders (5). According to the literature, obsessive–compulsive and avoidant personality disorders are frequently associated to eating disorder (6).

In adolescence, eating disorders often occurs in comorbidity with other disorders: particularly addictive and impulse control disorders. Recent studies have showed that lots of problems regarding food behaviors, impulse control, and addictive disorders share some common features in adolescent and young people (7).

Other studies have pointed out that sexual and/or physical abuse in childhood exposes the subject to the risk of developing eating disorder (8). According to them, a history of childhood abuse can be associated to eating disorder in 30% of cases (9).

Psychodynamic therapy is frequently used in clinical practice (10). The term refers to an "umbrella" concept for treatments that operate in an interpretive-supportive continuum (11). By interpretive intervention, insight into instincts, affects, object relations, or defense mechanisms may be enhanced. Supportive interventions include fostering a therapeutic alliance, setting goals, or strengthening psychosocial abilities by increasing reality testing or impulse control. The use of more supportive or more interpretive (insight-enhancing) interventions is tailored to the patient's needs. There is a range of manualized psychodynamic therapies varying in the extent to which they focus on supportive or expressive elements (12). "Psychodynamic psychotherapy has common factors, outlined by Blagys and Hilsenroth, including: focus on affect and expression of emotion, exploration of attempts

to avoid distressing thoughts and feelings, identification of recurring themes and patterns, discussion of past experience, focus on interpersonal relations, focus on the therapy relationship, and exploration of wishes and fantasies." (13).

The efficacy of the psychodynamic psychotherapy in patients with eating disorder has been established especially for anorexia, but promising results have been showed also for all feeding and eating disturbances (14).

Studies on adolescent patients affected by eating disorder have confirmed the efficacy of the psychodynamic therapy; particularly as to improving alimentary symptoms, complying with pharmacological treatments, and implementing the process of adolescent subjectivization (15).

Given the role of childhood abuse in the development of eating disorder and the efficacy of psychodynamic psychotherapy on these disorders even in adolescence, we wanted to investigate how the abuse can influence the psychotherapeutic outcome.

This is relevant also for providing a suitable treatment for abused patients with eating disorder in terms of frequency of sessions, duration and possible integrative approaches.

The first aim of our study was to compare characteristics and comorbidities of two types of patients affected by eating disorder: those who have suffered from a childhood abuse and those who had not. Our second aim was to analyze the psychodynamic therapy outcome in abused and not abused patients after 12 months of treatment. Patients were admitted to the Day Hospital of Psychiatry of the Catholic University and to the Day Hospital for Adolescents of "Sapienza University of Rome."

We used Eating Disorder Inventory-3 (EDI-3) to investigate the symptoms of eating disorder; Symptom checklist-90 (SCL-90), global assessment of functioning (GAF), and Structured Interview for DSM-IV Axis II (SCID-II) to evaluate psychopathology and comorbid personality disorders; Childhood Trauma Questionnaire-short form (CTQ-sf) to identify possible traumatic events or situations in the history; Barratt Impulsiveness Scale -11 (BIS-11) and Dissociative Experiences Scale (DES) to evaluate the characteristics of complex trauma (16). In fact, many patients with a history of traumatic abuse or neglect suffer from dissociative experiences and impulse dyscontrol which are the most frequent consequences of complex trauma.

PARTICIPANTS AND METHODS

Participants

During a period of 20 months (September 2014–May 2016), patients with eating disorders were observed in both Day Hospitals. The protocol was approved by local IRB and subjects took part in the project after signing an informed consent.

We enrolled 26 adolescents (13–18 years), who received a clinical diagnosis of Feeding and Eating disorders and comorbid

Addictive and/or Impulse Control Disorders. They underwent a psychodynamic psychotherapy for 12 months in the Day Hospital setting. Patients with other comorbid psychiatric disorders were excluded from the study. Each patient was scheduled for psychiatric and clinical evaluation at the beginning and at the end of the study.

The diagnosis of feeding and Eating Disorders was formulated at the first interview on the basis of medical history and according to the criteria established by the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). Likewise, patients were diagnosed as suffering from comorbid Addictive and/or Impulse Control Disorders according to the criteria of DSM-5.

Study Design and Clinical Sample

We enrolled adolescents who had not yet undergone any psychotherapeutic or pharmacological treatment until the study entry.

After the inclusion and before starting psychotherapy, a single experienced psychiatrist evaluated the patients by the following questionnaires and checklists: eating Disorder Inventory-3, SCL-90, Barratt Impulsiveness Scale -11, DES, GAF, Structured Clinical Interview for DSM-IV Axis II, CTO-sf.

Patients who reported in one or more of the Childhood Trauma Questionnaire dimensions scores equal to or above the clinical threshold in one or more of the Childhood Trauma Questionnaire dimensions were included in the second one (no childhood abuse).

After the first interview and assessment, patients of both clinical subsamples started a structured psychodynamic psychotherapy, in the hospital environment, for a period of at least 12 months. After 12 months, the same experienced psychiatrist evaluated the patients by the same tests, Childhood Trauma Questionnaire excluded.

Therapist Selection

Therapists were recruited in both hospital services where the sample was enrolled. Therapists from both services worked according to a common psychodynamic therapy pattern (17) and had been trained in psychotherapy by similar educational programs.

Therapists were in all 10, 7 females and 3 males, with at the least 10 years of clinical activity.

Sessions were once a week, lasting 45 min each, for a total of about 44–48 sessions in 1 year. All therapists supported and followed the work with patients through periodical individual and weekly group supervisions.

Psychodynamic therapy with the adolescents implies the elaboration of original experiences from infancy. According to the Monniello's model, psychotherapy aims at differentiating the onset of subjectivation from its actual completion. Just as in the neonatal period, intersubjectivity plays a crucial role in adolescence. The therapist function consists in elaborating unconscious and infant contents, and mentally integrating physical sensations of the adolescent newly sexualized body. These objectives are met through dream analysis, free associations, and by encouraging the narrative of the adolescent psychological life.

Questionnaire and Checklist

Eating Disorder Inventory-3 was released in 2004 and successively implemented to reflect more modern theories related to eating disorders (18). The questionnaire has 91 items divided into 12 subscales based on a 0- to 4-point scoring system. Three scales are specific to eating disorder: drive for thinness (DT), bulimia (B), body dissatisfaction; 9 are general psychological scales not directly relevant to eating disorders: low self-esteem (LSE), personal alienation, interpersonal insecurity (II), interpersonal alienation (IA), interoceptive deficits (ID), emotional dysregulation (ED), perfectionism (P), asceticism (A), maturity fears. The inventory yields six composites: eating disorder risk, ineffectiveness, interpersonal problems, affective problems, overcontrol, general psychological maladjustment. It is also a self-report questionnaire administered in 20 min. We have used the Italian version of EDI-3 (19).

Symptom Checklist-90 is a 90-item self-report symptom inventory designed to measure psychological symptoms and distress during the previous week through 10 primary symptom dimensions and one summary score termed global severity index (GSI) (20). Subjects provide a score from 0 (not at all) to 4 (very much). It is appropriate for individuals from the community, as well as for patients with either medical or psychiatric conditions. The main symptom dimensions include somatization (SOM), obsessive—compulsive, interpersonal sensitivity, depression, anxiety (ANX), hostility, phobic anxiety (PHOB), paranoid ideation (PAR), and psychoticism (PSY), sleep disorders (SLEEP). For each of them the relative score is calculated as the average of questions answered. Scores \geq 1 are considered significant. We have used Italian version of SCL-90 (21).

Barratt Impulsiveness Scale-11 [BIS-11 by Barratt (22)] is the most widely used questionnaire designed to assess the personality or the behavioral impulsiveness (22). It is composed of 30 items describing common impulsive or non-impulsive (for reverse scored items) behaviors and preferences: attention (A), Cognitive Instability (IC), Motor (IM) (M), Perseverance (P), Self control (SF), Cognitive Complexity (CC), Attentional (A), Motor (IM), and Non-planning (InonPlan). Items are scored on a 4-point scale: rarely/never = 1, occasionally = 2, often = 3, almost always/ always = 4. We have used Italian version of Barratt Impulsiveness Scale-11 (BIS-11) (23).

Dissociative Experiences Scale is a psychological self-assessment questionnaire measuring dissociative symptoms and is a screening not diagnostic test for Dissociative Identity Disorder (24) It is made of 28 questions and provides an overall score (cutoff = 30 for Dissociative Identity Disorder) as well as 4 subscale scores. Patients with lower scores may have other post-traumatic conditions. We have used Italian version of DES (25).

Global Assessment of Functioning is used by mental health clinicians and physicians to subjectively rate the social, occupational, and psychological functioning of adults (26). We have used Italian version of GAF (27).

The Semi-structured Interview for DSM-IV Axis II (SCID-II) is designed to diagnose DSM-IV Personality Disorders (28). It consists of open-ended questions to investigate the presence of the 10 DSM-IV Personality Disorders and the two categories included in the Appendix (Passive–Aggressive and

TABLE 1 | Patients' demographic and clinical characteristics.

	Total sample (26)	Abused patients (11)	Not abused patients (15)	p-Value
Sex				
M F	10 (38.5%) 16 (61.5%)	4 (36.4%) 7 (63.6%)	6 (40%) 9 (60%)	1
Age				
median interquartile range (IQR)	16 3	16 3	16 4	0.458
Anorexia Binge eating disorder Bulimia Avoidant/restrictive food intake disorder	5 (19.2%) 10 (38.5%) 2 (7.7%) 9 (34.6%)	1 (9.1%) 4 (364%) 1 (9.1%) 5 (45.5%)	4 (26.7%) 6 (40%) 1 (6.6%) 4 (26.7%)	0.629
Kleptomania Conduct disorder Intermittent explosive disorder Oppositional defiant disorder	1 (3.8%) 13 (50%) 3 (11.5%) 2 (7.7%)	1 (9.1%) 6 (54.5%) 2 (18.2%) 1 (9.1%)	0 7 (46.6%) 1 (6.7%) 1 (6.7%)	0.346
None	7 (26.9%)	1 (9.1%)	6 (40%)	
Substance abuse/ dependence Gambling Internet gambling None	6 (23.1%) 1 (3.8%) 7 (26.9%) 12 (46.2%)	5 (45.4%) 1 (9.1%) 2 (18.2%) 3 (27.3%)	1 (6.7%) 0 5 (33.3%) 9 (60%)	0.057
Avoidant Dependent Obsessive—compulsive Passive—aggressive Depressive Paranoid Schizotypal Schizoid Histrionic Narcissistic Borderline Antisocial	5 (19.2%) 2 (7.7%) 4 (15.4%) 11 (42.3%) 6 (23.1%) 8 (30.8%) 3 (11.5%) 0 0 2 (7.7%) 5 (19.2%) 2 (7.7%)	2 (18.2%) 0 1 (9.1%) 7 (63.6%) 3 (27.3%) 5 (45.5%) 1 (9.1%) 0 2 (18.2%) 4 (36.4%) 2 (18.2%)	3 (20%) 2 (13.3%) 3 (20%) 4 (26.7%) 3 (20%) 3 (20%) 2 (13.3%) 0 0 1 (6.7%)	1 0.492 0.614 0.109 1 0.218 1 - - 0.169 0.128 0.169

Depressive Personality Disorders). We have used Italian version SCID-II (29).

Childhood Trauma Questionnaire-short form is a retrospective, self-reportedscreening measure for traumatic experiences in the infancy with 5 subscales, 3 assessing abuse (emotional, physical, and sexual) and 2 neglect (emotional and physical) (30). Each subscale includes 5 items with a 5-point frequency of occurrence: (1) never true, (2) rarely true, (3) sometimes true, (4) often true, and (5) very often true, scores ranging from 5 (no history of abuse or neglect) to 25 (very extreme history of abuse and neglect). A 3-item Minimization-Denial subscale is designed to identify extreme response bias, specifically respondents' attempts to minimize their experiences. Other traumatic events that may occur in childhood, such as bereavement or major illness, are not assessed. We have used Italian version of CTQ-sf (31).

Statistical Analysis

Median and interquartile range (IQR) were used to describe quantitative variables, absolute and relative frequencies of

TABLE 2 | Baseline test values.

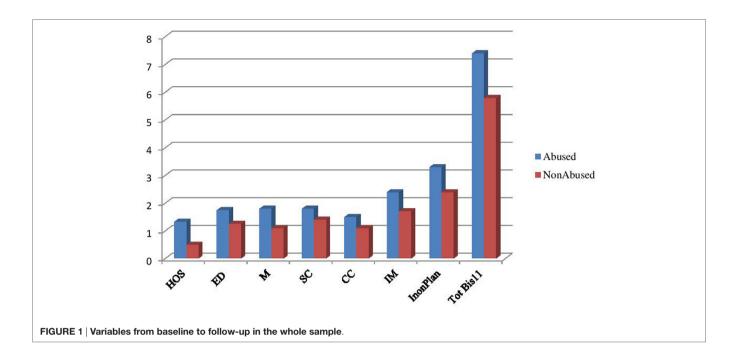
Symptom variables	Abused	patients	Not ab patie		р
	Median	IQR	Median	IQR	
SCL-90					
SOM	1.50	1.41	1	1.50	0.405
OC	2	1.7	1.3	2	0.550
IS	1.78	2.33	0.56	2	0.287
DEP	1.69	1.92	1.08	1.46	0.311
ANX	1.2	2	0.80	2.2	0.405
HOS	1.33	1	0.50	0.99	< 0.05
PHOB	0.57	0.85	0.57	1.14	0.465
PAR	1.68	2.66	0.83	1.17	0.349
PSY	0.80	1.8	0.40	1.2	0.076
GSI	1.41	1.75	0.84	1.41	0.233
SLEEP	1.57	1.43	0.71	2	0.132
EDI-3					
DT	1.29	2	1.71	3	0.897
В	0.63	2.62	0.87	1.38	0.917
BD	2.60	1.7	1.7	2.8	0.107
PA	2	1.14	1	2.01	0.177
LSE	2.16	2	1.66	2	0.274
II	2.14	1.57	1.71	1.86	0.499
IA	2.14	1.43	1.28	1.86	0.146
ID	1.63	2	1.63	2	0.979
ED	1.75	1	1.25	1	< 0.05
Р	1.33	2	1.16	1	0.639
A	0.86	1.29	1.42	1.57	0.585
MF	1.50	1.88	2	1.25	0.168
BIS-11					
A	12	4	11	4	0.228
IC	6	2	5	4	0.289
М	18	6	11	4	<0.01
Р	7	4	6	3	0.198
SC	18	4	14	5	<0.01
CC	15	3	11	4	<0.05
IA	19	4	17	7	0.201
IM	24	7	17	3	<0.001
Inon Plan	33	5	24	4	<0.001
Tot Bis11	74	12	58	10	<0.001
DES	12.5	33.58	10.71	17.93	0.392
GAF	50	10	51	11	0.087

SCL-90, symptom Checklist-90; SOM, somatization; Obs, obsessive-compulsive; IS, interpersonal sensitivity; DEP, depression; ANX, anxiety; HOS, hostility; PHOB, phobic anxiety; PAR, paranoid ideation; PSY, psychoticism; SLEEP, sleep disorders; GSI, Global Severity Index; EDI-3, Eating Disorders Inventory-3; DT, drive for thinness; B, bulimia; BD, body dissatisfaction; LSE, low self-esteem; PA, personal alienation; II, interpersonal insecurity; IA, interpersonal alienation; ID, interoceptive deficits; ED, emotional dysregulation; P, perfectionism; A, asceticism; MF, maturity fears; DES, Dissociative Experiences Scale; BIS-11, Barratt Impulsiveness Scale-11; A, attention; IC, cognitive instability; IM, Motor (M); P, perseverance; SF, self control; CC, cognitive complexity; A, attentional, IM, InonPlan, non-planning; GAF, global assessment of functioning.

Bold font indicates the test abbreviations and significant results.

categorical variables. The chi-square test was used to evaluate the association between CTQ (cut-off = 8) and sex, eating, impulse control and addiction disorders. Mann–Whitney test was used to test if age and baseline scores were different in abused and non-abused patients according to CTQ.

In order to test the change from the baseline to 12 months of follow-up, the Wilcoxon signed rank test and the McNemar test were used for quantitative and dichotomous variables, respectively. The effect size was investigated through the Wilcoxon Rank



test and phi(φ) for McNemar test (32). Effect sizes were evaluated using the following formulas: $r = Z/\sqrt{N}$ and $\varphi = \sqrt{(\chi^2/N)}$ and have been interpreted according to Cohen (32). An analysis of covariance (ANCOVA) was performed in order to investigate any significant differences in the effect of intervention between abused and not abused patients; the pre-test scores were used as covariate in order to adjust the analysis. Furthermore, a stratified analysis for patients with or without history of abuse was performed in order to assess the efficacy of the intervention in each group. A *p*-value <0.05 was considered significant, with no correction applied.

RESULTS

Subject's Characteristics at Baseline

Patients' characteristics are shown in **Table 1**. The median age was 16; 16 of 26 patients were female. Eleven patients (42.3%) had a history of abuse according to CTQ score, with respect to subscales high median values were found especially for emotional neglect: emotional abuse (median: 15, IQR:10), physical abuse (median: 11, IQR:18), sexual abuse (median: 6, IQR:7), emotional neglect (median: 36, IQR:13), and physical neglect (median:12, IQR:12); 10 out of 26 patients had a binge eating comorbidity.

Regarding comorbidities: impulse control and addiction disorders were found in 19 (73%) and 14 patients (53.8%), respectively. Thirteen patients presented conduct disorders, 1 (3.8%) had Kleptomania, 3 (11.5%) intermittent explosive disorder, 2 (7.7%) oppositional defiant disorder; 6 (23.1%) substance-related disorders, 1 (3.8%) gambling, 7 (26.9%) internet gambling. One or more personality disorders were found in 76% (20 patients) of our study sample, passive aggressive being the personality disorder most frequently observed (42.3% in the total sample and 63.6% in abused patients). No significant differences were found

between abused and non-abused patients with respect to patients' characteristics (sex, age, eating disorders, impulse control disorders, personality disorders, addictive disorders) even though, as far as addictive disorders are concerned, a trend was observed with abused patients showing more frequently substance abuse/ dependence and gambling (Table 1).

Baseline

At the baseline, abused patients showed significantly higher scores in hostility (SCL 90), emotional dysregulation (EDI 3), SF, CC, IM (M), and IM, non-planning, and TotBis11Motor (BIS-11) (**Table 2**; **Figure 1**).

Regarding the effects of the psychotherapeutic intervention, results from statistical tests and effect sizes are reported in **Table 3**. Variables showing a significant change from baseline to follow-up are highlighted in bold. At 12 months, intervention resulted in a significant decrease of score in the variables SOM, OC, ANX, PHOB, PSY, GSI, SLEEP as for SCL-90 scale, in ID, ED, and A as for EDI-3 test, in IC as for BIS-11, and in DES; in almost all these items intervention showed a medium effect size. On the contrary, a statistically significant increase, showing a large effect size, r = -0.55, was observed in GAF.

With respect to ANCOVA, after adjustment for pre-test values, statistically significant differences in response to treatment between abused and not abused patients were found for the following items of the BIS-11 scale: InonPlan $[F(1;23)=7.46\ p=0.01]$, A $[F(1;23)=12.08,\ p=0.002]$, P $[F(1;23)=6.60,\ p=0.017]$ with abused patients reporting higher values at followup. No further statistically significant differences between the two groups were found.

The stratified analysis showed that in patients with history of abuse, intervention resulted only in a significant decrease in PSY, whereas in patients with no history of abuse, a significant

TABLE 3 | Results from statistical tests.

Test	Basel	ine	12 moi	nths	Tes	t statistic	S
	Median	IQR	Median	IQR	Z	р	r
SCL-90							
SOM	1	1.31	0.63	0.9	-2.78	< 0.01	-0.39
OC	1.55	1.80	0.95	1.6	-2.09	< 0.05	-0.29
IS	1.06	2.06	0.73	1.69	-1.62	0.106	-0.23
DEP	1.16	1.77	0.89	1.83	-1.20	0.230	-0.17
ANX	1.15	2.20	0.55	1.4	-2.35	< 0.05	-0.33
HOS	1	1.71	0.33	2	-1.46	0.144	-0.20
PHOB	0.57	1	0.14	0.78	-2.81	<0.01	-0.39
PAR	1	2.04	0.60	1.99	-2.72	0.204	-0.38
PSY	0.50	1.30	0.25	1.1	-2.76	< 0.01	-0.38
GSI	0.98	1.46	0.48	1.34	-2.35	< 0.05	-0.33
SLEEP	1.07	1.75	0.86	1.43	-2.09	< 0.05	-0.29
EDI-3							
DT	1.57	2	1.14	1.74	-1.83	0.067	-0.25
В	0.75	1.41	0.50	1.13	-0.72	0.475	-0.10
BD	2	2.1	1.57	2.2	-1.72	0.085	-0.24
PA	1.28	1.75	1.35	1.31	-0.17	0.869	-0.02
LSE	1.83	2	1.42	1	-1.67	0.094	-0.23
II	1.78	1.64	1.64	1.18	-1.24	0.216	-0.17
IA	1.57	1.61	1.38	0.71	-0.30	0.764	-0.04
ID	1.63	2	1.06	1.45	-1.98	< 0.05	-0.28
ED	1.44	1	0.99	1.16	-2.13	< 0.05	-0.30
Р	1.25	1	1.33	1	-0.03	0.976	-0.0
Α	1.28	1.32	0.98	1.10	-2.04	< 0.05	-0.28
MF	1.75	1.50	1.37	0.65	-1.34	0.181	-0.19
BIS-11							
Α	11.50	4	11.50	4	-0.21	0.834	-0.03
IC	6	3	5	2	-2.40	< 0.05	-0.33
M	12.50	8	13.50	13	-0.32	0.746	-0.04
P	7	3	7	2	-0.16	0.870	-0.02
SC	15	8	13.50	14	-0.38	0.704	-0.05
CC	12	4	13	11	-0.29	0.771	-0.04
IA	18	5	15.50	6	-1.78	0.075	-0.25
IM	18.50	7	20	6	-0.87	0.385	-0.12
Inon Plan	26.50	9	27	10	-0.34	0.731	-0.05
Tot Bis11	65.50	15	63.50	13	-0.73	0.465	-0.10
DES	11.61	23.66	7.22	15.2	-2.57	0.010	-0.36
GAF	51	19	61	10	-3.95	<0.001	-0.55

No significant changes were found ion SCID II items.

decrease was found for SOM, OC, PHOB, GSI, ID, and DES. GAF significantly increased in both abused and not abused patients (**Table 4**). No significant changes were found in SCID II items in both abused and not abused patients (**Figure 2**).

DISCUSSION

Our research confirms the correlation between eating disorders and childhood abuse found in the literature (33): 42.3% of our sample reported an abuse history according to CTQ-sf. The most represented eating disorder was the binge eating disorder.

In adolescence, eating disorders are often observed in comorbidity especially with addictive and conduct disorders (34).

Passive–aggressive was the most frequently observed personality disorder. Grover et al. (35), analyzing a group of patients who suffered from a child maltreatment according to CTQ-sf and comparing them with another group without such a history,

outlined that many personality disorders, among which the passive-aggressive one, are associated with a child abuse (35).

It is worth pointing out that patients with a history of abuse tend to show more frequent addictive behaviors. Woerner et al. (36) underlined that these patients may have a major tendency to self-punishment, such as using drugs and showing dependent behaviors in general (36).

The history of abuse and/or neglect represents a negative prognostic factor for patients with eating disorder. Harper et al. (37) demonstrated that patients with eating disorder and history of abuse had higher levels of depression, LSE, and worse prognosis (37).

In our sample, at baseline, patients with history of abuse and/or neglect showed more impulsiveness, tendency to acting out, poor mentalization, hostility, and ED; feelings and behaviors related to a state of anger and impulsiveness were observed. This emotional state is likely to derive from early traumatic relationships, either overloaded with emotions or characterized by lack or discontinuous presence of the caregiver. Anger and impulsiveness may lead the patient to actively research sensations.

Jeffrey and Jeffrey (38) assessed the psychological aspects of sexual abuse in female adolescents and evidenced that these patients are at high risk for subsequent acting out behaviors, anxiety, depression, LSE, alcohol and drug abuse or dependence, and sleep and dissociative disorders, eating disorder, emotional numbing, guilt, shame, hyperarousal, and multiple psychiatric disorders (38).

Child sexual abuse is associated with emotion regulation deficits in childhood (39). A not sufficiently protective environment may induce feelings of hostility in the abused child and prevent him to establish positive relationships. The high stress levels suffered by the abused child also hinder his ability to understand and determine cognitive unsteadiness and ED, which are risk factors for eating disorder development (33).

Abused and not abused patients differed as to levels of hostility, ED, and above all, impulsivity, which were higher in the former ones.

Following the treatment, the SCL-90 somatization index and the EDI-3 psychological scale, interoceptive deficit, decreased in the adolescents. One of the main goals of the psychodynamic psychotherapy in individuals expressing a variable level of mental pain through physical symptoms is to attain a condition of subjective appropriation of his own perceptive experiences. In fact, the therapy should provide the adolescent with the ability of mentally representing what he acts and expresses with his body. Through this new awareness the subject can elaborate childhood problems and integrate dissociated parts of himself.

Therapy induced also an improvement of the SCL-90 obsessiveness—compulsiveness index which signals the presence of persistent, irresistible, egodystonic or unwanted thoughts, impulses, and behaviors. Particularly, during the process of subjectivization fantasies, images and anguishes occur together with repetitive and intrusive thoughts. In the therapeutic relationship, the curiosity and the availability of the therapist toward the adolescent vitality are necessary so that patient can afford anguishes and resolve conflicts of childhood. Psychodynamic psychotherapy acts especially by allowing the elaboration of anxious-phobic emotions of

TABLE 4 | Stratified analysis.

Test	Base	line	12 mor	nths	Test	Test statistics		
	Median	IQR	Median	IQR	Z	р	r	
(A) Not abu	used patien	ts						
	Checklist-9	•						
SOM	1	1.50	0.53	1	-2.90	<0.01	-0.53	
OC	1.3	2	0.80	1.1	-2.05	< 0.05	-0.37	
IS	0.56	2	0.50	1	-1.36	0.173	-0.25	
DEP	1.08	1.46	0.46	1.34	-1.50	0.133	-0.27	
ANX	0.80	2.2	0.40	0.9	-1.61	0.107	-0.29	
HOS	0.50	0.99	0.20	1	-1.57	0.117	-0.29	
PHOB	0.57	1.14	0	0.32	-2.20	< 0.05	-0.40	
PAR	0.83	1.17	0.44	1.40	-1.34	0.182	-0.24	
PSY	0.40	1.2	0.20	0.4	-1.45	0.142	-0.26	
GSI	0.84	1.41	0.40	0.72	-2.10	<0.05	-0.38	
SLEEP	0.71	2	0.76	0.81	-1.39	0.164	-0.25	
_	order Inven							
DT	1.71	3	0.86	1.67	-1.48	0.140	-0.27	
В	0.87	1.38	0.34	1.11	-0.98	0.328	-0.18	
BD	1.7	2.8	0.87	2.1	-1.37	0.172	-0.25	
PA	1	2.01	1.54	1.10	-0.51	0.609	-0.09	
LSE	1.66	2	1.30	1	-0.51	0.615	-0.09	
II	1.71	1.86	1.71	0.90	-0.82	0.410	-0.15	
IA	1.71	1.86	1.71	0.90	-0.62 -1.04	0.300	-0.19	
ID	1.63	2	0.88	1.42	-1.99	<0.05	-0.36	
ED	1.25	1	0.70	0.75	-1.50	0.132	-0.27	
Р	1.16	1	1.33	1	-0.04	0.972	-0.01	
A	1.42	1.57	1	1.09	-1.76	0.078	-0.32	
MF	2	1.25	1.4	1.70	-1.33	0.184	-0.24	
Barratt Im	pulsiveness	Scale-1	1 (BIS-11)					
Α	11	4	11	4	-0.07	0.944	-0.01	
IC	5	4	5	2	-1.21	0.227	-0.22	
	11	4						
M			13	5	-1.48	0.138	-0.27	
P	6	3	6	1	-0.04	0.972	-0.01	
SF	14	5	12	2	-0.28	0.776	-0.05	
CC	11	4	12	6	-1.03	0.304	-0.19	
IA	17	7	15	7	-0.60	0.550	-0.11	
IM	17	3	18	4	-1.80	0.072	-0.33	
Inon Plan	24	4	24	6	-0.50	0.614	-0.09	
Tot Bis11	58	10	58	8	-0.19	0.850	-0.03	
DES	10.71	17.93	5.71	6.4	-2.50	<0.05	-0.46	
GAF								
GAF	51	11	61	9	-3.09	<0.01	-0.56	
(B) Abused	d patients							
SCL-90								
SOM	1.50	1.41	1.02	1.1	-0.71	0.48	-0.15	
OC	2	1.7	1.90	1.7	-0.58	0.56	-0.12	
IS	1.78	2.33	1	2.45	-0.85	0.40	-0.18	
DEP								
	1.69	1.92	1.2	1.92	-0.27	0.79	-0.06	
ANX	1.2	2	0.90	1.4	-1.75	0.08	-0.37	
HOS	1.33	1	1.67	2	-0.47	0.64	-0.10	
PHOB	0.57	2.42	0.42	0.71	-1.87	0.06	-0.40	
PAR	1.68	2.66	1.54	2.50	-0.42	0.68	-0.09	
PSY	0.80	1.8	0.70	1.6	-2.25	0.02	-0.48	
GSI	1.41	1.75	1.19	1.63	-1.16	0.25	-0.25	
SLEEP	1.57	1.43	171	1.29	-1.72	0.09	-0.37	
				0		0.00	5.01	
EDI-3								
DT	1.29	2	1.14	2.43	-0.97	0.33	-0.21	
В	0.63	2.62	1	1	-0.9	0.93	-0.19	
BD	2.60	1.7	1.7	2.9	-1.28	0.20	-0.27	
PA	2	1.14	1.28	1.66	-1.02	0.31	-0.22	
LSE	2.16	2	2	1.00		0.07		
					-1.82		-0.39	
II	2.14 2.14	1.57 1.43	1.14 1.28	1.42 0.71	-0.66 -1.48	0.51	-0.14	
IA						0.14	-0.31	

(Continued)

TABLE 4 | Continued

Test	Base	line	12 mo	nths	Test	statistic	s
	Median	IQR	Median	IQR	Z	р	r
ID	1.51	2	1.12	1.63	-0.61	0.54	-0.13
ED	1.75	1	1.35	1.88	-1.60	0.11	-0.34
Р	1.33	2	1	1	-0.15	0.88	-0.03
Α	0.86	1.29	0.96	1.72	-1.36	0.17	-0.29
MF	1.50	1.88	1.25	0.32	-0.46	0.65	-0.10
BIS-11							
Α	12	4	13	3	-0.14	0.88	-0.03
IC	6	2	4	2	-1.90	0.06	-0.40
M	18	6	15	6	-1.21	0.23	-0.26
Р	7	4	8	3	-0.43	0.67	-0.09
SF	18	4	19	5	-0.27	0.79	-0.06
CC	15	3	14	8	-0.51	0.61	-0.11
IA	19	4	17	4	-1.89	0.06	-0.40
IM	24	7	23	5	-0.81	0.42	-0.17
Inon Plan	33	5	33	3	-0.05	0.96	-0.01
Tot Bis11	74	12	70	10	-1.36	0.17	-0.29
DES	12.5	33.58	13.57	21.8	-1.29	0.20	-0.27
GAF	50	10	61	29	-2.53	0.011	-0.54

Bold font indicates the test abbreviations and significant results.

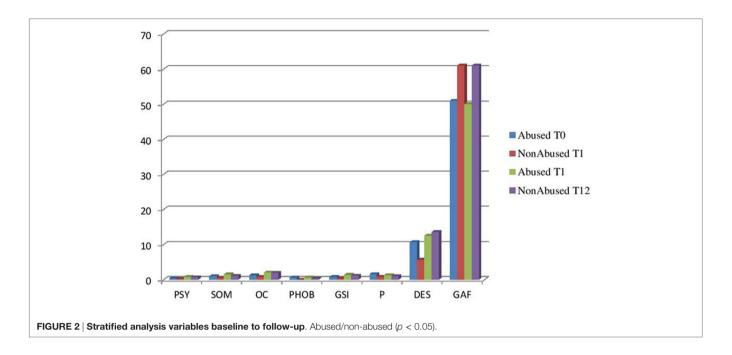
patient, improving his introspective abilities, and making him aware of the new somatosensory attitude.

After treatment, all patients improved in other psychopathological domains, including ED, asceticism, IC, dissociative traits, and global functioning.

The two main adaptive tasks of adolescence can be recognized in the psychic integration of pubertal bodily transformations and in the redefinition of identity. These two processes are characterized by strong ambivalence and both generalized and phobic anxiety. Addressing the conflict underlying anxiety is one of the main objectives of the psychodynamic therapy. Other authors, such Cropp et al. (40) examined the results of psychodynamic therapy in adolescents and found an improvement in symptoms and in the psychological general structure (40). Therefore, the improvement in the entire sample of the index of global severity, which reflects the intensity of the subjective discomfort, and the increase of global functioning, which reflects social, working, and psychological functioning, were significant results. The improvement in anxiety indices, ED, asceticism, and IC confirms the efficacy of dynamic therapy in remodeling the adolescent's mind and allowing him to represent his own emotional states, to take contact with his body and to gain a mentalization attitude, by preventing impulsive manifestations.

However, in the group of patients with a history of abuse and/or neglect, the improvement was much less evident: abused patients remained with higher levels of impulsivity and other psychopathological traits with respect to not abused patients. The improvement of symptoms after psychotherapy was evident in not abused patients in various psychological domains, including impulsivity, dissociation, and global functioning, whereas in abused patients only for psychoticism.

Nevertheless, the index of Psychoticism, including items of seclusion and retirement in addition to relevant symptoms of the schizophrenic dimension, significantly decreased in these



patients, which, because of trauma, may be more exposed to deficits in the ego structure and major difficulties in subjectivization. As Rössler et al. (41) underline, child sexual abuse can stand among the risk factors for psychotic disorder. Through dynamic psychotherapy a decrease of possible prodromal schizophrenic symptoms was observed, what is relevant to the prevention of psychotic breakdowns in the presence of a traumatic history. In fact, trauma exerts a very disruptive action on the adolescent's mental organization (41). In a rater-blinded randomized controlled trial conducted by Weijers et al. (42), patients with a not affective psychotic disorder after 18 months of psychodynamic psychotherapy showed an improvement in positive, negative, anxious, and depressive symptoms (42). The role of psychodynamic psychotherapy could be important in preventing psychotic disorders in adolescents with and without a history of abuse, even though a statistically significant improvement may be clear cut only in the presence of the most severe symptoms.

In conclusion, the limits of our study were the small sample size and the variability determined by a treatment applied by different therapists. However, this latter limit was minimized by the strict adoption of well-established therapeutic rules and by the case supervision by a single supervisor.

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Although it is difficult to find patients meeting all the criteria required by the protocol, our target is to enlarge the sample size in further studies.

ETHICS STATEMENT

This study was approved by the Institutional Review Board of Catholic University of the Sacred Heart, Rome, Italy. Subjects over the age of 18 took part in the project after signing an informed consent. For all the participants under the age of 18 who took part in the project, parental consent was also obtained.

AUTHOR CONTRIBUTIONS

Full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis: LJ. Study concept and design: AS, LR, GM, and LJ. Acquisition of data: AS. Analysis and interpretation of data: AS, LS, and CW. Drafting of the manuscript: AS. Critical revision of the manuscript for important intellectual content: LR, GM, and LJ. Statistical analysis: CW and LS. Obtaining funding: none. Supervision: LJ.

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Behavioral and Neural Manifestations of Reward Memory in Carriers of Low-Expressing versus High-Expressing Genetic Variants of the Dopamine D2 Receptor

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Dopamine is critically important in the neural manifestation of motivated behavior, and alterations in the human dopaminergic system have been implicated in the etiology of motivation-related psychiatric disorders, most prominently addiction. Patients with chronic addiction exhibit reduced dopamine D2 receptor (DRD2) availability in the striatum, and the DRD2 TagIA (rs1800497) and C957T (rs6277) genetic polymorphisms have previously been linked to individual differences in striatal dopamine metabolism and clinical risk for alcohol and nicotine dependence. Here, we investigated the hypothesis that the variants of these polymorphisms would show increased rewardrelated memory formation, which has previously been shown to jointly engage the mesolimbic dopaminergic system and the hippocampus, as a potential intermediate phenotype for addiction memory. To this end, we performed functional magnetic resonance imaging (fMRI) in 62 young, healthy individuals genotyped for DRD2 TagIA and C957T variants. Participants performed an incentive delay task, followed by a recognition memory task 24 h later. We observed effects of both genotypes on the overall recognition performance with carriers of low-expressing variants, namely TaqlA A1 carriers and C957T C homozygotes, showing better performance than the other genotype groups. In addition to the better memory performance, C957T C homozygotes also exhibited a response bias for cues predicting monetary reward. At the neural level, the C957T polymorphism was associated with a genotype-related modulation of right hippocampal and striatal fMRI responses predictive of subsequent recognition confidence for reward-predicting items. Our results indicate that genetic variations associated with DRD2 expression affect explicit memory, specifically for rewarded stimuli. We suggest that the relatively better memory for rewarded stimuli in carriers of low-expressing DRD2 variants may reflect an intermediate phenotype of addiction memory.

Keywords: dopamine D2 receptor, TaqIA, C957T, episodic memory, reward, fMRI, intermediate phenotype

INTRODUCTION

Dopamine (DA) is crucially involved in motivated behavior, and dysfunctional dopaminergic neurotransmission has been implicated in the pathophysiology of neuropsychiatric disorders like schizophrenia and substance dependence (Heinz and Schlagenhauf, 2010). Therefore, numerous genetic association studies of these disorders have focused on the dopaminergic system. In humans, the DRD2 gene on Chr 11q23.2, which encodes the dopamine D2 receptor, harbors several genetic variants previously linked to variability of D2 receptor expression as well as individual differences in motivated behavior and risk for psychiatric disorders. A common single nucleotide polymorphism (SNP, rs1800497; minor allele frequency 0.33 in dbSNP) located in the neighboring ANKK1 gene, also known as TaqIA polymorphism, has repeatedly been linked to reduced striatal D2 receptor expression in A1 allele carriers in both post mortem expression investigations and in vivo radioligand binding studies using Positron emission tomography (PET; Noble et al., 1991; Thompson et al., 1997; Pohjalainen et al., 1998; Jonsson et al., 1999; Ritchie and Noble, 2003; Hirvonen et al., 2009a). One study employing single photon emission tomography (SPECT) did not find a difference in D2 receptor binding between A1 carriers and A2 homozygotes (Laruelle et al., 1998), but that study was later criticized for the combination of healthy participants and patients with schizophrenia in one sample and for the lower resolution of the SPECT compared to the PET method (Ritchie and Noble, 2003). The synonymous exonic DRD2 C957T polymorphism (rs6277) has also been linked to striatal D2 receptor expression (Hirvonen et al., 2009a) and is in linkage disequilibrium (LD) with TaqIA (Ritchie and Noble, 2003; Doehring et al., 2009). Given the strong, but incomplete, LD between the polymorphisms, it is plausible to employ the haplotype defined by the two variants as a genetic proxy for D2 receptor expression (Gelernter et al., 2006; Doehring et al., 2009; Hirvonen et al., 2009a; Voisey et al., 2012). In clinical association studies, haplotypes containing both polymorphisms have been associated with impulsivity-related psychiatric disorders, most prominently addiction (Morton et al., 2006; Doehring et al., 2009; Voisev et al., 2012).

While the results of genetic association studies are thus far inconclusive with respect to actual disease risk (Samochowiec et al., 2014), studies of intermediate phenotypes have successfully demonstrated effects of genetic variability in the dopamine system on human motivational and cognitive processing (Meyer-Lindenberg and Weinberger, 2006; Yacubian et al., 2007; Richter et al., 2013, 2014; Wittmann et al., 2013). Most neurobiological investigations of addiction in humans and animals have highlighted the role of dysfunctional dopaminergic transmission in the ventral striatum/nucleus accumbens (NAcc) and reduced striatal D2 receptor availability (Kienast and Heinz, 2006; Everitt, 2014), but some authors have also pointed out the role of the hippocampus, which is critically involved in the formation of long-term memories (Robbins and Everitt, 2002; Robbins et al., 2008). Dopamine has been suggested to promote neural mechanisms underlying long-term memory formation and persistence, and this notion is supported by the previously reported preferential hippocampus-dependent encoding of reward-associated stimuli (Lisman and Grace, 2005; Wittmann et al., 2005; Adcock et al., 2006; Krebs et al., 2009; Lisman et al., 2011). With respect to genetic influences on reward memory, an imaging genetics study by Wittmann et al. (2013) has revealed that a genetic variation associated with dopamine transporter expression modulates the co-activation of the hippocampus and NAcc during the encoding of reward-associated information. Regarding potential effects of DRD2 genetic variants on hippocampus-dependent memory, the C957T CC genotype has been associated with better episodic memory (Li et al., 2013; Papenberg et al., 2013), albeit studies on potential influences of the TaqIA polymorphism on explicit memory have yielded conflicting evidence. While Bartres-Faz et al. (2002) observed a protective effect of the A1 allele on long-term verbal memory performance among cognitively impaired elderly humans, Persson et al. (2015) found relatively lower memory performance in aged A1 carriers, particularly in tasks requiring verbal memory updating. Furthermore, McAllister et al. (2005, 2008) observed an adverse influence of the A1 allele on episodic memory for a word list in both healthy participants and patients with head injury. Importantly, none of those studies investigated a putative role of DRD2 genetic variants on memory for reward-associated stimuli.

Bringing together the previous observations that the TaqIA A1 and C957T C alleles were associated with lower DRD2 expression, modulated neural processing in the striatum and limbic system, conferred a higher risk for substance abuse, and potentially affected episodic memory functions, we hypothesized that these genetic variants would influence hippocampus-dependent memory for reward-predicting stimuli. Specifically, we expected carriers of these variants to show increased reward-related memory and memory-related hippocampal and striatal activation as a potential intermediate phenotype for addiction memory. To this end, we performed functional magnetic resonance imaging (fMRI) during an incentive delay task followed by a delayed memory test (Wittmann et al., 2005, 2013; Barman et al., 2014, 2015) in a cohort of young healthy subjects genotyped for the TaqIA and the C957T polymorphisms. To investigate a potential influence of reward strength, we employed two reward conditions: a monetary and a social condition. In a previous study, we had found that the monetary condition elicited faster reaction times (RTs) and a more pronounced NAcc reward anticipation response than the social condition (Barman et al., 2015).

MATERIALS AND METHODS

The experimental paradigm, study cohort, data acquisition and fMRI data processing have been described previously in the context of another imaging genetics study and in a study on individual differences in autistic traits (Barman et al., 2014, 2015). In the first study, a modulation of the hippocampal recognition-encoding response for monetary reward-predicting items by a polymorphism of the guanine nucleotide exchange

factor RASGRF1 was observed (Barman et al., 2014). The latter study investigated interactive effects of gender and subclinical autistic features on the anticipation and feedback processing of social reward (Barman et al., 2015). Here, we analyzed the memory parameters and their neural manifestation with respect to *DRD2* polymorphisms. Neither the inclusion of the RASGRF1 genotype nor of the Autism Quotient (AQ; Baron-Cohen et al., 2001) as covariates in our analysis leads to a qualitative change of the presented results.

Participants

Sixty two participants (mean age \pm SD: 24.58 \pm 2.75 years) were recruited from a larger cohort of healthy and young volunteers of a large-scale behavioral genetics study conducted at the LIN Magdeburg (n=719, age: mean \pm SD = 23.77 \pm 2.76 years; for detailed description of the sample see, Barman et al., 2014). Participants were recruited based on age, sex, and absence of MRI contraindications. All participants were of Caucasian origin, right-handed, had no history of neurological or psychiatric illness and did not use any illicit drugs or centrally acting medication according to self-report. Participants were stratified regarding the AQ to consider potential autistic traits as factor for social reward processing in a previous study (Barman et al., 2015).

Since TaqIA and C957T polymorphism have also been implicated in attentional processing and executive functions (Klein et al., 2007; Jocham et al., 2009; Markett et al., 2011; Colzato et al., 2013; Richter et al., 2013), the participants also performed standard neuropsychological tests like a flanker task (Eriksen and Eriksen, 1974), as well as the alertness and task switching subtests of the Test of Attentional Performance [Testbatterie zur Aufmerksamkeitsprüfung (TAP); Zimmermann and Fimm, 1993].

All participants gave written informed consent in accordance with the Declaration of Helsinki and received financial compensation for participation. The work was approved by the Ethics Committee of the University of Magdeburg, Faculty of Medicine.

Genotyping

TaqIA polymorphism (NCBI accession number: rs1800497) was genotyped using a previously described protocol (Richter et al., 2013). Genomic DNA was extracted from blood leukocytes using the GeneMole[®] automated DNA extraction system (Mole Genetics AS, Lysaker, Norway) according to the manufacturer's protocol. Genotyping was performed using PCR with previously described primers (Grandy et al., 1989), followed by allele-specific restriction analysis with TaqI at 65°C.

For genotyping of C957T polymorphism (rs6277) a Competitive Allele Specific PCR assay (KASP; LGC Genomics GmbH, Berlin, Germany) was used. The reaction was performed in a final reaction volume of 10 μl containing 10 ng genomic DNA, 5 μl of 2x KASP Master mix (LGC Genomics) and 0.14 μl of primer mix with the two allele specific forward and the reverse primer. PCR-based amplification and read-out were performed in 96-well microtiter plates on the Roche LightCycler $^{\$}$ 480 Instrument II (Roche Diagnostics Germany, Mannheim, Germany) according to the manufacturer's recommendation

for this specific KOD assay. Data analysis was carried out using the LightCycler® 480 Software release 1.5.0 (Roche Diagnostics Deutschland GmbH). Genotyping experiments were made with quality control of automated allele calling by two independent operators blinded to phenotype (100% concordance). The call rate for the genotyped marker was 100%.

Because the COMT Val108/158Met (rs4680), DAT1/VNTR (rs28363170), and RASGRF1 (rs8027411) polymorphisms have previously been linked to memory function and reward processing (Bertolino et al., 2006; Meyer-Lindenberg and Weinberger, 2006; Schott et al., 2006; Yacubian et al., 2007; Wittmann et al., 2013; Barman et al., 2014), participants were also genotyped for these polymorphisms (details available upon request).

Procedure

We used a modified version of a previously employed categorical monetary incentive delay task conducted at two consecutive days (Wittmann et al., 2005; Krebs et al., 2009). On the first day participants performed a number comparison task in the MR tomograph. Besides monetary reward (1) participants could earn a positive social feedback (a photograph of smiling women, men, children, or couples) upon successful responding. Both reward types were investigated separately in two sessions. Each of the two sessions consisted of 100 trials (50 reward and 50 no-reward trials; event-related design), and the order of the runs was counterbalanced across participants. Before each session participants were given a short demonstration of the task and completed a practice session (20 trials) to learn the association between the cues and each condition. This practice session was employed to minimize learning effects during functional MR data acquisition and to induce the shift of the ventral striatal response from outcome to anticipation (Wittmann et al., 2005). Cue pictures consisted of photographs of simple objects that belonged to one of six categories (vehicles, bags, furniture, music instruments, clothes, kitchen devices). For each participant and session (monetary vs. social), two categories were randomly chosen to signal a potential reward or neutral outcome, respectively. Each trial started with the presentation of a cue picture for 1000 ms. Participants were asked to attend to the cues in order to be aware of the reward status and to respond via button press whether they expected a reward or not. After a variable delay (500–3500 ms), a number comparison task followed (target, 250 ms; Wittmann et al., 2005). Participants were requested to give a speeded response whether a target number was larger or smaller than five. The response deadline was adjusted individually based on RTs in the preceding trials to attain a correct response rate of approximately 80% (after four consecutive wins, the time limit was reduced by 20 ms, after one incorrect or slow reaction the time limit was increased by 20 ms). After a further variable time interval (500-2500 ms) a feedback was presented (750 ms). In reward trials either a picture of money coins or of a smiling face was presented upon fast and correct responses, and after a wrong or/and slow response black/white-noise image was shown. During neutral trials, the black/white-noise image was presented irrespective of outcome. The variable inter-trial interval was between 1000 and 4000 ms.

Twenty four (±4) hours after the start of the fMRI session, participants performed a recognition memory task outside the MR tomograph. Stimuli included the 200 cue images from the fMRI session, presented randomly intermixed with 100 distractors that had not been shown before. Subjects rated their recognition confidence on a scale ranging from 1 to 5 ("1": definitely old; "2": likely old; "3": unsure; "4": likely new; "5": definitely new). These confidence ratings were used to model the relationship between successful encoding of the cue pictures and brain responses during the initial presentation of the pictures.

MRI Data Acquisition

Functional MRI was performed using a 3 Tesla Siemens Magnetom Trio MR tomograph (SIEMENS Medical Systems, Erlangen, Germany) with a 12-channel phased array head coil. We collected structural (T1-weighted MPRAGE: 256 \times 256 matrix; FOV = 256 mm; 96 2 mm sagittal slices) and functional images (Gradient-Echo echo-planar imaging [EPI] sequence; TR = 2000 ms; TE = 30 ms; FOV = 240 mm; flip-angle = 90°; matrix = 96 \times 96; slice-thickness = 3 mm; 34 oblique slices parallel to the line from anterior to posterior commissure; voxel size = 2.5 mm \times 2.5 mm \times 3 mm; two runs of 420 volumes).

fMRI Data Processing and Analysis

Image processing and statistical analyses were performed using Statistical Parametric Mapping (SPM121). EPIs were corrected for acquisition time delay and head motion, spatially warped into the Montreal Neurological Institute (MNI) stereotactic reference frame, and spatially smoothed (isotropic Gaussian kernel; FWHM = 8 mm). A high-pass filter with a cut-off frequency of 128 s was applied to the data. Statistical analysis was carried out using a two-stage mixed-effects model. At the first stage, encoding-related hemodynamic responses were analyzed as a function of reward category-specific encoding and subsequent recognition confidence. Separate regressors for each reward category were created modeling the mean brain response. Recognition confidence-associated variance in brain responses was modeled by a trial-by-trial weighting of these regressors by the corresponding confidence ratings. Thus, the model contained eight regressors representing the memoryassociated neural effects. Brain responses of no interest were modeled via regressors for targets and feedbacks, with the latter complemented by a parametric regressor for the feedback type (success/failure). Signal fluctuations caused by interactions of susceptibility and motion were modeled by means of the six rigidbody movement parameters determined from motion correction. Finally a constant regressor represented the signal mean of the time course. Model estimation was performed using a restricted maximum likelihood (ReML) fit as implemented in SPM. Since our research was focused on the effect of genotype on memory formation, linear contrasts of rewarded minus neutral trials were computed for the parametric modulated statistical maps for monetary and social reward categories separately. Thus, two linear contrast images per subject were submitted to second-level random-effects analyses of covariance (ANCOVA) with reward

category (monetary vs. social) and genotype/haplotype (TaqIA: A1+ vs. A1-; C957T: CC vs. CT vs. TT; Haplotype: A1+/C+ vs. A1-/C+ vs. A1-/C-) as factors, and age and sex as covariates. Region of interest (ROI)-based analyses of recognition-encoding responses to reward-predicting items were performed using anatomical ROIs of the hippocampus (CA regions, as previously employed; Barman et al., 2014) generated with the SPM Anatomy Toolbox (Eickhoff et al., 2005) and of the striatum, generated with automated anatomical labeling (AAL; Tzourio-Mazoyer et al., 2002) implemented in the WFU-Pickatlas (Wake Forest University). Alpha error probabilities were adjusted for ROIvolumes [small volume correction (SVC)]. To this end, we first computed statistical maps with a significance level of p < 0.001uncorrected and a minimum cluster size of 10 adjacent voxels. In a second step, the alpha errors for significant effects within the ROIs were corrected for the corresponding ROI-volume. Report and discussion was restricted to those findings with a resulting family-wise error (FWE) corrected alpha probability p < 0.05.

Behavioral Data Analyses

To analyze the effects of motivation on the performance in the number comparison task, we calculated relative difference values between the RTs of correct responses in the neutral versus rewarded conditions divided by the mean RT for neutral trials, to account for confounding effects of individual variability of unspecific sensorimotor processing speed (Schott et al., 2007; DiffRT = [(RT_{neutral} - RT_{reward})/RT_{neutral} * 100] for each subject. We then computed ANCOVAs with the genotype/haplotype as between-subject factor, reward type (monetary vs. social) as within-subject factor and age and sex as covariates.

To analyze the recognition of previously seen items, we calculated the corrected hit rate by subtracting the percentage of new items incorrectly judged as old (false alarms) from the percentage of correctly recognized old items (hits). To derive estimates of recollection and familiarity for each participant, receiver operating characteristics (ROCs) were generated by plotting the proportion of hits against the proportion of false alarms as a function of confidence and fit to a dual process model (Yonelinas et al., 2002; Duzel et al., 2011). The ANCOVAs were computed separately for each SNP and for the haplotype. All ANCOVAs included the genotype/haplotype (TaqIA: A1+vs. A1-; C957T: CC vs. CT vs. TT; Haplotype: A1+/C+ vs. A1-/C+ vs. A1-/C-) as between-subject factor, trial type (rewarded vs. neutral), and reward category (monetary vs. social) as withinsubject factors, and age and sex as covariates. When appropriate, correlational analyses (Pearson's correlations), paired t-test or independent-sample *t*-test were used as *post hoc* tests.

To match the parametric modulation in the fMRI data analyses (see above), in an additional analysis, the medians of the Likert-scaled confidence ratings on the subsequent day were computed for each item type (old vs. new), trial type (rewarded vs. neutral) and reward category (social vs. monetary). Low values indicated that items were declared as old, and high values indicated that items were declared as new. To gain an initial all-encompassing overview including all within-subject factors, between-subject factors, and covariates, repeated-measures ANCOVAs were computed. Owing to the non-parametric

¹http://www.fil.ion.ucl.ac.uk/spm/

nature of the dependent variable, non-parametric *post hoc* tests (Mann–Whitney-*U*, Kruskal–Wallis) were used to compare genotypes/haplotypes when appropriate. The ANCOVAs were computed separately for each SNP and for the haplotype. All ANCOVAs included the genotype or haplotype (TaqIA: A1+ vs. A1-; C957T: CC vs. CT vs. TT; Haplotype: A1+/C+ vs. A1-/C+ vs. A1-/C-) as between-subject factor, item type (old vs. new item), trial type (rewarded vs. neutral), and reward category (monetary vs. social) as within-subject factors, and age and sex as covariates.

RESULTS

Genotyping

Among the 62 participants, we identified three A1 homozygotes, 28 heterozygotes, and 31 A2 homozygotes of the TaqIA polymorphism. A1 carriers (A1+: A1/A1 and A1/A2) were grouped together for all subsequent analyses and compared to A2 homozygotes (A1-: A2/A2) as in previous behavioral and imaging studies (Richter et al., 2013, 2014). The allelic

distributions for the polymorphisms are displayed in **Tables 1–3**. The distribution of the SNPs did not violate Hardy–Weinberg equilibrium (HWE; TaqIA: $\chi^2=1.12$, p=0.289; C957T: $\chi^2=1.08$, p=0.300). As TaqIA and C957T are in LD, a combined analysis was conducted. Therefore we also grouped together C carriers of the C957T (C+: C/C and C/T; C-: T/T; Voisey et al., 2012), thus forming four possible haplotype combinations, of which only three were found in our cohort (**Table 3**). The groups of each genotype and the haplotype did not significantly differ in sex, age, allele distributions of the COMT Val108/158Met, RASGRF1 and DAT1/VNTR polymorphisms, smoking status or the AQ score (see **Tables 1–3**). Genotype/haplotype groups did also not differ in tests of attentional processes and executive functions (see Supplementary Tables S1–S3).

Behavioral Results

Genotype/Haplotype-Related Modulation of Reward-Related Processing Speed

In the number comparison task, we observed a significant interaction of reward category and C957T genotype ($F_{2.57} = 4.71$,

TABLE 1 | Demographic data and behavioral data of the memory parameters regarding TaqlA polymorphism.

TaqlA	A1+	A2A2	Statistics
Women/Men	16/15	14/17	$\chi^2 = 0.26, p = 0.611$
Mean age	25.1 ± 3.3	24.0 ± 2.0	$t_{60} = 1.61, p = 0.114$
AQ	14.9 ± 7.0	15.4 ± 7.1	U = 464.00, p = 0.816
C957T CC/CT/TT	12/19/0	3/16/12	$\chi^2 = 17.66, p < 0.001^*$
COMT MM/VM/VV	6/22/3	8/14/9	$\chi^2 = 5.06, p = 0.080$
RASGRF1 GG/TG/TT	11/13/7	9/17/5	$\chi^2 = 1.07, p = 0.587$
DAT1 10-10/10-09/11-09	20/10/1	19/12/0	$\chi^2 = 1.21, p = 0.547$
Smoking status (no/yes)	19/11	26/5	$\chi^2 = 3.32, \rho = 0.068$
Corrected hit rates – monetary condition	1		
Neutral [%]	20.45 ± 12.50	20.26 ± 11.28	Main effect of TaqIA
Reward [%]	19.61 ± 12.06	15.61 ± 10.90	genotype
Corrected hit rates – social condition			$F_{1,58} = 3.29, p = 0.075,$
Neutral [%]	18.97 ± 14.18	18.45 ± 10.45	$\eta^2 = 0.05$
Reward [%]	24.06 ± 14.32	18.19 ± 12.21	
Familiarity estimates – monetary condition	on		
Neutral	0.46 ± 0.35	0.39 ± 0.27	Main effect of TaqlA
Reward	0.45 ± 0.29	0.32 ± 0.26	genotype
Familiarity estimates – social condition			$F_{1,58} = 4.10, p = 0.047^*,$
Neutral	0.44 ± 0.39	0.39 ± 0.32	$\eta^2 = 0.06$
Reward	0.43 ± 0.34	0.38 ± 0.32	
Median confidence ratings – monetary c	condition		
Neutral	3.50	3.50	Interaction of TaqIA
Reward	3.00	3.25	genotype \times trial type \times
Median confidence ratings – social cond	lition		reward category
Neutral	3.50	3.50	$F_{1,58} = 2.89, p = 0.094,$
Reward	3.50	3.50	$\eta^2 = 0.05$

Demographic data: sex distribution, age (years, mean \pm SD), AQ score (mean \pm SD), number of smokers and non-smokers (data available for N = 61), and allelic distributions for C957T polymorphism, COMT Val108/158Met polymorphism (MM: Met homozygotes; VM: Val/Met heterozygotes; VV: Val homozygotes), RASGRF1 polymorphism and DAT1/VNTR polymorphism (10-10: 10 repeat homozygotes; 10-09: heterozygotes with 10 and 9 repeats; 11-09: heterozygotes with 11 and 9 repeats). Behavioral data: corrected hit rates (mean \pm SD), familiarity estimates (mean \pm SD), and median of confidence ratings. *Significant effect p < 0.005.

TABLE 2 | Demographic data and behavioral data of the memory parameters regarding C957T polymorphism.

C957T	CC	СТ	тт	
Women/men	9/6	18/17	3/9	$\chi^2 = 3.57, p = 0.168$
Mean age	23.9 ± 2.3	25.1 ± 3.1	23.9 ± 1.8	$F_{2,59} = 1.53, p = 0.226$
AQ	15.6 ± 6.6	15.3 ± 7.6	14.2 ± 5.7	$\chi^2 = 0.21, p = 0.901$
COMT MM/VM/VV	3/10/2	7/22/6	4/4/4	$\chi^2 = 3.94, p = 0.415$
RASGRF1 GG/TG/TT	3/6/6	15/17/3	2/7/3	$\chi^2 = 8.89, p = 0.064$
DAT1 10-10/10-09/11-09	10/4/1	23/12/0	6/6/0	$\chi^2 = 4.58, p = 0.333$
Smoking status (no/yes)	12/2	23/12	10/2	$\chi^2 = 2.77, p = 0.250$
Corrected hit rates – monetary co	ndition			
Neutral [%]	23.67 ± 11.68	18.69 ± 12.25	19.83 ± 10.04	Main effect of C957T
Reward [%]	20.13 ± 12.18	18.69 ± 10.98	11.33 ± 11.26	genotype
Corrected hit rates - social condit	ion			$F_{2,57} = 4.32, p = 0.018^*$
Neutral [%]	23.73 ± 12.58	17.49 ± 12.51	16.00 ± 10.69	$\eta^2 = 0.13$
Reward [%]	26.27 ± 19.73	21.20 ± 9.61	14.50 ± 12.24	
Familiarity estimates – monetary of	ondition			
Neutral	0.58 ± 0.33	0.35 ± 0.32	0.42 ± 0.21	Main effect of C957T
Reward	0.43 ± 0.33	0.40 ± 0.27	0.30 ± 0.26	genotype
Familiarity estimates – social cond	lition			$F_{2,57} = 3.75, p = 0.029^*$
Neutral	0.55 ± 0.44	0.35 ± 0.30	0.42 ± 0.36	$\eta^2 = 0.12$
Reward	0.55 ± 0.45	0.39 ± 0.28	0.27 ± 0.25	
Median confidence ratings – mone	etary condition			
Neutral	3.50	3.50	3.00	Interaction of C957T
Reward	3.00	3.00	3.50	genotype \times trial type \times
Median confidence ratings – socia	al condition			reward category
Neutral	3.50	3.50	3.75	$F_{2,57} = 4.37, p = 0.017^*$
Reward	3.00	3.50	3.50	$\eta^2 = 0.13$

Demographic data: sex distribution, age (years, mean \pm SD), AQ score (mean \pm SD), number of smokers and non-smokers (data available for N = 61), and allelic distributions for COMT Val108/158Met polymorphism (MM: Met homozygotes; VM: Val/Met heterozygotes; VV: Val homozygotes), RASGRF1 polymorphism and DAT1/VNTR polymorphism (10-10: 10 repeat homozygotes; 10-09: heterozygotes with 10 and 9 repeats; 11-09: heterozygotes with 11 and 9 repeats). Behavioral data: corrected hit rates (mean \pm SD), familiarity estimates (mean \pm SD), and median of confidence ratings. *Significant effect p < 0.005.

p = 0.013, $\eta^2 = 0.14$), with C957T C carriers showing more reward-related RT decrease in the monetary versus social reward trials (CC: $t_{14} = 6.62$, p < 0.001; CT: $t_{34} = 4.99$, p < 0.001), while there was no difference for the TT homozygotes (p = 0.393). No further significant effects were observed (all p > 0.112).

Genotype/Haplotype-Related Modulation of the Corrected Hit Rates

With respect to delayed recognition, we observed a main effect of C957T genotype on the corrected hit rates, with trends in the same direction for TaqIA and for the haplotype (TaqIA: p = 0.075; C957T: $F_{2,57} = 4.32$, p = 0.018, $\eta^2 = 0.13$; haplotype: p = 0.055; see **Tables 1–3**). C957T C homozygous subjects showed an overall better performance than heterozygous and T homozygous subjects (CC > CT: $t_{48} = 2.10$, p = 0.041; CC > TT: $t_{25} = 2.60$, p = 0.016; CT > TT: p = 0.083; see **Figure 1**).

Moreover there was a main effect of age in the model containing the haplotype (TaqIA: $F_{1,58}=4.29$, p=0.043, $\eta^2=0.07$; C957T: p=0.059; haplotype: $F_{1,57}=5.36$, p=0.024, $\eta^2=0.09$), indicating a negative correlation between age and memory performance (r=-0.276, p=0.030). All other effects or interactions were not significant (all p>0.170).

Genotype/Haplotype-Related Modulation of Recollection and Familiarity Estimates

The analyses of the recollection estimates revealed no significant effects (all p > 0.066).

The analyses of the familiarity estimates revealed significant main effects of TaqIA and C957T genotype (TaqIA: $F_{1,58}=4.10$, p=0.047, $\eta^2=0.07$; C957T: $F_{2,57}=3.75$, p=0.029, $\eta^2=0.12$; haplotype: p=0.119). TaqIA A1 carriers compared to A2 homozygotes ($t_{60}=1.48$, p=0.146; t-test with standardized residues accounting for age and sex: $t_{60}=2.03$, p=0.047), and C957T C homozygous subjects compared to heterozygous showed higher overall familiarity estimates (CC > CT: $t_{48}=2.12$, p=0.048). For the comparison between C957T C and T homozygous subjects we found only an – even equally directed – trend (CC > TT: p=0.051). The comparison between C957T heterocygotes and T homocygotes revealed no significant differences in familiarity (CT > TT: p=0.690). A graphical depiction of these results could be found in **Figure 1**.

Again there was a main effect of age in the model containing the haplotype, and the TaqIA genotype (TaqIA: $F_{1,58} = 5.83$, p = 0.019, $\eta^2 = 0.09$; C957T: p = 0.062; haplotype: $F_{1,57} = 6.07$, p = 0.017, $\eta^2 = 0.10$), indicating

TABLE 3 | Demographic data and behavioral data of the memory parameters regarding the TaglA/C957T haplotype.

Haplotype	A1+/C+	A1-/C+	A1-/C-	
Women/men	16/15	11/8	3/9	$\chi^2 = 3.45, p = 0.179$
Mean age	25.1 ± 3.3	24.1 ± 2.1	23.9 ± 1.8	$F_{2,59} = 1.32, p = 0.275$
AQ	14.9 ± 7.0	16.1 ± 7.9	14.2 ± 5.7	$\chi^2 = 0.28, p = 0.868$
COMT MM/VM/VV	6/22/3	4/10/5	4/4/4	$\chi^2 = 6.21, p = 0.184$
RASGRF1 GG/TG/TT	11/13/7	7/10/2	2/7/3	$\chi^2 = 2.84, p = 0.585$
DAT1 10-10/10-09/11-09	20/10/1	13/6/0	6/6/0	$\chi^2 = 2.31, p = 0.679$
Smoking status (no/yes)	19/11	16/3	10/2	$\chi^2 = 3.33, \rho = 0.190$
Corrected hit rates – monetary cor	ndition			
Neutral [%]	20.45 ± 12.50	20.53 ± 12.25	19.83 ± 10.04	Main effect of
Reward [%]	19.61 ± 12.06	18.32 ± 10.03	11.33 ± 11.26	haplotype
Corrected hit rates - social conditi	ion			$F_{2,57} = 3.05, p = 0.055,$
Neutral [%]	18.97 ± 14.12	20.00 ± 10.29	16.00 ± 10.69	$\eta^2 = 0.10$
Reward [%]	24.06 ± 14.32	20.53 ± 11.92	14.50 ± 12.24	
Familiarity estimates – monetary of	ondition			
Neutral	0.46 ± 0.35	0.37 ± 0.31	0.42 ± 0.21	Main effect of
Reward	0.45 ± 0.29	0.34 ± 0.27	0.30 ± 0.26	haplotype
Familiarity estimates - social cndit	ion			$F_{2,57} = 2.21, p = 0.119,$
Neutral	0.44 ± 0.39	0.37 ± 0.29	0.42 ± 0.36	$\eta^2 = 0.07$
Reward	0.43 ± 0.34	0.45 ± 0.35	0.27 ± 0.25	
Median confidence ratings – mone	etary condition			
Neutral	3.50	3.50	3.00	Interaction of
Reward	3.00	3.00	3.50	haplotype \times trial type \times
Median confidence ratings – socia	l condition			reward category
Neutral	3.50	3.50	3.75	$F_{2,57} = 4.50, p = 0.015^*,$
Reward	3.50	3.00	3.50	$\eta^2 = 0.14$

Demographic data: sex distribution, age (years, mean \pm SD), AQ score (mean \pm SD), number of smokers and non-smokers (data available for N = 61), and allelic distributions for COMT Val108/158Met polymorphism (MM: Met homozygotes; VM: Val/Met heterozygotes; VV: Val homozygotes), RASGRF1 polymorphism and DAT1/VNTR polymorphism (10-10: 10 repeat homozygotes; 10-09: heterozygotes with 10 and 9 repeats; 11-09: heterozygotes with 11 and 9 repeats). Behavioral data: corrected hit rates (mean \pm SD), familiarity estimates (mean \pm SD), and median of confidence ratings. *Significant effect p < 0.005.

a negative correlation between age and memory performance ($r=-0.263,\ p=0.039$). Additionally an interaction of trial type (rewarded vs. neutral) and sex was observed in the model containing the TaqIA genotype (TaqIA: $F_{1,58}=4.21,\ p=0.045,\ \eta^2=0.07;\ C957T:\ p=0.089;\ haplotype:\ p=0.092$), indicating slightly higher familiarity estimates in women compared to men in the rewarded, but not in the neutral condition (rewarded: $t_{60}=1.73,\ p=0.089;$ neutral: p=0.768). All further analyses yielded no significant effects (all p>0.069).

Genotype/Haplotype-Related Modulation of Reward-Related Recognition Confidence Ratings

When analyzing the medians of the confidence ratings, all three ANCOVAs revealed a main effect of the item type (all p < 0.029), indicating that previously seen items were indeed recognized as old (lower medians for old vs. new items).

Moreover we observed significant three-way interactions of C957T genotype and haplotype with trial type and reward category (TaqIA: p = 0.094; C957T: $F_{2,57} = 4.37$, p = 0.017, $\eta^2 = 0.13$; haplotype: $F_{2,57} = 4.49$, p = 0.015, $\eta^2 = 0.14$), most notably, in absence of an interaction with item type

(four-way interaction: all p > 0.435). Post hoc tests showed that in the monetary reward category, differential confidence ratings (rewarded vs. neutral) in C975T C homozygotes versus T homozygotes revealed a bias to declare rewarded items as old, independent of their actual item type (old vs. new; CC > TT: monetary: U = 40.50, p = 0.015, social: p = 0.500; see **Figure 1**). A1+/C+ haplotype carriers compared to A1-/C- haplotype carriers (A1+/C+> A1-/C-: monetary: U = 99.50, p = 0.018, social: p = 0.377; see **Tables 2**, 3 for details) also showed significant differences of confidence ratings, but as no effect was observed for the A+/C+ haplotype carriers compared to A1-/C+ haplotype carriers (A1+/C+> A1-/C+: monetary: p = 0.959, social: p = 0.760), this effect was most likely driven by LD with the C957T polymorphism.

In the model containing the TaqIA genotype, on the other hand, a significant three-way interaction of trial type \times reward category \times sex was observed ($F_{1,58} = 5.09$, p = 0.028, $\eta^2 = 0.08$), most likely reflecting a response bias of men in the social and of women in the monetary category (men \times women: monetary: U = 315.50, P = 0.018; social: U = 335.00, P = 0.037).

All other effects were not significant (all p > 0.077).

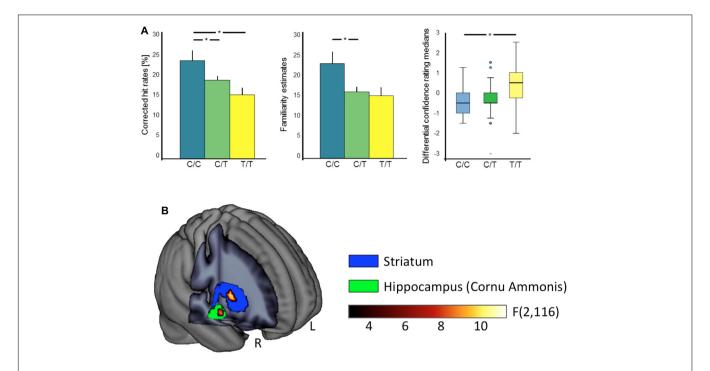


FIGURE 1 | **Effects of the C957T polymorphism on behavioral and fMRI correlates of reward memory. (A)** Significant behavioral C957T genotype effects on episodic memory performance. Bar plots depict overall corrected hit rates (left) and familiarity estimates (middle) with standard errors. The C957T C allele is associated with an overall higher recognition performance. The box plot (right) depicts differential confidence rating medians (rewarded vs. neutral) in the monetary reward category. Horizontal lines represent the medians, the box represents the 25th and 75th percentiles, the whiskers indicate the 5th and 95th percentiles, dots mark outliers, and the colored asterisks indicate the extremes. Lower values of the C homozygotes indicate a bias to declare rewarded as compared to neutral items as old, independent of their actual item type. *p < 0.05. (B) Neural manifestations of the interaction between C957T genotype and reward category during encoding. Significant interactions of C957T genotype and reward category in right hippocampus (green) and striatum (blue). Statistical F-map and ROIs for small volume alpha error correction overlaid on a mean anatomical image. L, left; R, right.

Brain Activation Patterns

Genotype/Haplotype-Related Modulation of Neural Correlates of Reward-Dependent Memory

To investigate the neural correlates of reward-related memory, we modeled recognition confidence-associated variance in brain responses via linear parametric regressors (see Materials and Methods). Reward category-specific contrast images between reward and neutral trials were submitted to group level ANCOVA. We observed significant interactions of C957T genotype and reward category in right hippocampus and striatum (right hippocampus: $F_{2,116} = 8.80$, p = 0.032, [x y z] = [24 –13 –14], 9 voxels; right striatum: $F_{2,116} = 10.43$, p = 0.026, [x y z] = [30 5 1], 14 voxels; p < 0.05, FWE-corrected for the respective ROI volumes; see **Figure 1**), indicating a C957T-related modulation of hippocampal and striatal correlates of reward-dependent memory.

DISCUSSION

Our results show a genotype-dependent modulation of hippocampal and striatal brain responses during encoding of reward-predicting items. Importantly, this modulation manifested also at the behavioral level, with genotypes previously linked to lower D2 receptor expression, i.e., the TaqIA A1 and C957T C alleles, being associated with an overall higher recognition performance and a response bias for reward-predicting items.

Dopamine D2 Receptor Gene Variants and Recognition Performance

In the present study, we observed significant effects of both the DRD2 C957T and the DRD2/ANKK1 TaqIA gene variants on recognition memory, with carriers of the low-expressing alleles showing higher corrected hit rates and familiarity estimates. Our findings are compatible with two previous studies demonstrating relatively superior memory performance in C957T C homozygotes (Li et al., 2013; Papenberg et al., 2013). Previous results regarding the TaqIA polymorphism have been inconsistent (see Introduction; Bartres-Faz et al., 2002; McAllister et al., 2005, 2008; Persson et al., 2015). Effects of TaqIA might have been driven by its LD with C957T, but none of the previous studies investigated both SNPs together, nor have those studies tested memory for rewardassociated stimuli. In the present study, we had hypothesized that DRD2 genotypes would preferentially affect the encoding of picture stimuli that predicted a reward. While we found lowexpressing DRD2 variants to be associated with overall memory performance and with a more liberal response criterion for rewarded stimuli, we did not observe a specific interaction of genotype and reward on the actual memory performance at the behavioral level. On the other hand, such an interaction was observed at the level of memory-related brain activity. The most likely explanation for this is, in our view, the relatively small sample size. It has previously been suggested that differences in BOLD signal changes are likely to be more closely related to the cellular effects mediated by genetic variations than the between-group differences of behavioral readouts (Meyer-Lindenberg and Weinberger, 2006; Mier et al., 2010).

A further somewhat unexpected finding was that genotyperelated differences in memory performance were found for familiarity, but not recollection estimates. This observation is to some extent in contrast to the previously reported higher recollection rates for reward-predicting items (Wittmann et al., 2005). One explanation for this discrepancy comes from modeling work by Elfman et al. (2008) who postulate that recollection versus familiarity in explicit memory processes is influenced by item similarity. Specifically, as the level of feature similarity across items increases, the hippocampus loses its ability to encode items distinctively, and the threshold nature of recollection - as opposed to familiarity, which follows signal detection theory - breaks down. In line with this explanation, the stimuli used in the original study by Wittmann et al. (2005) were considerably less similar to each other, and the categories were more broadly defined (living vs. non-living objects).

Dopaminergic Modulation of Hippocampus-Dependent Memory Formation

Our data analyses revealed that, in addition to effects of both the DRD2/ANKK1 TaqIA and the C957T genotypes on recognition memory, the C957T polymorphism also modulated hippocampal and striatal activation during encoding of reward-predicting stimuli. The hippocampus and the striatum, particularly the NAcc, are core structures of a neural circuit that has been suggested to mediate the encoding of novel and reward-associated information into long-term memory, the so-called hippocampal-VTA loop (Lisman and Grace, 2005). According to this model, dopamine release in the hippocampus and NAcc promotes long-term memory by stabilizing plasticity mechanisms, which may underlie the well-documented superior memory performance for rewarded relative to unrewarded stimuli (Wittmann et al., 2005; Adcock et al., 2006; Krebs et al., 2009).

It may seem counterintuitive that individuals carrying genetic variations associated with lower striatal D2 receptor density exhibit better reward-related memory. It should be noted, though, that higher baseline dopaminergic tone, as indexed by PET imaging of dopamine synthesis capacity has been linked to detrimental rather than beneficial effects of reward on attentional performance (Aarts et al., 2014). With respect to memory, a similar observation has been

reported in participants who performed a recognition memory task with a reward manipulation. Reward affected recognition performance adversely when participants had received the dopamine precursor L-DOPA (Apitz and Bunzeck, 2013). Both studies convergingly support the previously suggested inverted U-shape of dopaminergic effects on human cognitive processing (Vijayraghavan et al., 2007).

An additional or possibly alternative explanation for the observed pattern might be a potential role of extrastriatal D2 receptors in reward memory. It should be noted though, that D2 receptor expression outside the striatum is sparse and constitutes to a considerable degree of presynaptic inhibitory autoreceptors (for reviews see Wolf and Roth, 1990; Schmitz et al., 2003). With respect to the TaqIA polymorphism, lower expression of autoinhibitory D2 receptors has been proposed to elicit increased presynaptic dopamine synthesis (Laakso et al., 2005), which may conceivably also influence extrastriatal dopamine release. While this notion is compatible with both animal studies (Bello et al., 2011; de Jong et al., 2015), and a pharmacological study in humans (Buckholtz et al., 2010). Along the same line Wittmann et al. (2013) observed a modulation of striatal and hippocampal activation during successful encoding of reward-related pictures by a polymorphism previously associated with striatal dopamine transporter expression (meta-analysis Costa et al., 2011; Shumay et al., 2011; Spencer et al., 2013) and presumably resulting extracellular DA availability. Compatibly, reward circuit activity has been linked to interindividual variability of striatal dopamine release (Schott et al., 2008), and increased midbrain and NAcc activity in nine-repeat carriers has also been observed during successful episodic memory formation, independently of reward (Schott et al., 2006). However, the existing data regarding C957T on striatal versus extrastriatal D2 receptor binding are thus far inconclusive (Hirvonen et al., 2009a,b; see Limitations and Directions for Future Research), and it seems therefore premature to simply attribute the observed association of C957T with reward memory to reduced extrastriatal presynaptic autoinhibition.

Response Bias as a Further Risk Mechanism for Addiction Memory?

Our data analyses revealed that, in addition to overall better reward memory performance, C957T C homozygotes exhibited also a response bias for rewarded items. That is, that the analysis of the medians of the confidence ratings of the recognition test 24 h after encoding revealed that carriers of low-expressing alleles showed a tendency to judge images that predicted monetary reward as old, irrespective of whether they had actually been presented during encoding. The observation that this bias was only apparent in the monetary and not the social condition may reflect the stronger propensity of the monetary condition to elicit reward responses (Barman et al., 2015). High false alarm rates can be induced experimentally, for example by a well-known paradigm described by Roediger and McDermott, in which the context of a lure item -that is not actually presented during

study- is induced, leading to increased false recognition of the lure item at test (Roediger and McDermott, 1995). While the original finding by Roediger and McDermott has been replicated by a number of different groups, the underlying neurocognitive mechanisms are not yet completely understood, and it is unlikely that a single process leads to the increased recognition of the lures (Jou and Flores, 2013). In the original paradigm, lure items were typically category words, while a number of associate words were presented during study. In the present study, carriers of low-expressing DRD2 alleles showed a tendency to judge items from the monetary reward category as old, even though these items did not differ qualitatively from other images of the same category. One mechanism that has been proposed to underlie the tendency to judge new items as old is a shift of response criterion (Miller and Wolford, 1999). Such a criterion shift could also happen when an entire category is more salient than another. Given the previously reported increased risk of substance-related disorders in carriers of low-expressing DRD2 alleles (Morton et al., 2006; Doehring et al., 2009; Swagell et al., 2012; Voisey et al., 2012; also underpinned by a nominal TaqIA genotype effect on the smoking status in our cohort, see Table 1), the higher false alarm rate could also be considered a tendency to generalize reward-associated stimuli and to show a reduced ability to inhibit a response to such stimuli (see, for example, Machulska et al., 2016). This interpretation is also compatible with our previous observation in a motivated Go/Nogo learning task, in which TaqIA A1 carriers showed a selective deficit in learning the "NoGo-to-win" condition, i.e., the suppression of a motor response to obtain a reward (Richter et al., 2014). While these studies cannot elucidate the precise molecular mechanisms, they may nevertheless deliver potential intermediate phenotypes.

Limitations and Directions for Future Research

The most important limitation of the present study is the relatively small sample size, which is the most likely reason why no significant interaction effects of genotype and reward on memory performance could be observed (see above). Furthermore, given that genetic variations do not exert their effects in isolation, it would be of interest to assess potential interactions with other gene variants in the dopamine system. For example Wittmann et al. (2013) observed a modulation of striatal and hippocampal activation during successful encoding of reward-related pictures by the DAT1/VNTR polymorphism, and in our own group we observed effects of a polymorphism of the guanine nucleotide exchange factor RASGRF1 that is an important regulator of intracellular signaling and neural plasticity in the brain (Barman et al., 2014). Another potential variant of interest would be the COMT Val108/158Met (rs4680) polymorphism that has been previously associated with both memory function and reward processing (Bertolino et al., 2006; Meyer-Lindenberg and Weinberger, 2006; Schott et al., 2006; Yacubian et al., 2007). The sample size, however, did not allow us to systematically investigate such combined genetic effects. We did, however, test the allelic distribution

of those variants in order to exclude them as potential confounds.

Another limitation, albeit not unique to the present study, is that the exact effects of C957T on dopamine D2 receptor availability are yet incompletely understood. While in vitro studies have suggested lower mRNA stability associated with the T allele (Duan et al., 2003), an in vivo PET investigation has demonstrated that, unexpectedly, C homozygotes had the lowest striatal D2 receptor binding potential (Hirvonen et al., 2004). In a follow-up study, Hirvonen et al. (2009a) further suggested that this effect was better attributable to receptor affinity rather than actual expression levels. For extrastriatal D2 receptors, one study has actually suggested increased rather than decreased binding potential in C homozygotes (Hirvonen et al., 2009b), which would, in case of presynaptic D2 receptors, be in conflict with our interpretation that lower extrastriatal presynaptic DRD2 expression might result in higher activity of the hippocampal-VTA loop in C957T C carriers. On the other hand, Hirvonen et al. (2009b) suggested that their results could be rather attributable to the - generally sparsely expressed - post-synaptic extrastriatal D2 receptors, as D2 autoreceptor functioning in the cortex was less efficient compared to the striatum (Cubeddu et al., 1990), and the cortical expression pattern might thus more likely reflect the regulations at mRNA level described by Duan et al. (2003). It should further be noted that the lifelong presence of a genetic variant associated with altered gene expression or regulation is likely to lead to long-term plasticity at the large-scale network level. With respect to the DRD2 C957T polymorphism, for example, Markett et al. (2013) have reported reduced striatal gray matter density in C homozygotes, which may in turn lead to long-term changes in cortico-striatal loop function, thereby exerting subtle effects on cognitive functions like memory.

CONCLUSION

Our results provide evidence for a role of *DRD2*-SNPs in human reward memory with carriers of low-expressing *DRD2* alleles being associated with an overall higher recognition confidence and a response bias for reward-predicting items. This pattern may reflect a phenomenon contributing to a complex endophenotype, which at a clinical level manifests as addiction memory (see also Robbins et al., 2008) and reward-related impulsivity.

AUTHOR CONTRIBUTIONS

Designed experiment: AR, AB, AD, JS, BS. Performed experiment: AB, DS, AD, GB, AA, MK, MZ. Analyzed data: AR, AB, TW, JS. Wrote manuscript: AR, DS, CS, BS. All authors edited and/or approved the manuscript.

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SUPPLEMENTARY MATERIAL

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Description of Various Factors Contributing to Traffic Accidents in Youth and Measures Proposed to Alleviate Recurrence

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Gicquel L, Ordonneau P, Blot E, Toillon C, Ingrand P and Romo L (2017) Description of Various Factors Contributing to Traffic Accidents in Youth and Measures Proposed to Alleviate Recurrence. Front. Psychiatry 8:94. doi: 10.3389/fpsyt.2017.00094 Traffic accidents are the leading cause of hospitalization in adolescence, with the 18-24-year-old age group accounting for 23% of deaths by traffic accidents. Recurrence rate is also high. One in four teenagers will have a relapse within the year following the first accident. Cognitive impairments known in adolescence could cause risky behaviors, defined as repetitive engagement in dangerous situations such as road accidents. Two categories of factors seem to be associated with traffic accidents: (1) factors specific to the traffic environment and (2) "human" factors, which seem to be the most influential. Moreover, the establishment of a stronger relation to high speed driving increases traffic accident risks and can also be intensified by sensation seeking. Other factors such as substance use (alcohol, drugs, and "binge drinking") are also identified as risk factors. Furthermore, cell phone use while driving and attention deficit disorder with or without hyperactivity also seem to be important risk factors for car accidents. The family environment strongly influences a young person's driving behavior. Some interventional driving strategies and preventive measures have reduced the risk of traffic accidents among young people, such as the graduated driver licensing program and advertising campaigns. So far, few therapeutic approaches have been implemented. Reason why, we decided to set up an innovative strategy consisting of a therapeutic postaccident group intervention, entitled the ECARR2 protocol, to prevent recurrence among adolescents and young adults identified at risk, taking into account the multiple risk factors.

Keywords: traffic accidents, recurrence, young drivers, adolescence, prevention, therapeutic programs

INTRODUCTION

Traffic accidents are the leading cause of death among young people aged 15–29 years in industrialized countries (1). For example, in Britain in 2011, 22% of road accidents involved at least one young driver aged 17–24 years. In fact, accidents including young drivers typically represented about a quarter of all deaths on the road (2).

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In France, traffic accidents also represent a major and persistent public health problem. They are by far the leading cause of death among young people aged 15–24 years (3). A global process of reducing fatal traffic accidents has been applied for all age groups since 1979. According to an annual report from the Organization for Economic Co-operation and Development (4), a 15% decrease in the number of road deaths was observed between 2010 and 2014, a drop similar to the one observed period between 2006 and 2010.

However, this declining trend is still fluctuating. In fact, in January 2016, the French Ministry of the Interior stated that road deaths were up by 2.4% in 2015, for the second consecutive year, while the number of injury accidents has declined by 3.6%.

Since 1979, traffic accidents fatalities mainly affect three age groups (5) (**Figure 1**).

Furthermore, according to the French epidemiological center on the medical causes of death (5) (**Figure 1**), the age group 25–44 years seems to be the most affected by road fatalities. However, when divided by the number of constituent years of each age group, the 15–24 age group had the highest average mortality rate (**Figure 2**). Indeed, in view of the nine constituent years of the 15–24 age group, the number of accidents is greater than the 19 constituent years of the other two age groups (i.e., 25–44 age group and 46–64 age group).

The 15–24 age group represented alone about 20–30% of deaths from traffic accidents, making it the most affected age group by road fatalities. According to the data from the French ONISR (6), young people aged 18–24 years still contributed to 17% of road deaths in 2014, although only representing 8% of the population. Hence, they seem to be twice as likely as other age groups to lose their lives on the roads.

Moreover, according to the International Road Traffic and Accident Database (7), young French adults aged 18–24 years have among the highest mortality and morbidity rates in European countries.

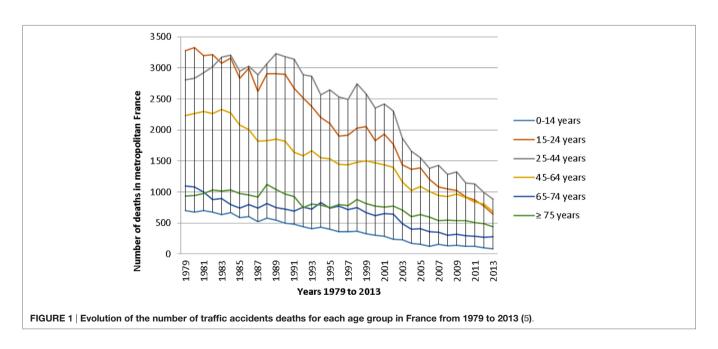
The high levels of risks faced by young drivers are the product of both their own developmental characteristics and their specific environment.

TRAFFIC ACCIDENTS, ADOLESCENCE, AND BRAIN MATURATION

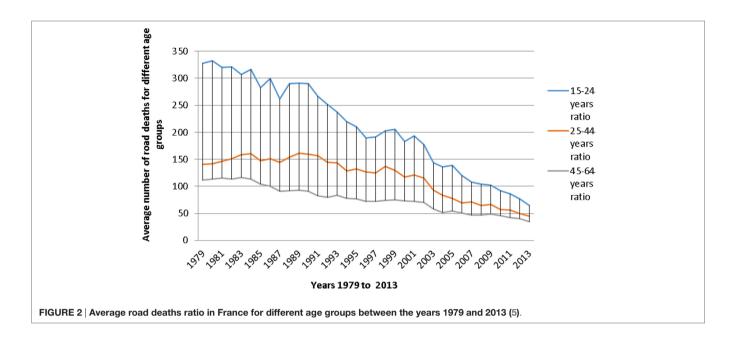
According to Courtois (8), risk taking is normal during adolescence, a distinguished period of an individual's development. It is indeed a phase during which neurological data display a significant maturation of the frontal and temporal lobes. According to Dayan and Guillery-Girard (9), adolescent behaviors (impulsivity, sensation seeking, and risky behaviors) are more frequent between 15 and 25 years, reaching a maximum at 18 years and decreasing after 25 years. These behaviors are related to a major brain reorganization that selectively affects the prefrontal cortex. The specific adolescent behaviors could be the consequence of cognitive control impairment due to this brain maturation. Thus, the cortical structures involved in high-level decision-making processes (prefrontal cortex) become transiently immature. Barbalat et al. (10) imply that adolescents tend to choose riskier options because they feel less risk aversion than adults and devaluate the future consequences of their choices.

From an economic and neurologic point of view, some studies have shown that two cerebral areas are implicated in risk taking (10) as follows.

- The anterior cingulate cortex and the posterior prefrontal cortex whose function is to optimize decision-taking. It allows to normally take advantage of previous unfavorable outcomes and to better manage conflicts between the different choices.
- The insular cortex involved in negative affects such as disgust.
 It inhibits risky decision-making.



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Furthermore, Mantyla et al. (11) conducted an experiment on students to determine whether the development of the executive control system located in the prefrontal lobe could be associated with driving performances. For that purpose, they evaluated young people's driving performances with a driving simulation test and six other experimental tasks. Results showed that individual differences in brain maturation had an impact on driving performance during the simulation task.

Various studies have shown that the dysfunction of these brain regions in adolescents was significantly correlated with behavioral measures of risk taking during the last MRI task. These risk behaviors are as much about substance use, sports accidents as they are about road accidents. Coslin (12) stresses that all risk behaviors reveal a common characteristic: whatever causes them, these conducts can be very destructive for one's self as for others and must be taken seriously. According to this author, the sought sensations associated with these behaviors will tend to be self-reinforcing. Repeated sensation seeking is hypothesized to fill the narcissistic void experienced by a young person passing through an identity crisis, particularly, sensations associated with speed and risks taken on the road.

TRAFFIC ACCIDENTS AND THEIR RISK IN ADOLESCENCE

Adolescence is a transitional period marked by a more in-depth environmental exploration than by safety seeking. Thus, according to Courtois (8), "the most vulnerable adolescents are more likely to implement more dangerous and/or less structured risk behaviors." In fact, for teens entering the new world of adults, their poor knowledge of rules as well as high-risk behaviors increases their frequency of hazard exposures (13).

According to Michel et al. (14), risk behaviors are established during adolescence and are defined as a deliberate and repetitive

engagement in dangerous situations. They are also divided into two types of risk: short-term and long-term risk. The first type leads to behaviors involving the notion of acts and falls directly into the somatomotor register. Here, the alternative is restricted to either victory or failure in terms of accident or death. As for the second type, it reflects the potential danger that occurs in duplicating an activity, such as the one occurring during the repeated use of psychoactive substances. Furthermore, these authors also identified a risk based on the individual's participation in his activity, particularly when it comes to the driver's choice to take risks or not. He could decide to violate safety rules, and in this case, risk taking is considered active and does not solely depend on external factors such as other motorists' driving styles. Thus, risk taking is a decision that involves a choice characterized by a certain degree of uncertainty about the probabilities of failure or success. In fact, Chumpawadee et al. (15) found that Thai students who have engaged in risky behaviors during motorcycle driving were more likely to view these behaviors as normal, in addition to being less likely to have adequate self-control. These authors also found that having a greater awareness of motorcycle accident risk behaviors was significantly associated with a lower risk of engagement in risky behaviors.

Moreover, Pérez-Diaz (16) suggested that it was not only about risk exposure, assessed by the time spent on the road and the type of vehicle, but also about a much more complex genetic predisposition to risk. In fact, it takes into account each person's individual aspects (sensorimotor and intellectual abilities, hyperactivity, aggressiveness, impulsivity, psychopathological aspects such as antisocial behavior trends, etc.), in addition to environmental aspects (influence of family background, peers, etc.). Additionally, Higelé and Hernja (17) concluded that the emotional and psychological components of young drivers' behavior, particularly through their relation to risks, were nowadays identified as being the main causes of these drivers' big involvement in traffic accidents.

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TRAFFIC ACCIDENTS, ADOLESCENCE, AND RISK FACTORS

Accidents and Individual Risk Factors

Accidents and Personality Dimensions

There seems to be two categories of factors associated with car accidents (18). On one hand, there are factors specific to the traffic environment and the vehicle in question, and on the other hand, there are factors linked to "human" determinants (i.e., the driver himself). Generally, the majority of car accidents seem to be associated with the "human" factor. Irritability and anger, for example, are factors included in the latter category. Many researchers have implied that these factors greatly undermine road safety and highlighted their important contribution to car accidents. Along these lines, Chliaoutakis et al. (18) suggested that high involvement of young drivers in car crashes was associated with having no tolerance on the road, getting easily (or without serious reason) irritated, expressing aggression or hostility toward other drivers, not being able to cope with stress, and not being able to control his/her emotions. These results are complementary to those of Norris et al. (19) who found that future motor vehicles accidents were strongly predicted by high hostility combined with poor self-esteem.

Javadi et al. (20) aimed to determine how each of the personality factors, including mental health, depressive disorders, self-esteem, aggression, and parenting, contribute to traffic accidents of young boys aged between 18 and 24 years old. The authors explain that among the mental health aspects, depression is a type of negative emotion, which might negatively affect the driver's interpretation of the traffic environment, his/her driving behaviors and concentration, so that he/she cannot react and behave properly in the required circumstances. Depressed mood and failure schema (which means that failure is inevitable for the individual) could predict violations and mistakes in boys. The authors suggest having a better understanding of the contributing factors in adolescent's driving behaviors and early interventions toward high-risk driving behaviors can help prevent life-threatening consequences in adulthood.

Furthermore, the study by Vassallo et al. (21) showed that the strongest correlations associated with risky driving patterns were antisocial behavior, excessive alcohol consumption, and relational status. Gender, school completion, temperament, civic engagement, and antisocial peer relationships were also correlated with the different patterns of risk behavior.

Moreover, Waylen and McKenna (22) found that risky attitudes toward road use were observed in adolescents long before they learned to drive. Thus, this shows that a driver's risky behaviors are not only the function of being in control behind the wheel but are also determined by individual characteristics. Hence, in order to be effective, preventive interventions must target young people before they are old enough to be allowed to drive

In their review, McDonald et al. (23) identified poor hazard anticipation skills as factors determining young drivers' car crash risk. Few training programs have been developed to improve these skills. All studies included in this meta-analysis found that young drivers showed an improvement in anticipating risk.

However, none of these studies assessed their long-term effects on road accidents.

Accidents and Relation to Speed

Michael et al. (24) evaluated young two-wheeler riders' speeding inclination and other factors linked to it including general attitude to riding, riding behaviors (i.e., engaging in competition and stunts), emotional states associated with riding, motives associated with riding fast, sensation seeking, traffic violations, age, gender, years of riding, riding frequency, and self-report of riding speed. They found that men reported significantly greater inclination to speed than women and that more years of riding were linked to a greater tendency for riding fast. These results are in accordance with the results by Styles et al. (25) who found that more driving years increased drivers' confidence and thus increased their risk taking while driving. Rathinama et al. (26) found similar results in young motorcyclists (aged between 10 and 16 years): the more the child motorcycle rider had experience, the higher was his traffic accident risk. They also found that 35% of boys did not respect safety distances from other vehicles and that 20% of them were already involved in an accident. Michael et al. (24) also pointed out that speeding was related to the emotional states it triggered. In short, driving fast seems to be influenced by psychological factors such as beliefs and perceptions associated with speeding, motives for speeding, and perceived speed and safety. Nevertheless, it is also influenced by behavioral factors such as sensation seeking, risk taking, the desire to reduce travel time, stress, and affect states.

Accidents and Consumer Behaviors

Alcohol Consumption

Previous studies have widely examined the effects of alcohol and drugs on traffic crashes. They highlighted the strongly negative impact the abuse of these substances had on road accidents' incidence.

The SAM study [short for "drugs and fatal accidents" by Elsande et al. (27)] found that the risk of being held accountable for a fatal accident appears to be multiplied by 8.5 times among drivers with a blood alcohol level over the legal limit. This added risk is all the more important given that alcohol consumption is associated with cannabis consumption; here, the risk appears to be multiplied by approximately 15 times. Interestingly, 24% of fatal accidents in 2014 involving individuals aged 18–29 years are associated with the driver having consumed alcohol (28). In this manner, as regularly specified by the French ONISR in its annual reports, alcohol consumption contributes to high rates of fatal accidents mainly caused by speeding, drug consumption, and non-use of seat belts.

According to Waylen and McKenna (22), alcohol greatly increased the probability of having a car accident and the severity of its consequences. Espada et al. (29) added that the occupant of a vehicle is three times more likely to die of a fatal injury after a car accident if having consumed alcohol compared to being sober. In fact, alcohol could impair driving capacities and cause accidents and/or collisions. Indeed, Dang et al. (30) demonstrated a relationship among the precociousness of the first alcohol intoxication and risky behaviors on the road among

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young drivers. Al-Abdallat et al. (31) showed that alcohol use significantly reduced a person's motor skills due to its impact on concentration, alertness level, and reflexes. Brubacher et al. (32–34) found that the risk of car crashes increased with alcohol use and was higher among young drivers. Thus, alcohol seems to be the leading cause of road accidents, being involved in one-third of serious crashes. These authors also found alcohol in 17.8% of injured British Columbia drivers and cannabis in 12.6% of them. Both these substances have been associated with a decrease in psychomotor skills required for safe driving.

It is important to mention the emergence of a particularly singular alcohol consumption among young people: the "binge drinking" phenomenon. In fact, recent European surveys showed an increase in alcohol and cannabis use among teenagers (33, 34). According to the World Health Organization (35), the harmful use of alcohol accounts for a substantial portion of the global burden of disease, in addition to being the third highest premature death risk and disability factor worldwide. In 2004, more than 2.5 million people worldwide have died from alcoholrelated causes, including 320,000 young people aged 15-29 years. These studies pinpointed the common increase among young people of a pattern of excessive alcohol drinking associated with euphoric effects (36). This phenomenon is better known as "binge drinking," a model defined by consuming a maximum amount of alcohol in a minimum time period. It is a different from any other practice related to alcohol consumption. Buelga and Musitu (36) found that 36% of Portuguese and 89% of Danish teens aged 15-16 years had already experienced drunkenness. The effects of this excessive-episodic drinking can lead to very serious brain damage. In their study on 121 participants aged 18-25 years, Bo et al. (37) assessed the effects of binge drinking on cognitive performance. They used the three last questions of the Alcohol Use Questionnaire and combined them into a binge score that was entered as a predictor of cognitive performance. They found that binge drinking significantly predicted faster reaction times and impairment in response adjustment.

Consumption of Psychoactive Substances

Alcohol and drug use are known to increase the risk of traffic crashes, especially among youth (38). Over the past two decades, the prevalence of cannabis and alcohol use in drivers involved in fatal car crashes has increased approximately fivefold from below 2% in 1991 to above 10% in 2008 (39).

In France, despite taking early security measures to decrease drunk driving, the first decree for the systematic search of narcotics among drivers involved in serious road crashes did not appear before 2001. This gap between reforms against alcohol and those against drugs can be explained in several ways. On one hand, society's awareness of the dangers of certain drugs (such as cannabis) took longer to acknowledge than those of alcohol. Indeed, the impact of alcohol's effects could be analyzed as it was listed in the bulletins of accidents indexed by the police for every accident (fichiers BAAC, *Bulletin d'Analyse des Accidents Corporels de la Circulation*, 2005). This was not the case with drugs where information was not available immediately. On the other hand, the resources needed to detect these substances have been placed into service well after those used to test blood alcohol level.

In the study conducted in Jordan, Al-Abdallat et al. (31) showed a link between the use of alcohol and psychotropic drugs and increased road accidents' risks. This is due to the effects of these drugs on the central nervous system by impairing a driver's intellectual functions, judgment, and reflexes. Similarly, the results of the study by Dang et al. (30) showed that factors associated with risky driving behavior are, in boys, having a degree, sports practices, involvement in a fight in the last year, as well as the precocity of cannabis consumption. The latter being one of the major factors involving driving risk taking in girls, with entry into sexuality.

According to a meta-analysis conducted by Gjerde et al. (40), it seems that the combined use of two or more psychoactive substances was significantly associated with higher risks of traffic crashes. In fact, the biggest increase of road accidents was observed when alcohol and drugs were simultaneously consumed. Furthermore, Dubois et al. (39) found that drivers who were positive for cannabis alone had a 16% increase in the odds of an unsafe driving action. However, these odds increased by approximately 8–10% when alcohol and cannabis were combined.

The association between the simultaneous consumption of drugs and higher traffic accidents could be explained by the fact drug use induced greater involvement of youth in other risky behaviors (i.e., night driving, driving in the snow, constant change of radio station, driving above the speed limit) (38).

Accidents and Attention Disorders

Attention Deficit Disorder with or without Hyperactivity

Alcohol and drugs are main factors contributing to accidents, such as highlighted above. However, in Europe and the United States, the greatest cause of deaths seems to be due to unintentional injuries. The risk of these injuries is increased with the presence of an attention deficit hyperactivity disorder (ADHD) (41). Overall, the risk of death is doubled compared to individuals without ADHD, and this risk is even higher 1 year after diagnosis. In fact, the occurrence of this diagnosis in adulthood significantly increased the risk of death compared to its diagnosis in childhood or adolescence. According to Dalsgaard et al. (41), ADHD is closely linked to the use of psychoactive substances. Thus, the combination of ADHD and substance abuse can be particularly dangerous and could potentially increase the risk of a traffic accident and its recurrence. Indeed, Vingilis et al. (42) found that the majority of patients with an ADHD had associated problems such as psychological distress, antisocial behavior, anti-anxiety and antidepressant medication use, substance use disorders, and social problems. Thus, these authors have shown that the status of antisocial personality disorder and cannabis use is significant predictors of road accidents or at least negative driving-related outcomes when associated with ADHD.

Additionally, it seems that teenagers with ADHD are more prone to all sorts of accidents compared to the ones without ADHD (43). Clancy et al. (44) tried to determine whether ADHD adolescents, aged 13–24 years, showed more unsafe road-crossing behaviors than healthy controls. They found that individuals with ADHD had a lower margin of safety and

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evidenced twice as many collisions as compared to controls. In their study, El Farouki et al. (45) hypothesized that ADHD increased the effect of external distractions and traffic crash responsibility. They found that ADHD and external and/or internal distractions were important factors leading to a higher risk of traffic crashes and injuries. This could be due to the fact that participants with ADHD had a greater difficulty in managing the dual task situation, in addition to having insufficient attention and inadequate behavioral responses. It can also be explained by the impulsivity of adolescents with ADHD and their motor coordination difficulties (43). Furthermore, in their meta-analysis of behavioral outcomes and a review of effect size of pharmacological studies, Jerome et al. (46) found that patients with ADHD committed significantly more traffic violations, had less safe driving habits, and were more involved in traffic accidents compared to controls. It could be due to the fact that adults and adolescents with ADHD seem to be more prone to driving anger (aggressive driving), aggression, impulsivity, risk taking, and driving under the influence of alcohol and/or drugs. Nevertheless, some of these results should be interpreted with caution. In fact, another recent meta-analysis by Vaa (47), based on 16 accident studies, showed that all these studies failed to confirm that ADHD drivers had more drunk driving than drivers without ADHD. Smorti and Guarnieri (48) evaluated the contribution of impulsiveness and aggressive and negative emotional driving to predict traffic violations and accidents, taking into account potential mediation effects. They concluded that impulsiveness was not associated, neither directly or indirectly, with traffic accidents. However, it modulated the behavioral and emotional states of young drivers while driving, which in turn could have influenced risky driving.

Consequently, according to Sargant and Finlay (49), health professionals should encourage the management of anger, frustration, and irritability, in addition to implementing an adapted and systematic treatment to decrease the risk of accidents among young people with ADHD.

Mobile Phone Use

The use of a mobile phone has previously often been associated with positive outcomes such as allowing long distance communication (50). However, with time, its use has increasingly been associated with harmful or problematic behaviors. Indeed, according to the French ONISR (51), this emerging factor could be responsible of 25-50% of injury accidents. Additionally, the collective expertise of the French institute of science and technology for transport, development, and networks (52) and the French institute of health and medical research (53) claimed that a phone call could triple the risk of road accidents. In France, the first decree to forbid the use of handheld phones while driving, considered to distract the driver, came into effect in 2003. Many studies have assessed the negative impact of mobile phone use on driving skills. Strayer et al. (54) showed that driving impairments associate with using a mobile phone could be as profound as those associated with driving while drunk.

Saifuzzaman et al. (55) found that mobile phone use while driving was a significant distraction, especially in young drivers, that impaired driving performance, thus becoming a leading

cause of traffic motor vehicle crashes. For example, drivers were more likely to miss traffic signals (stop signs, traffic lights, etc.) and were involved twice as often in car crashes when having a phone conversation while driving. Generally, drivers maintained slower driving speed, larger vehicle spacings, and had longer time headways when engaged in phone conversations. This could suggest possible risk compensatory behaviors associated with phone conversations while driving, or it could be the consequence of the distraction itself on driving performance. Finally, the general conclusion on the effects of mobile phone use while driving suggests that both the use of handheld and hands-free mobile sets significantly increased the risk of having a car accident (56). This is in accordance with the results of the meta-analysis conducted by Caird et al. (57), concerning the effects of cell phones on driving performance. They found that the use of either phone types mentioned above was associated with a mean increase of 40% of reaction time and an accident risk multiplied by 4.

According to Billieux et al. (58), it seems that mobile phone use while driving is associated with a high level of sensation seeking *via* impulsive and dangerous behaviors. Thus, in situations in which the driver needs to concentrate, the consciousness of the risks arising from the situation (i.e., phoning while driving), is likely to create intense excitement.

Accidents and Family Risk Factors Accidents and Family Climate

Additional research tried to identify behavioral and non-behavioral factors among adolescents in relation to traffic accidents. In their longitudinal study on patterns of adolescent psychosocial behavior and substance use of risky driving groups, Bingham and Shope (59) used the Problem Behavior Theory to model risky driving among adolescents and young adults' risky driving from adolescent problem behavior. They found that characteristics of young adults in the riskiest driving groups included a low level of parental monitoring, an increased parental permissiveness, and a weaker social bond. In fact, these developmental traits seem to identify individuals who are likely to endanger themselves and others through risky driving. They are the ones who should receive early interventions to reduce the likelihood of subsequent risky driving.

Furthermore, Taubman-Ben-Ari and Katz-Ben-Ami (60) evaluated family climate in relation to road accidents in adolescents in four different studies. In their first study, they used the "family climate for road safety scale" (FCRSS) to assess seven aspects of the parent–child relationship (i.e., modeling, feedback, communication, monitoring, non-commitment, messages, and limits) and reported the associations between these factors and dangerous driving. In their third study, they found that positive correlations between the FCRSS and youngsters' reported proneness to take risks while driving. These factors were in fact positively associated with various dimensions of family functioning. Finally, in their second and fourth study, they found significant associations between the FCRSS factors and both driving style (risky, angry, anxious, careful) and family cohesion. These studies eventually showed that young drivers who perceived their parents

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as good role models, encouraging autonomy and commitment to safety, and setting clear limits on the infringements of the highway code, tended to take less risks while driving and drove more carefully and less aggressively. However, teenagers who did not perceive their parents as guarantors of their safety may take more risks (61). These studies highlighted the importance of both family climate and environment in a person's risk taking.

These results are in accordance with the study by Sabaté-Tomas et al. (62), who found that family and peers were the most influential factors on the creation of a high-risk profile in young drivers. In addition, driving schools seemed to be the strongest protective factor in preventing the appearance of risky driving profiles. The authors explained that the same driving behavioral pattern was generally repeated in at least two generations in the same family in both the low- and high-risk young drivers' groups. Consequently, high-risk drivers maintained the reckless driving behavior their parents had, whereas low-risk drivers had attitudes to road safety similar their parents.

Curry et al. (63) found that interventions targeting parents and directed toward parents' cognitions, behaviors, and skills allowed the improvement of parental supervisory behaviors during the learning driving stage and at the start of the independent driving stage. These interventions also promoted teen driver's skills acquisition and reduction of their risky driving behaviors.

PREVENTIVE THERAPEUTIC STRATEGIES FOR RECURRENCE OF TRAFFIC ACCIDENTS IN ADOLESCENCE

Current Preventive Strategies

Example of Political Measures: The Graduated Driver Licensing

Accidents involving young drivers resulted in significant morbidity and mortality in France and other countries such as Great Britain, the United States, etc. (64). In the last few years, the GDL program was developed and used in some countries, like United States, Great Britain, Canada, South Africa, and Australia, in order to address this scourge. It allowed drivers to gain experience in low-risk driving conditions by adding an "intermediate" phase between the learning stage and the acquisition of the driving license. This new licensing program required young drivers to advance through several stages where they were subject to a variety of restrictions that reduced their exposure to high-risk driving conditions (i.e., adult supervision, daytime driving, passenger limits, etc.) (65). Kaafarani et al. (66) aimed to determine the effect of this 2007 law on the incidence of total motor vehicle crashes and accidents they called "fatal" motor vehicle crashes among drivers aged between 16 and 29 years, divided into three age groups (16-17, 18-20, and 25-29 years). They found that total motor vehicle crashes significantly decreased following the law for all three age groups, with a greater decrease in the 16-17 years (37%) and the 18-20 years (25%) compared to the 25-29 years (15%). The rates of fatal motor vehicle crashes also significantly decreased in all three groups. Thus, it seemed that this type of political measure was able to decrease the accident rates among youth.

Moreover, the effectiveness of the GDL programs varied according to its components. Chen et al. (67) showed that the comprehensive GDL programs were associated with a 20% reduction in 16-year-old drivers' fatal crash involvement rates. The greatest benefit appeared to be associated with programs that included age requirements and a waiting period of 3 months and above before the intermediate stage, nighttime driving restriction, and either 30 h or more of supervised driving or passenger restrictions.

In an effort to improve the quality of the experience of young drivers during the mandatory supervised driving period, a new program entitled "Green Light for Life" was conducted in 2005 in Israel. This program included a meeting with the young driver, his parents, and a supervisor, during which guidance was given regarding the best practices for the accompanied driving period, as well as advises for dealing with in-vehicle parent-teen dynamics. In order to evaluate the effectiveness of the program, Toledo et al. (68) compared official crash records of young drivers who participated in the program with crash records of all other license holders at the same period. The analysis indicated a significant 10% decrease of crash records for those who participated in the program, within 24 months after obtaining their driving license. Therefore, this program seemed to raise awareness to the importance of the accompanied driving phase in order to reduce the incidence of young drivers' road accidents.

In addition, the GDL is unique in the history of road safety *via* its great impact on the targeted group, in one U.S. state, showing a steady decrease of teens drivers' accident risks by at least 25% (69). The implementation of GDL programs could therefore save a substantial number of lives. In fact, several studies evaluating many angles of the GDL confirmed its effectiveness. In their study, Jones et al. (64) found that this program could prevent up to 114 deaths and 7,366 victims per year in Great Britain. According to Foss (70), improving the functioning of GDL programs would probably require a better understanding of adolescent driving behaviors.

Finally, according to Chen et al. (67), pediatricians and family physicians could play an important role in working with legislators to implement GDL programs by encouraging parents of young drivers to enforce the requirements of GDL.

Advertising Campaigns for Road Safety

Regarding road-related risks, many studies showed that the effectiveness of educational and preventive road safety programs is yet to be confirmed (71). Despite the popularity of road safety advertisements, speeding is still considered socially acceptable. The lack of efficiency in advertising campaigns could be due to the fact they are often based on intuition rather than principles of psychology. Thus, they seemingly fail to target the right factors (72). In fact, advertisement and educational campaigns in favor of road safety are primarily based on persuading drivers in complying with speed limits (by providing drivers, for example, with information about speeding consequences).

Although there is still no consensus on the effectiveness of road safety preventive strategies, research showed that advertising based on threats (highlighting dangers such as being injured Gicquel et al. Traffic Accidents' Reccurence in Youth

or killed in a crash) was very effective (73). In fact, the technique incorporating physical threats of death and injuries in advertisements increased the intensity of emotional and cognitive responses compared to advertisements based on less threatening and more informative or humorous messages.

A study in Quebec conducted by Daignault and Paquette (74) also examined the effectiveness of threatening advertisements by evaluating television messages varying on 3° of realism (symbolic/realism/hyperrealism). They found that messages illustrating a threat in a hyperrealistic manner were the most effective at highlighting the importance of emotional and cognitive processes related to advertising information processing.

Current Therapeutic Strategies

Twisk et al. (75) tested five road safety educational programs for pedestrians and cyclists. Three programs were based on a cognitive approach (road safety education, practical exercise, stimulation of empathy...), whereas the two others were based on fear or negative emotions. Young people, aged 12 and 18 years, were divided into five groups according to their age and each age group received one of the five programs. Results showed that the three programs based on road safety education significantly improved self-reported safety behavior. It would, however, be interesting to compare the effect of these educational programs on other groups of the same age.

Young people generally achieved a psychological balance in their lives by experimenting risk taking behaviors. This process is a personal exploration of their identity while seeking for their autonomy (14). Carbone (76) insisted on implementing psychological counseling for young drivers following an accident. This is mainly the reason why she proposed the inclusion of a support group for hospitalized adolescents after an accident. The author indicated that teens communicated their experiences of fear, loneliness, and danger. In fact, the experience of speaking in a peer group in the presence of a therapist confirmed the important need of these teenagers to express themselves while being supported by an adult.

Preventing Recurrence of Traffic Accidents in At-Risk Adolescents and Young Adults: Protocol ECARR2

To compensate for the lack of effectiveness of road safety campaigns and considering the well-established interest in psychological group care during adolescence, we decided to evaluate an innovative strategy: a postaccident group therapeutic intervention aimed at preventing recurrence of traffic accidents. For this to happen, we proposed a randomized, multicenter, interventional, case–control study in the west of France.

Every teenager included in the experimental group would attend three group sessions 1 month after being involved in an accident. Each group session would be 1 week apart and would consist of integrative sessions combining motivational interviewing and cognitive-behavior therapy.

The ongoing study started in January 2016 and included 12 adults and pediatrics emergency departments in the West of

France. Its main purpose is to show a minimum decrease, at 12 months after study inclusion, of 20% in the number of traffic accidents in a group of adolescents and young adults involved in a road accident and with a high risk of recurrence. To do so, we will compare two groups of patients at high risk of recurrence: a group receiving therapeutic prevention intervention and a control group. The intervention will consist of three sessions per week for three consecutive weeks. The inclusion period is estimated to last 1 year in order to include 300 participants, divided equally in the two groups mentioned above. Each patient will be followed up for 1 year after his/her initial inclusion in the study. In addition, all participants will be evaluated by phone at three (T3), six (T4), and 12 (T5) months after their inclusion.

Ultimately, from a public health perspective, proving the effectiveness of this program could allow it to be generalized in France.

CONCLUSION

This work analyzes some factors involved in traffic accidents in youth. Two categories of factors seem to be associated with traffic accidents: (1) factors specific to the traffic environment and (2) "human" factors, which seem to be the most influential.

Some interventional driving strategies and preventive measures have reduced the risk of traffic accidents among young people; so far, few therapeutic approaches have been implemented. We decided to set up an innovative strategy consisting of a therapeutic postaccident group intervention, ECARR2 to prevent recurrence among adolescents and young adults identified at risk, taking into account the multiple risk factors.

AUTHOR CONTRIBUTIONS

LG determined the topic, managed this review, corrected, and translated it and is organizing the associated research. PO, EB, and CT contributed to bibliographic researches and to the redaction of the article. LR contributed to bibliographic research and redaction of the article.

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Hoarding Disorder: A Case Report

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Hoarding disorder is characterized by a persistent difficulty discarding items, the desire to save items to avoid negative feelings associated with discarding them, significant accumulation of possessions that clutter active living areas and significant distress or impairment in areas of functioning. We present a case of a 52-year-old married man who was referred to the psychiatry department for collecting various objects that were deposited unorganized in the patient's house. He reported to get anxious when someone else discarded some of these items. This behavior had started about 20 years earlier and it worsened with time. The garage, attic, and surroundings of his house were cluttered with these objects. On admission, in the mental status examination, it was observed that the patient was vigil, calm, and oriented; his mood was depressed; his speech was organized, logic, and coherent; and there were no psychotic symptoms. A psychotherapeutic plan was designed for the patient, including psychoeducation, cognitive restructuring, and exposure to discarding objects. A pharmacological treatment with fluvoxamine 100 mg tid and guetiapine 200 mg was added to the therapeutic plan, with the progressive improvement of the symptoms. Nine months later, the patient was able to sell/recycle most of the items. Studies evaluating treatment for HD are necessary to improve the quality of life of the patients and to reduce the hazards associated with the disorder.

Keywords: hoarding disorder, obsessive-compulsive disorders, antipsychotics, psychotherapy, clinical case study

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INTRODUCTION

The concept of hoarding was defined in 1996 as a behavioral phenomenon of acquisition of objects and failure to discard objects (1).

Compulsive hoarding was first included as diagnostic criteria for obsessive–compulsive personality disorder in the Diagnostic and Statistical Manual of Mental Disorders—third Edition Revised. Clinical hoarding began to be considered secondary to some disorders, such as dementia, residual schizophrenia, eating disorders, brain injury, autism spectrum disorders, or compulsive buying (2). Later, hoarding was considered a subtype or dimension of obsessive–compulsive disorder (OCD), with this behavior being seen in about 18–40% patients (2). However, hoarding would be seen frequently independent from other psychiatric disorders. After focusing on the epidemiological, phenomenological, and neurobiological aspects of hoarding, hoarding disorder (HD) was included as an isolated entity, in OCD spectrum, in the Diagnostic and Statistical Manual of Mental Disorders fifth Edition (DSM-V). The criteria for diagnosis of HD in DSM-V are a persistent difficulty discarding items, the desire to save items in order to avoid negative feelings associated with discarding them, significant accumulation of possessions that clutter active living areas, and significant distress or

TABLE 1 Diagnostic criteria for Hoarding disorder in the Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM-V).

- A Persistent difficulty discarding or parting with possessions, regardless of their actual value
- B This difficulty is due to a perceived need to save the items and to distress associated with discarding them
- C The difficulty discarding possessions results in the accumulation of possessions that congest and clutter active living areas and substantially compromises their intended use. If living areas are uncluttered, it is only because of the interventions of third parties (e.g., family members, cleaners, and authorities)
- D The hoarding causes clinically significant distress or impairment in social, occupational, or other important areas of functioning (including maintaining
 - a safe environment for self and others)
- E The hoarding is not attributable to other medical conditions (e.g., brain injury, cerebrovascular disease, and Prader–Willi syndrome)
- F The hoarding is not better explained by the symptoms of other mental disorders (e.g., obsessions in obsessive–compulsive disorder, decreased energy in major depressive disorder, delusions in schizophrenia or another psychotic disorder, cognitive deficits in major neurocognitive disorder, and restricted interests in autism spectrum disorder)

impairment in areas of functioning (**Table 1**) (3). Usually, these items are perceived to be useful in the future or to be esthetic or cause an emotional attachment (1, 4). If clutter is severe, it can cause threats to public health and safety (such as fire hazards and falls) (5).

In contrast to hoarding in OCD, the thoughts of not discarding in patients with HD are not considered by the patients to be intrusive, repetitive, or egodystonic (6). Besides, stress in HD is associated with the consequence of the clutter of the items and not related to the content of the thoughts associated with the reasons to not discard objects.

Compulsive hoarding affects about 2–5% of the population (7–9). Hoarding behaviors usually start at a subclinical level in early adolescence and worsens with each decade (10–12). Often the disorder becomes clinically significant only in middle-aged patients, with the distress associated to HD being caused by the intervention of others, such as relatives or local authorities (13). Stressful or traumatic events may be associated with the onset of hoarding symptoms (11).

Other psychiatric disorders often co-occur with HD. The most frequent comorbidity is a major depression, which can be present in up to 50% of the cases (14). Attention deficit/hyperactive disorder (ADHD) is also a common comorbidity with HD, with some studies suggesting association with inattentive symptoms of the disorder (15). Poorer general health is also associated with HD (16).

The cognitive behavioral model conceptualized for HD proposes that compulsive hoarding develops through emotional responses associated with the beliefs about possessions. This model proposes (1, 17):

 Information processing deficits (including avoiding/delaying decisions with fear of making wrong decisions, self-report of inattentiveness and difficulty remembering/recording memories, and deficits in categorization/organization).

- Emotional attachment and beliefs (of responsibility and control) for the possessions.
- 3. Maladaptive behavioral patterns (avoiding discarding objects which is associated with negative emotions, and acquiring and saving associated with positive emotions).
- 4. The cognitive behavioral treatment (CBT) designed to address HD involves assessment and psychoeducation on symptoms, motivation enhancement, cognitive restructuring, exposure to non-acquiring, and discarding and prevention of relapse (17, 18). One meta-analysis that focused on the results of CBT in patients with HD showed that symptoms decrease significantly after treatment with large effect size, especially with the difficulty to discard component of the disease (17). In the same study, rates of clinically significant changes were modest, with most patients continuing to score in the clinical range at posttreatment (17). Pharmacological treatment of HD disorder is not well established, since most studies evaluating treatment were made in patients with an OCD diagnosis with a hoarding component. Most of these studies used serotonin reuptake inhibitors, and the results were associated with poor response to treatment (19). A meta-analysis evaluated the effect of pharmacotherapy in patients with pathological hoarding (either diagnosed with OCD with hoarding component or HD) and response to treatment observed was 37-76% (20). In this study, only two studies focused on patients with HD. An open label trial used venlafaxine in monotherapy, in which 70% of the patients were classified as responders (decrease of ≥30% in the UCLA Hoarding Severity Scale and Saving Inventory—Revised and at least "much improved" on the Clinical Global Impression-Improvement) (21). The second study, a case series (n = 4) using methylphenidate, since there are some studies that point out the association between HD and ADHD, did not have significance in the resolution of hoarding symptoms (22).

CASE REPORT

We present a case of a 52-year-old married man, who has the sixth grade, and works as a mechanic. He has no previous history of medical conditions. As a psychiatric background, he reported depressive symptoms following the death of his only son 22 years ago.

The patient was referred to treatment at the psychiatry department of Hospital de Braga for the first time by his family doctor for collecting various objects, predominantly stones, papers, and damaged pieces of cars that were deposited unorganized in the patient's house. The patient collected these items because he thought they were valuable and/or usable in the future, but recognized that the collection was exaggerated. He could not discard any of these items, even if he never used them when needed. He reported to get anxious when someone else discarded some of these items. This behavior had started about 20 years earlier and it worsened with time. Despite, the thoughts of the possible use of these items were the reason why he could not throw out the possessions, these thoughts were not considered intrusive, repetitive, or egodystonic. The garage, attic, and surroundings of his house were cluttered with these objects (Figure 1). The clutter in his

house is classified in to seven categories according to the clutter image rating (23, 24).

On admission, in the mental status examination, it was observed that the patient was vigil, calm, and oriented; his mood



FIGURE 1 | Patient's house at beginning of medical intervention. Photo was taken and provided by patient. Consent for publication was obtained.

was depressed; his speech was organized, logic, and coherent; and there were no psychotic symptoms.

A psychotherapeutic plan for the patient was designed. The goals were to understand and educate the patient on his symptoms and beliefs, so he could understand the need of treatment. Cognitive restructuring of the beliefs and exposure to non-acquire and discard the objects saved were also explored. Along with the psychotherapeutic plan, a pharmacological treatment with fluvoxamine 100 mg id and trazodone 150 mg id was made, to treat the coexistent depressive symptoms and insomnia. During the first 6 months of treatment, the patient continued to buy and collect objects. Then, fluvoxamine was gradually augmented to 100 mg tid and quetiapine 200 mg was added to the treatment plan, with progressive improvement in the symptoms and the patient being able to sell/recycle most of the items after 9 months of this treatment (Figure 2). The patient is currently medicated with quetiapine 100 mg id for insomnia and organized the spaces cluttered (Figure 3). The patient and his wife were very gratified with the results.

This study was performed in accordance with the provisions of the Declaration of Helsinki 2008 and was approved by the ethics eommittee of Hospital of Braga. We obtained informed written consent from the patient authorizing publication of

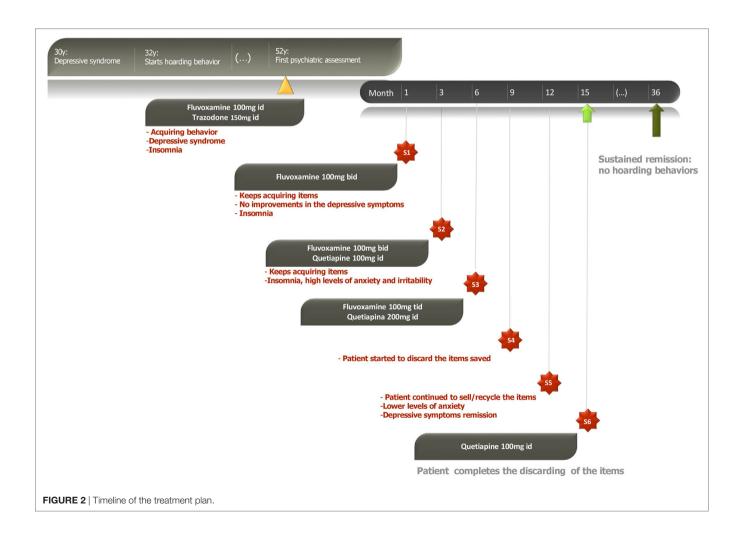




FIGURE 3 | Patient's house after medical treatment. Photo was taken and provided by the patient. Consent for publication was obtained.

clinical case and his photographs. His anonymity has been preserved.

DISCUSSION

We presented a patient who suffered from HD. The case was managed with both pharmacotherapy and a reduced number of psychotherapeutic sessions, which may be of interest in times of restrictions on available psychiatric and psychotherapeutic resources.

The clinical features of his object hoarding showed a typical pattern. The patient had an inability to discard objects and had an accumulation behavior with a long evolution over time. He was referred to the psychiatric treatment about 20 years after the beginning of the accumulation symptoms. Delay in seeking treatment for HD is very common and, if not treated, the evolution of the disorder occurs with progressive worsening of the behaviors.

The possessions collected did not have any value, and the thought that the possessions may be needed in the future did not have any characteristics of an obsession, such as being repetitive or egodystonic. In the same vein, the anxiety caused by the disorder was associated with the fact that he did not want to get rid of the items because he thought they could be valuable and no thought of something bad could happen, as typical in OCD. In addition, collected items disturbed the normal organization of his house and were cluttered.

Interestingly, the accumulation behavior began a few years after the death of his son. In fact, HD onset (as other obsessive-related disorders) is commonly associated with chronic stress and important life events (11, 25).

Hoarding disorder is mainly treated with CBT, including psychoeducation, motivational interviewing, classic cognitive techniques focused on dysfunctional beliefs, and exposures targeting sorting and discarding. Patients could also benefit with some pharmacological interventions.

In the presented case, the psychotherapeutic plan included a reduced number of sessions (basically due to limitations on available resources) and a combined pharmacologic approach.

Although no medications are currently marketed to treat HD, some studies identified benefits with the use of serotoninergic drugs in this disorder as in other disorders of the obsessive spectrum (19, 26). Treatment with fluvoxamine was chosen, not only for its characteristics of reduction of anxiety but also to address insomnia and depressive symptoms presented by the patient. Given that the patient did not tolerate trazodone, it was necessary to optimize the treatment for this problem, which constituted an opportunity for the use of quetiapine. Although there are no studies to evaluate the efficacy of quetiapine in this disorder, this case study illustrates its benefit that besides improving the sleep it seems to have contributed to lower the levels of anxiety in this patient.

Overall, the conjugation of described psychotherapeutic and pharmacotherapeutic approach contributed to significant improvement of the patient's symptoms until sustained remission.

Future studies regarding the treatment of HD are necessary to address the difficulties of these patients and to improve their quality of life.

ETHICS STATEMENT

This study was performed in accordance with the provisions of the Declaration of Helsinki 2008 and was approved by the ethics Committee of Hospital of Braga. We obtained informed written consent from the patient authorizing publication of clinical case and his photographs. His anonymity has been preserved.

AUTHOR CONTRIBUTIONS

DV and PM observed the patient, collected and analyzed the data. DV, JG, and PM wrote the paper. All authors approved the final work.

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Integrative Understanding of Familial Impulsivity, Early Adversity and Suicide Risk

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Introduction: Impulsivity is a core characteristic of bipolar disorder and it was observed as elevated in individuals with the disorder and in their relatives. Both impulsivity and history of maltreatment are risk factors for suicide attempts, however, these two key variables may not be independent, given the fact that parental impulsivity and associated social context could increase the risk of child maltreatment. In this study it was examined the association between the impulsivity of relatives and child maltreatment taking into consideration the conjoint and unique effects of these two variables on the risk of suicide attempts among the patients.

Materials and Methods: Participants of the study consisted of 117 patients diagnosed with bipolar disorder and 25 first-degree relatives. Linear regression model was conducted to describe associations between facets of impulsivity of relatives and levels of child maltreatment reported by patients. The independent associations of suicide attempt history with the dimensions of impulsivity of the patient and maltreatment were tested by multinomial logistic regression.

Results: Impulsivity of relatives and, more specifically, inhibitory control can predict the maltreatment of the patient. Inhibitory control and emotional abuse were related, conjointly, to a greater likelihood of having a history of more than one suicide attempt.

Discussion: Considering that the impulsivity of relatives predicts child maltreatment, it is possible that a genetically shared impulsivity is an underlying feature associated with the history of multiple suicide attempts. These findings highlight the importance of considering child maltreatment, impulsivity and suicide attempt history in integrative models.

Keywords: bipolar, impulsive behavior, suicide, attempted, relatives, child maltreatment

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INTRODUCTION

Bipolar bisorder (BD) consists of a heterogenic group of mood pathologies, which varies in terms of amount and severity of depressive and/or manic episodes, presence of psychotic symptoms, comorbid diagnostics, number of hospitalizations and suicide risk.

There are at least two main BD subtypes. *Bipolar I* disorder is characterized by the presence of at least one manic episode. Mania, in turn, is characterized by a period of at least 1 week of elevated, expansive or irritable mood, increased energy, and more talkativeness and engagement in risky activities (American Psychiatric Association [APA], 2013). *Bipolar II*

is described as the presence of at least one previous major depressive episode for at least 2 weeks and one hypomanic episode that lasts a minimum of 4 days (American Psychiatric Association [APA], 2013).

Approximately one quarter of patients with *Bipolar I* report suicide attempts (Merikangas et al., 2011) and suicide accounts for 10 and 6.7% of deaths in *Bipolar I* and *II*, respectively (Angst et al., 2013). Hence, BD presents the highest absolute risk of suicide among different psychiatric conditions (Nordentoft et al., 2011). The focus of this paper is to understand the conjoint effects of two key factors for suicidality within BD: child maltreatment and impulsivity. With the aim to shed light into how impulsivity, maltreatment and suicidality interact, the goal of this study is to develop and test a more integrative model of these variables.

Impulsivity is considered to be a core feature of BD (Swann et al., 2003). To begin with, the diagnostic criteria for mania involves impulsivity. Even after manic episodes clear out, however, a growing body of research suggests that high levels of impulsivity persist (Swann et al., 2003). It is also noteworthy that impulsive behaviors can be transmitted through generations since it is observed to be elevated even in family members who do not meet diagnostic criteria for BD (Fortgang et al., 2016). According to the Self-Regulation Intergenerational Transmission Model, the diminished self-regulation that contributes to impulsive behavior is multifactorial, involving prenatal, social mechanisms of transmission, such as marital and parentchild interaction, as well as neurobiological mechanisms (Bridgett et al., 2015). Impulsivity is associated with low quality of life (Victor et al., 2011) and dysfunctional behaviors such as aggressiveness within BD (Johnson and Carver,

Particularly, impulsivity seems to be related to suicidality within BD (Johnson et al., 2016). Impulsive behavior triggered by emotion is related to history of suicidal ideation, self-harm, and suicide attempt in BD (Johnson et al., 2016) and also among those without BD (Kasen et al., 2011; Black and Mildred, 2013; Auerbach et al., 2016). These findings converge with the results of a longitudinal study, which indicates that impulsivity may predict suicide attempts over a 15-year period in the general population (Kasen et al., 2011).

A separate literature indicates that early adversity and maltreatment are major concerns within BD. Rates of child abuse and neglect are quite high in those with the disorder, with exposure estimates as high as 51% (Daruy-Filho et al., 2011). Early adversity and maltreatment have been associated with early bipolar onset and also to contribute to a poor prognosis within BD, including more symptom severity, more relapse and lower levels of functioning (Daruy-Filho et al., 2011). Child maltreatment is also a predictor of the risk of suicide within BD (Norman et al., 2012). Indeed, a wide range of forms of child maltreatment, including sexual abuse, emotional abuse, physical abuse and emotional neglect, have been individually associated with the risk of attempted suicide within BD (Norman et al., 2012).

Although both impulsivity and childhood adversity seem to be important in understanding bipolar suicidality, these two variables have been studied separately in the literature on BD. However, it is possible that impulsivity among family members may increase the risks of exposure to childhood adversity in offspring.

Considering this background, it was hypothesized that patients whose relatives have high levels of impulsivity may be in a social context that could increase the risk of abuse. First, the degree of overlap of early adversity and impulsivity among individuals with BD was assessed, then the conjoint and unique effects of early adversity and patient impulsivity as correlates of suicide attempt were considered. That is, it was examined: (1) whether the impulsivity of relatives can predict the levels of child maltreatment; (2) the extent to which the impulsivity of the patients and maltreatment dimensions are associated with suicide attempts.

MATERIALS AND METHODS

Sample

The sample consisted of a group of 117 bipolar patients and 25 first-degree relatives. The inclusion criteria taken were being aged between 18 and 60 years. Exclusion criteria were based on neurological conditions. The bipolar group consisted of individuals who had been previously diagnosed with BD by a psychiatrist and were being treated in a bipolar outpatient clinic which is part of Brazilian Public Health System. The bipolar diagnosis was confirmed through the administration of the MINI Plus 5.0 diagnostic interview (Sheehan et al., 1997). Each patient was asked to indicate a first-degree adult relative to compose the sample of relatives. However, only part of them attended to the scheduled appointment. Only a few of them met the inclusion criteria, resulting in a small sample of 25 relatives. Inclusion and exclusion criteria were the same applied to patients with the addition that they could not present psychiatric diagnosis, assessed by the administration of MINI Plus 5.0 diagnostic interview (Sheehan et al., 1997). First degree relative was considered as being parents' siblings or children of patients. No more than one relative per patient was assessed. Fifteen of the 25 relatives assessed were parents of patients, on the majority being their mothers. The Ethics Committee of the Federal University of Minas Gerais approved this study (N° 064/09) and all of the participants filled a written informed consent procedures before taking part in the study procedures.

Measures

Interviews and instruments were administered to patients in order to assess impulsivity, child maltreatment, suicide attempt history and mood states. Family members completed parallel measures of their personal levels of impulsivity and mood states.

Barrat Impulsiveness Scale – BIS – 11 (Patton et al., 1995)

The BIS – 11 is a 30-item self-rated scale designed to assess impulsive thought and behavior. The Brazilian version of the scale was used, which has already been validated (Malloy-Diniz et al., 2010, 2015). Previous analysis identified two factors from the extracted of the Brazilian version of the scale:

Inhibition control ($\alpha=0.79$), defined as the ability to inhibit a proponent behavior and attentional control, and Non-planning ($\alpha=0.62$), defined as the decision making that requires costbenefit evaluation between short and long term consequences within an emotional context (Malloy-Diniz et al., 2015).

Childhood Trauma Questionnaire – CTQ (Bernstein et al., 2003)

The CTQ is a 28-item self-report questionnaire of frequency of traumas experienced before the age of 12, in 5-point likert scale, ranging from *never* to *always*. The Brazilian version of this scale was taken into consideration, which presents five subscales: emotional ($\alpha = 0.88$), physical ($\alpha = 0.92$), and sexual abuse ($\alpha = 0.97$), as well as emotional ($\alpha = 0.94$) and physical neglect ($\alpha = 0.66$), (Grassi-Oliveira et al., 2006, 2014).

Suicide attempt history Suicide attempt history was assessed through a self-report question that classified patients as those who never attempted suicide, the ones that attempted once or those who attempted more than once. The question was "Have you ever attempted suicide?" The patient was asked to mark one of three options: Never attempted suicide, attempted once, attempted more than once. In the end, suicide attempt was defined as an act with clear intention to kill oneself.

Beck Depression Inventory – BDI (Beck, 1961)

The BDI is one of the most commonly used self-rated depression scales. The 21-item cover depressive symptoms such as energy level, hopelessness, suicide ideation and self-punishment. Each item is rated on a scale of 0–3 and higher scores reflect greater depression severity. The Brazilian version shows internal consistency of 0.81 (Gorenstein and Andrade, 1996).

Young Mania Rating Scale – YMRS (Young et al., 1978)

The YMRS scale is a semi-structured interview and rating system used to quantify severity of mania symptoms observed during clinical interview and in the past 48 h. It consists of 11 questions that asses mood, activity level, psychomotor agitation, sexual interest, appearance, irritability, insight, sleep, aggressiveness and content of thoughts. Each item is scored on a scale of 0–4, with the exception of items assessing irritability, speech, content of thoughts and disruptive behavior. These have double the scoring weight and are scored from 0 to 8. Maximum score possible is 56 points. A trained clinician who had at least 2 years of experience in a bipolar outpatient clinic completed the interview and ratings. The Brazilian version of YMRS was used, which presented intraclass correlation coefficient of 0.80 and internal consistency of 0.67 (Vilela et al., 2005).

Statistical Analysis

All of the statistical analysis were performed in SPSS software, version 21.0. The following methods were selected to describe the associations of (1) impulsivity of relatives and levels of child maltreatment of patient; and (2) impulsivity and maltreatment dimensions of patient with history of suicide attempts and its reoccurrence. Since the sample size was unbalanced for

relatives and patients, the analysis were divided in those two steps. First, principal components factor was conducted, using the oblimin rotation on the child maltreatment items of all 117 patients, in order to determine the number of statistically independent dimensions of trauma and reduce subsequent dependent variables in subsequent linear regression model. This was considered a preliminar requirement for step one, since the sample size was not enough to allow consideration of all dimensions of maltreatment as a dependent variable in further regression.

To examine the effect of impulsivity of relatives scores on child maltreatment of patients, a linear regression model was conducted with both BIS factors as independent variables. This step considered 25 patients and their respective relatives.

As a second step, a multinomial logistic regression model was computed to assess whether maltreatment and impulsivity predicted suicide attempt history among the 117 individuals with BD. The targeted categories were *No history of suicide attempt;* One previous suicide attempt; and More than one previous suicide attempt.

Depression and mania ratings were considered as potential confounds and were controlled as needed in both steps.

RESULTS

The demographic characteristics of the sample, as well as levels of impulsivity and child maltreatment, are described in **Table 1**. Approximately 67% of the patients met diagnostic criteria for *Bipolar I* and 32.3% for *Bipolar II* disorder.

Principal Components Analysis of the Childhood Abuse Scale

Principal component analysis are shown in Table 2. The results showed no multicollinearity and the sample size was in accordance to Kaiser-Meyer-Olkin measure of sample adequacy (KMO = 0.71), and KMO for individual variables were equal or higher than 0.67. Sphericity as tested by Bartlett's test indicated that the correlations between variables were adequate for Principal Components Analysis ($X^2 = 177.41$, df = 10, p < 0.001). One factor surpassed Kaiser's criterion of Eigenvalue higher than 1 and explained 52.58% of the variance. Considering that the statistical requirements to consider maltreatment as an unique factor were met, maltreatment was taken as one factor on analysis regarding associations between impulsivity of relatives and maltreatment. These results show that the frequency of specific types of maltreatment are not dissociated from others. That is, those patients who tend to experience elevated levels of one type of maltreatment may also have higher probability to experience other forms of it.

Impulsivity of Relatives Levels Correlate with Levels of Childhood Maltreatment of Patients

Before conducting the analysis of the impulsivity effects, potential confounds of manic (YMRS) and depressive (BDI) symptoms

were considered by testing correlations with maltreatment of patient scores. Neither the YMRS, r (DF) = -0.07 (24), p = 0.74 nor the BDI, r (DF) = 0.31 (24), p = 0.13 were correlated with maltreatment. More specifically (as shown in **Table 3**), results of the linear regression show that first-degree BIS Inhibitory Control scores of relatives correlate significantly with patient report of General maltreatment, although Non-planning scores did not contribute to additional variance. Impulsivity of relatives explains a considerable proportion of the variance, r^2 = 0.30, N = 25, p < 0.05. Therefore, relatives impulsivity of relatives accounts for 30 percent of variance in self reported levels of maltreatment, showing that inhibitory control in relatives seem to impact on frequency of perceived maltreatment of patients.

TABLE 1 | Sample characteristics.

	Patient	Patients (N = 117)		es (N = 25)
	N	%	N	%
Level of education				
Secondary education or below	69	58.9	15	60.0
Partial undergraduat	14	12.0	4	16
Undergraduate	29	24.8	5	20.0
Graduate degree	5	4.3	1	4
Gender – Women	78	66.7	17	68.0
Suicide attempt history				
No history of suicide attempt	81	69.2	_	-
One previous suicide attempt	20	17.1	_	-
More than one previous suicide attempt	16	12.7	-	-

	Mean	SD	Mean	SD
Age	43.60	12.16	41.89	15.75
Beck Depression Inventory	14.34	11.29	11.32	10.67
Young Mania Rating Scale	1.90	3.18	3.09	3.86
BIS - Inhibition control	40.55	9.14	35.52	6.96
BIS - Non-planning	23.87	6.01	25.28	4.54
Physical neglect (3 items)	4.60	1.96	-	-
Emotional neglect (7 items)	13.87	6.12	-	-
Physical abuse (5 items)	7.99	3.92	-	-
Emotional abuse (5 items)	10.32	4.99	-	-
Sexual abuse (5 items)	6.85	3.80	-	-

TABLE 2 | Factor loading of Childhood Trauma Questionnaire subscales

Subscale	Factor 1: Maltreatment
Emotional neglect	0.877
Physical neglect	0.736
Emotional abuse	0.802
Psysical abuse	0.699
Sexual abuse	0.431

Extraction Method: Principal Component Analysis. Rotation Method: Oblimin with Kaiser Normalization.

Maltreatment of Patients and Impulsivity Predict the Number of Previous Suicide Attempt

As shown in **Table 4**, multinomial logistic regression was performed with BIS and Maltreatment scores as predictors of suicide attempt (never, once, more than once) as an outcome variable. Diminished inhibitory control was robustly correlated with number of suicide attempts, distinguishing specifically those who attempted suicide once or more from those who never attempted.

Child Maltreatment scores were considered separately to provide richer information regarding factors associated with presence and/or recurrence of suicide attempt. Only the Emotional abuse factor was significantly related to suicidality and it was only significant in differentiating repeated attempters from those with only one attempt. The correlations between impulsivity and maltreatment dimensions are shown in **Table 5**.

DISCUSSION

Many studies indicate that impulsivity and early adversity experiences are both correlated with suicidality within BD. Despite evidence that familial impulsivity may feature a context prone to greater risk of abuse, researchers have tended to consider these two variables separately. The goal of this study was to develop a more integrative understanding of familial impulsivity and early adversity, and also to consider whether patient's impulsivity and abuse contributed independently to the risk of suicide attempts for individuals with BD. Since those that repeatedly attempted suicide may represent a subset of more severe patients, beyond discrimination of the presence of suicide attempt history, it was also an aim to describe aspects that could account for reincidence of suicide attempt.

Our findings confirmed that problems of patients with inhibitory control were tied to suicidality. Furthermore, findings extended previous work outside the BD diagnosis by showing that poor inhibitory control in relatives was related to the frequency of child maltreatment experienced by patients. Although these findings do not test direct influences of impulsivity of relatives and risk of suicide attempt in patients, it highlights that emotional abuse is related to a greater risk of recurrent suicide attempts even after accounting for deficits in inhibitory control in patients. These novel findings provide initial data to foster investigations on further unified and transgenerational perspective on impulsivity, adversity and suicidality.

TABLE 3 | Linear regression of Family Impulsivity Scores as Predictors of Maltreatment of Patients Scores (N = 25).

	В	SE B	b
Constant	-0.10	1.12	
BIS - Inhibitory Control	0.05	0.02	0.43*
BIS - Non-Planning	-0.06	0.03	-0.36

 $r^2 = 0.30$, N = 25, *p < 0.05.

This study, such as previous ones, suggests that the effects of impulsivity on suicidality within BD do not seem to generalize across measures of impulsivity, which indicates that it must be considered a multifaceted construct (Malloy-Diniz et al., 2009, 2011; Watkins and Meyer, 2013; Johnson et al., 2016). Previous works have found that impulsivity in the context of emotion is particularly predictive of suicidality, moreover this form of impulsivity would be helpful to be considered in future models of links between early adversity, impulsivity and bipolar suicidality.

The findings of this study dovetail with other researches that increasingly documents the complex interplay between maltreatment and impulsivity. Child maltreatment may not be independent of impulsivity of relatives. However, the results do not show the underlying causes that link them. Within BD, relatively few relatives meet full diagnostic criteria for the disorder, but many experience high levels of impulsivity when compared to healthy controls (Hıdıroğlu et al., 2013). One

TABLE 4 | Multinomial logistic regression for history of suicide attempt.

		95%	CI for Odds Ra	tio
	B (SE)	Lower	Odds Ratio	Upper
No history of SA vs. m	ore than one SA			
Intercept	7.56 (2.81)			
BIS - Inhibition control	-0.11 (0.04)*	0.83	0.89	0.97
BIS - Non-planning	0.01 (0.06)	0.90	1.01	1.13
Physical neglect	0.21 (0.23)	0.79	1.23	1.93
Emotional neglect	-0.14 (0.08)	0.74	0.87	1.02
Sexual abuse	-0.07 (0.08)	0.80	0.93	1.09
Physical abuse	-0.14 (0.09)	0.73	0.87	1.04
Emotional abuse	0.14 (0.09)	0.96	1.15	1.38
One previous SA vs. n	nore than one SA			
Intercept	6.71 (3.34)			
BIS - Inhibition control	-0.15 (0.05)*	0.78	0.86	0.95
BIS - Non-planning	-0.09 (0.08)	0.79	0.92	1.07
Physical neglect	0.23 (0.25)	0.77	1.26	2.08
Emotional neglect	-0.08 (0.09)	0.77	0.92	1.11
Sexual abuse	0.02 (0.08)	0.87	1.02	1.20
Physical abuse	-0.11 (0.11)	0.73	0.89	1.10
Emotional abuse	0.27 (0.11)*	1.06	1.31	1.62

 R^2 = 0.29 (Cox and Snell), 0.36 (Nagelkerke). Model x^2 = 39.99, ρ < 0.001. df = 14, $^*\rho$ < 0.05.

TABLE 5 | Spearman's rho correlations between BIS-11 and CTQ patient's subscale scores.

	1	2	3	4	5	6
(1) BIS – Inhibition control	_	_	_	_	_	_
(2) BIS - Non-planning	-0.35**	-	_	_	_	-
(3) Physical neglect	0.10	-0.14	_	-	-	_
(4) Emotional neglect	0.15	-0.21*	0.64**	-	-	_
(5) Sexual abuse	0.18	-0.02	0.18	0.20*	_	-
(6) Physical Abuse	0.13	-0.00	0.36**	0.45**	0.23*	_
(7) Emotional Abuse	0.36**	-0.09	0.30**	0.58**	0.40**	0.51**

^{*}p < 0.05; **p < 0.001.

possibility is that lack of inhibitory control in relatives is a marker of familial contexts which are prone to maltreatment behaviors. Higher familial impulsivity may lead to a more chaotic family environment that allows these other adversities to unfold. History of maltreatment, in turn, influence cognitive and emotional development, which intensify the risks of impulsivity and poor constraint over harmful behaviors (Braquehais et al., 2010; Daray et al., 2016). Inhibitory control shared by patients and relatives as an impulsivity dimension fosters dysfunctional behaviors such as maltreatment and suicide behavior. The reasons for relatives and patients to present dysfunctional may be diverse, possibly involving learnt behavior, developmental interferences of one behavior over another as well as shared genetic aspects that this study could not assess. That is, above and beyond the genetic influences, maltreatment has been shown to predict impulsivity over time (Braquehais et al., 2010; Daray et al., 2016).

Current findings indicated that inhibitory control and emotional abuse set the stage for recurrent suicide attempts rather than single attempts. The number of suicide attempts is a particularly robust predictor of suicide completion (Watkins and Meyer, 2013). Those that attempted suicide repeatedly also tend to present more severe dysfunctionality, as evidenced by their higher numbers of hospitalizations. Therefore, the clarification of inhibitory control as an specific aspect related to this subset of patients may be a promising target for treatments that aim to reduce recurrent suicide behavior and its dysfunctional consequences. If replicated, the current findings highlight the importance of considering specific types of early abuse as serious markers of more pronounced suicide risk.

Despite the potential clinical importance of these findings, the study is limited by the reliance on self-report measures of impulsivity and maltreatment, and also by the small number of relatives assessed. It is also important to consider that siblings and children were included in sample of relatives. Therefore, since it is less plausible that their impulsivity leads to maltreatment, it is not possible to conclude that the impulsivity observed in relatives leads to maltreatment. Instead, it may be more plausible to consider that impulsivity observed in relatives can be considered a family vulnerability marker to impulsive behaviors such as maltreatment. The small sample size precluded the ability to examine more refined dimensions of suicide attempts, such as lethality and age of onset. Furthermore, medication or comorbidities were not controlled. Despite the limitations, this study supports the relevance to develop approaches encompassing the transgenerational perspective on impulsivity and maltreatment in relation to suicide attempts in BD.

Current findings, if replicated, would have important clinical implications. First, emotional abuse and inhibitory control were independently associated with number of suicide attempt so they both represent important potential treatment targets. Second, interventions to address impulsivity may need to consider that this personality trait evolved in a family context. One possible approach for those who are seeking family therapy might be to integrate a consideration of family levels of impulsivity into that work. Impulsive behaviors of patients and family members

could be addressed by teaching self-regulatory strategies, but also by considering communication effects and strategies in contexts in which multiple members of a family may have these concerns. By doing so, it may reduce the risk of high levels of conflict and potentially provide some protection from emotional abuse. As a whole, it is expected that these preliminary findings provide insight into some important links between variables that have been studied separately in understanding suicidality within bipolar disorder. Future studies should investigate causal relationships using larger samples and longitudinal designs.

ETHICS STATEMENT

This study was carried out in accordance with the recommendations of the Ethics Committee of the Federal University of Minas Gerais with written informed consent from all subjects. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was

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AUTHOR CONTRIBUTIONS

IL: Contributed on writing, performing statistics and delineating method. LM-D: Contributed on discussion, data collection and writing. DdM: Contributed on writing, discussion and data collection. ADS: Contributed on writing and reviewing. FN: Contributed on data collection, method and on delineating the study designed. SJ: Contributed on delineating, methods, statistics, discussion and writing.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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An Analysis of the Associations among Cognitive Impulsiveness, Reasoning Process, and Rational Decision Making

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Impulsivity may lead to several unfortunate consequences and maladaptive behaviors for both clinical and nonclinical people. It has a key role in many forms of psychopathology. Although literature has discussed the negative impact of impulsivity, few have emphasized the relationship between cognitive impulsiveness and decision making. The aim of this study is to investigate the effects of cognitive impulsiveness on decision making and explore the strategies used by participants to solve problems. For this purpose, we apply two measures of impulsivity: the self-report Barratt Impulsiveness Scale (BIS-11) and the performance based Cognitive Reflection Test (CRT). Moreover, we evaluate participants' reasoning processes employed to answer CRT questions based on the calculation expressions, data organization, and erasures they made while answering the CRT (note that we utilized the instruments using pen and paper). These reasoning processes are related to the role of executive functions in decision making, and its relationship with impulsiveness. The sample consists of 191 adults, who were either professionals or undergraduate students from the fields of business, management, or accounting. The results show that cognitive impulsiveness may negatively affect decision making, and that those who presented the calculation to answer the CRT questions made better decisions. Moreover, there was no difference in the strategies used by impulsive vs. nonimpulsive participants during decision making. Finally, people who inhibited their immediate answers to CRT questions performed better during decision making.

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1. INTRODUCTION

Cognitive impulsiveness may lead people to make mistakes on simple reasoning tasks. A study conducted by Frederick (2005) proved that even students from the best universities in the world, make mistakes on simple reasoning questions due to misuse of their cognitive resources. Frederick applied the Cognitive Reflection Test (CRT), a three-item task with simple reasoning problems, to measure cognitive reflection ability (reflectivity and impulsivity) on undergraduate students from well-known universities. Frederick found that Harvard students scored, on average, only 1.43, while students from Princeton University scored 1.63 (on a score ranging from 0 to 3).

These intriguing results may be explained based on what researchers call cognitive dual process (Wason and Evans, 1975; Evans, 2003; Osman, 2013). Literature has suggested that people use two types of cognitive processes: System 1 and System 2 (Stanovich and West, 2000; Kahneman and Frederick, 2002; Shafir and LeBoeuf, 2002), or Type 1 and Type 2, according to a recent study (Evans and Stanovich, 2013). While Type 1 is related to an impulsive way of thinking, Type 2 is a reflective style of decision making. Thus, even when people know how to answer specific questions and how to make good decisions, they may misjudge if they use the impulsive cognitive type.

Although it is well-known that people may provide correct or incorrect answers due to the use of different cognitive processes, the strategies that could distinguish when they are using Type 1 or Type 2 to make decisions are currently unknown. Executive functions may explain and clarify the underlying reasoning processes of different strategies performed during a rational decision making.

Executive functions are mental processes that allow us to mentally play with ideas; consider alternatives rather than being impulsive; resist temptations; solve problems; and be creative when meeting unanticipated challenges (Diamond, 2013). They act as a manager of our cognitive resources—such as planning, decision making, and flexibility—which are used to accomplish objectives, including rational and mathematical problems (Blair et al., 2008; Toll et al., 2011; Bull and Lee, 2014). Cognitive flexibility, for instance, involves being flexible enough to adjust to changed demands or priorities, to admit we are wrong, and to take advantage of unexpected situations (Diamond, 2013). Planning, in turn, plays a key role in finding satisfactory solutions for a problem (Krikorian et al., 1994), and consists of the ability to create the best way to achieve a defined goal, regarding the rank of steps and the necessary tools to accomplish it (Malloy-Diniz et al., 2014). Finally, according to Zelazo and Müller (2002), executive functions are composed of "hot" and "cool" components related to emotional and cognitive processes, respectively and, their interaction involves the ability to control impulsive behaviors.

Impulsivity has a key role in many forms of psychopathology (Verdejo-García et al., 2007; Malloy-Diniz et al., 2011), and Barratt's impulsivity model is one of the most widely applied and recognized approaches (Stanford et al., 2009) used to investigate it. According to this model, the impulsiveness personality trait is composed of three subtypes: nonplanning impulsiveness (orientation toward present and cognitive complexity), motor impulsiveness (acting on the spur of the moment), and attentional impulsiveness (lack of attention and concentration) (Patton et al., 1995). However, only two factors (inhibition control and nonplanning) have been found for adults in the Brazilian context (Vasconcelos et al., 2012; Malloy-Diniz et al., 2015). From a neurobiological perspective, the nonplanning subtype from Barratt's model is analogous to a "cognitive impulsiveness" associated with the act of making decisions (Bechara et al., 2000). According to Bechara's model, cognitive impulsiveness is related to an inability to delay gratification, which is in line with the "orientation toward the present" characteristic of Barratt's nonplanning impulsiveness subtype.

Therefore, this study investigates the effect of impulsivity on rational decision making, and explores the strategies people use to solve problems. Although Frederick contributed significantly to the literature on cognition and decision making, he and other authors using the same instrument (Toplak et al., 2011, 2014; Cueva Herrero et al., 2015; Alos-Ferrer et al., 2016; Primi et al., 2016) did not investigate whether participants could present impulsive personality traits, and did not explain the process of reasoning used to make rational decisions. Moreover, regarding psychometric measures of impulsivity, most studies that use selfreport and behavioral measures have examined the relationship between impulsivity and mental disorders, such as substance abuse (Petry and Casarella, 1999; Tarter et al., 1999; McGue et al., 2001; Dougherty et al., 2009) and obesity (Fields et al., 2013), or investigated the reliability of impulsivity measures (Reynolds et al., 2006) but not the relationship between impulsivity and decision making related to logical and abstract reasoning.

Additionally, nonplanning is an important subtype of impulsivity that is difficult to evaluate, at least using self-reported measures (Barratt, 1993). Our data-collection approach provided spontaneous and ecological data to evaluate this subtype of impulsivity and to investigate participants' executive function abilities. Our data emerged from an individual and singular procedure with no explicit instructions, unlike in usual neuropsychological tasks (Heaton et al., 1993; Bechara et al., 1994; Krikorian et al., 1994). In this regard, no study has used both CRT and the Barratt Impulsiveness Scale (BIS-11) as measures of impulsivity; this study intends to fill these gaps.

Based on the discussion in the literature on cognitive dualprocess, executive functions, and impulsivity, as presented in this section, we propose and test four hypotheses. Regarding the inability to delay gratification and to plan in a long-term which are characteristics of the nonplanning impulsiveness trait (Patton et al., 1995), the first hypothesis predicts that high levels of this trait negatively affect performance in rational decision making. Following the same line, for successful accomplishment of several daily activities, including the solution of rational and mathematical problems, people should clearly identify their final objective, building a plan of goals and using hierarchical organization that makes its execution feasible (Malloy-Diniz et al., 2014). Thus, the second hypothesis states that high levels of the nonplanning impulsiveness trait negatively affect manipulation of apparent information needed to solve problems. Given that appropriate performance of executive functions has a key role in achieving objectives and making decisions (Diamond, 2013), the third hypothesis suggests that the more participants manipulate data following structured reasoning, the better their performance on rational decision making. Finally, cognitive flexibility involves being flexible enough to adjust to changed demands or priorities, to admit we are wrong, and to take advantage of unexpected situations (Diamond, 2013). Hence, our fourth hypothesis predicts that people who initially provide an impulsive answer during decision making, but later rethink and change it, perform satisfactorily when solving problemsi.e., cognitive flexibility positively affects rational decision making.

2. MATERIALS AND METHODS

2.1. Participants

The sample was comprised of 191 participants who were professionals (74.3%) or undergraduate students (25.6%) from the fields of business, accounting, or management. It included 44.3% women, and the participants' mean age was 33.9 years (SD = 10.24). In total, 191 participants answered the survey, but seven participants did not reveal their monthly income, 11 did not answer all CRT questions, and one left one BIS-11 question unanswered. Thus, due to these missing values, the final sample for analysis was between 183 and 180 for the hypotheses tests¹.

Participants were volunteers recruited from a well-known Brazilian entertainment company; from an executive education program in the public sector at Getulio Vargas Foundation (FGV); and from the accountancy undergraduate program at the State University of Rio de Janeiro. The latter two institutions are prestigious universities in Brazil; hence, we assume that all participants were able to read, interpret questions, and perform the four basic math operations (add, subtract, multiply, and divide). Inclusion criteria were aged above 18 years, and higher education completed or underway (participants who did not meet these criteria were excluded from the study). The study was approved by the Human Subjects Review Committee of FGV-EBAPE (Cod: 18032016-1710).

2.2. Instruments

Impulsivity was measured based on two validated instruments:

- BIS-11, translated version (Malloy-Diniz et al., 2010): This is a self-report Likert scale from 1 to 4 (1 = rarely/never; 4 = almost always/always) consisting of 30 items that evaluate the behavior construct and personality trait of impulsivity. This scale measures the three subtypes of impulsivity (nonplanning impulsiveness, attentional impulsiveness, motor impulsiveness) and total impulsiveness, which is the sum of the subtypes. Nevertheless, for the Brazilian context, a two-factor division (inhibition control and nonplanning impulsiveness), besides the total score, was adopted (Malloy-Diniz et al., 2010, 2015).
- CRT (Frederick, 2005): This is a performance-based task comprising the following three reasoning questions: (1) A bat and a ball cost \$1.10 in total. The bat costs \$1.00 more than the ball. How much does the ball cost? (2) If it takes 5 machines 5 min to make 5 widgets, how long would it take 100 machines to make 100 widgets? (3) In a lake, there is a patch of lily pads. Every day, the patch doubles in size. If it takes 48 days for the patch to cover the entire lake, how long would it take for the patch to cover half of the lake? The scores range from 0 (no correct answer) to 3 (all answers correct), and measures one type of cognitive ability: the tendency to override a premature response that is usually incorrect, and to engage in reflective reasoning, which usually leads to correct answers. Translation into Portuguese was carried out by the researchers. The first

question in the CRT was adapted to the Brazilian price level reality and culture, since baseball is not popular in the country. Thus, we replaced the bat and ball with candy (*bala*) and bubble gum (*chiclete*).

2.3. Procedures

Participants completed the survey in a single session lasting 30 min maximum. The media corporation workers answered the survey during an event organized by their employer, while students completed it in their classrooms, after they had returned from a break.

Surveys were completed individually, with participants answering the CRT, BIS-11, and demographics questions after signing a consent form. The CRT questionnaire had a blank space for participants to use for their calculations if necessary. However, in order to avoid influencing participants on their decisions as to whether to use this blank space, nothing was said about the possibility of conducting calculations in those spaces. The researchers provided directions to respondents on how to answer the questions by themselves, without consulting external sources. When in doubt, participants were told to ask the researchers, who remained present in the classroom during the procedures for help. At the end of the survey, participants returned the sheet with their answers, along with their consent form. We stored both documents separately, and coded the participants to ensure anonymity.

With the aim of better understanding the main features of the respondents, the sample was divided among *impulsive* and *nonimpulsive* groups, following the normative parameters proposed by Malloy-Diniz et al. (2015). Participants at the 75th percentile or above on the BIS-11 total impulsiveness variable were assigned to the *impulsive* group, while those below the 75th percentile were assigned to the *nonimpulsive* group. However, to test hypotheses we used the whole sample.

For the BIS-11 assessments, we analyzed the data using a two-factor structure, as suggested by Vasconcelos et al. (2012) and Malloy-Diniz et al. (2015) for a sample comprised of Brazilian adults. The nonplanning factor was determined based on the same 11 items from the original study (Patton et al., 1995) (i.e., 1, 7, 8, 10, 12, 13, 14, 15, 18, 27, and 29). The other factor, inhibitory control, was determined based on the remaining 19 items that were originally split between motor and attentional impulsiveness factors.

In turn, the CRT was applied for the purposes of measuring rational decision making (i.e., the CRT scores) and to investigate participants' abilities to manage their executive functions during their reasoning processes. To achieve this objective, participants were required to use pen and paper, leading to more spontaneous and ecological performance-based data.

Thus, we were able to observe four types of reasoning process to answer the CRT: those that did not present any externalization or calculation expression or reasoning (*no expression*), as depicted in **Figure 1**; those that showed some data organization but with no persistence in terms of development of calculation (*organization*), as shown in **Figure 2**; and those with a high manipulation of data, demonstrating a rationale with some structured sequences of reasoning (*calculation*), as demonstrated

¹Table 1 in the Supplementary Material presents the hypotheses tests using variables with no missing values, which shows that the results do not change in this case.

100 minutos.

FIGURE 1 | Illustration of no expression reasoning strategy. No expression is the no externalization or expression of calculation or reasoning.

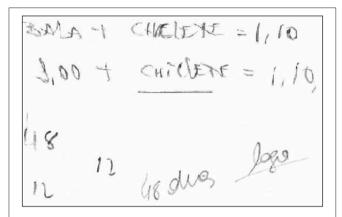


FIGURE 2 | Illustration of organization reasoning strategy. *Organization* is the presentation of some organization but with no persistence regarding calculation.

FIGURE 3 | Illustration of calculation reasoning strategy. *Calculation* is the high manipulation of data, demonstrating a rationale with some structured sequences of reasoning.

in **Figure 3**. Interestingly, some people answered the question and then erased and changed the answer, showing calculation or not. It seems that these participants first answered impulsively, but then reconsidered their answers and changed their minds, presenting cognitive flexibility during decision making. This variable was termed as *erasure*, and is illustrated in **Figure 4**. As for CRT, the scores range from 0 (any organization or calculation; no organization; no calculation; or no erasure depending on the variable) to 3 (no organization or calculation; organization; calculation; or erasure to all three questions, depending on the variable).

To evaluate the strategies used by participants, we evaluated how they answered the CRT questions on their sheets. Two researchers and an assistant analyzed and coded the different types of reasoning processes of each questionnaire. To reach a consensus, each researcher evaluated each variable separately to allocate it to the observed types of reasoning processes. Following the individual analysis of each reasoning process, the researchers discussed the few divergences until consensus was reached. Data were analyzed using Stata version 14.1.

3. RESULTS

Descriptive analysis was used in order to characterize the sample. Age, gender, occupation, and income are the demographic

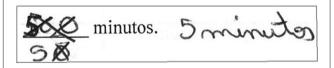


FIGURE 4 | Erasure variable. Erasure: It seems that this participant, initially, answered impulsively, reconsidered her answer, and then changed her mind.

characteristics of the sample Annual income is a categorical variable ranging from US\$ 7,536.23 to over US\$ 48,985.50².

Regarding performance on CRT, 36.9% of the subjects did not answer any question correctly; 21.9% correctly answered one question; 24.1% two questions; and 17.1% answered all three questions correctly, as depicted in **Table 1**.

Table 2 presents the correlation analysis applying Pearson correlation coefficients. The investigated variables are the total of the two subtypes of impulsivity (inhibition control impulsiveness and nonplanning impulsiveness), the total impulsiveness, the sum of the *no expression*, *organization*, *calculation*, and *erasure* reasoning process variables in answering the CRT, and the CRT score (sum of correct answers in the CRT) for each respondent.

 $^{^2}$ Participants were asked their monthly income in the Brazilian currency (Real, BRL), which was converted into U.S. dollars at the average rate for the period of data collection (i.e., USD $1 = BRL\ 3.45$) and then multiplied by 13 (i.e., 12 months plus the thirteenth salary).

TABLE 1 | Summary statistics.

Panel A: Quantitative variables	Impulsive subsample Mean (SD)	Nonimpulsive subsample Mean (SD)	Overall Mean (SD)
Nonplanning	27.9 (3.08)	21.77 (3.63)	23.38 (4.42)
Inhibition control	43.2 (5.36)	33.14 (3.78)	35.78 (6.13)
Total impulsiveness	71.1 (5.37)	54.92 (6.03)	59.16 (9.23)
Age (years)	33.97 (9.57)	33.86 (10.49)	33.90 (10.24
N	50	141	191
Panel B: Qualitative variables	Impulsive subsample N (%)	Nonimpulsive subsample N (%)	Overall N (%)
CRT SCORE			
0 (no correct answer)	20 (40.82)	49 (35.51)	69 (36.90)
1 (only one correct answer)	9 (18.37)	32 (23.19)	41 (21.93)
2 (two correct answers)	12 (24.49)	33 (23.91)	45 (24.06)
3 (all three correct answers)	8 (16.33)	24 (17.39)	32 (17.11)
NO EXPRESSION			
0 (organization or calculation for all three questions)	5 (10)	14 (9.93)	19 (9.95)
1 (organization or calculation for only one question)	6 (12)	12 (8.51)	18 (9.42)
2 (organization or calculation for two questions)	8 (16)	20 (14.18)	28 (14.66)
3 (no organization or calculation)	31 (62)	95 (67.38)	126 (65.97)
ORGANIZATION			
0 (no organization)	41 (82)	127 (90.07)	168 (87.96)
1 (organization for only one question)	7 (14)	12 (8.51)	19 (9.95)
2 (organization for two questions)	2 (4)	2 (1.42)	4 (2.09)
3 (organization for all three questions)	0	0	0
CALCULATION	00 (00)	100 (70 0 1)	105 (70.00)
0 (no calculation)	33 (66)	102 (72.34)	135 (70.68)
1 (calculation for only one question)	12 (24)	19 (13.48)	31 (16.23)
2 (calculation for two questions)	3 (6)	9 (6.38)	12 (6.28)
3 (calculation for all three questions)	2 (4)	11 (7.80)	13 (6.81)
ERASURE			
0 (no erasure)	41 (82)	120 (85.11)	161 (84.29)
1 (erasure for only one question)	8 (16)	19 (13.48)	27 (14.14)
2 (erasure for two questions)	1 (2)	1 (0.71)	2 (1.05)
3 (erasure for all three questions)	0	1 (0.71)	1 (0.52)
GENDER			
0 (male)	28 (57.14)	75 (55.15)	103 (55.68)
1 (female)	21 (42.86)	61 (44.85)	82 (44.32)
OCCUPATION			
0 (student)	12 (24)	37 (26.24)	49 (25.65)

(Continued)

TABLE 1 | Continued

Impulsive subsample N (%)	Nonimpulsive subsample N (%)	Overall N (%)
38 (76)	104 (73.76)	142 (74.35)
11 (22.92)	27 (19.85)	38 (20.65)
3 (6.25)	9 (6.62)	12 (6.52)
6 (12.50)	18 (13.24)	24 (13.04)
7 (14.58)	27 (19.85)	34 (18.48)
11 (22.92)	28 (20.59)	39 (21.20)
10 (20.83)	27 (19.85)	37 (20.11)
	subsample N (%) 38 (76) 11 (22.92) 3 (6.25) 6 (12.50) 7 (14.58) 11 (22.92)	subsample N (%) subsample N (%) 38 (76) 104 (73.76) 11 (22.92) 27 (19.85) 3 (6.25) 9 (6.62) 6 (12.50) 18 (13.24) 7 (14.58) 27 (19.85) 11 (22.92) 28 (20.59)

CRT = sum of correct answers on CRT; Nonplanning = total nonplanning impulsiveness; Inhibition control = total inhibition control impulsiveness; Organization = sum of answers using Organizations;

Calculation = sum of answers using Calculations; Erasure = sum of answers using Erasures; No expression = sum of answers using No expressions

Gender: mean = percentage of women in the respective samples

The sum of No expressions, Organization and Calculation is 3: CRT has 3

questions and in each one participants could presented only one of the three variables. Impulsive = Total impulsiveness = or > 65. Nonimpulsive = Total impulsiveness < 65.

TABLE 2 | Pearson cross-correlation table.

Variables	1	2	3	4	5	6	7	8
1-CRT								
2-Nonplanning	-0.22							
3-Inhibition control	-0.00	0.52						
4-Total impulsiveness	-0.11	0.82	0.91					
5-No expression	-0.29	0.07	-0.04	0.00				
6-Organization	0.06	0.01	0.11	0.08	-0.49			
7-Calculation	0.30	-0.08	-0.00	-0.04	-0.92	0.10		
8-Erasure	0.22	0.04	0.10	0.09	0.03	-0.08	0.00	

CRT, sum of correct answers on CRT; Nonplanning, total nonplanning impulsiveness; Inhibition control = total inhibition control impulsiveness; Organization = sum of answers using Organizations;

Calculation = Sum of answers using Calculations; Erasure = Sum of answers using Erasures; No expression = sum of answers using No expressions.

The ordinary least squares (OLS) method and ordered logistic regression (Ologit) were performed to test the hypotheses based on the whole sample (i.e., the *overall* sample depicted in the last right column of **Table 1**). The dependent variables are interval and ordinal; thus, the results of both methods may be useful to evaluate the robustness of the findings. The OLS method presents a simple result, and its coefficient allows for direct interpretation. On the other hand, Ologit is also appropriate for the analyses since dependent variables may be ordered from 0 (highest level of impulsive trait), for the participants who did not provide any correct answer, or who did not conduct any calculations, to 3 (highest level of reflectivity), for participants who answered all three CRT questions correctly or who wrote calculations on

the sheet of paper to answer all of them. Finally, both methods allow for the control of important variables that could influence outcomes of the dependent variables, such as income (Dohmen et al., 2010). Inhibition control impulsiveness was added to the model as a control variable for the nonplanning impulsiveness effects. Moreover, *organization* was used as a control variable for the effect of *calculation*³.

For the hypotheses tests, the results of the regression methods differed only for the first hypothesis regarding the *p*-value, as depicted in **Table 3**. In this regard, OLS coefficients are reported because they allow for direct interpretation. Coefficients are not standardized because the variables are on the same scale.

Hypothesis 1 predicted that high levels of nonplanning impulsiveness would negatively affect performance on decision making (CRT). After entering the demographic variables and controlling for the inhibition control subtype of impulsiveness, the regressions showed that hypothesis 1 was supported ($\beta=-0.05, p<0.05$). Despite the low coefficient value, this result suggests that people who are usually present-oriented and do not think carefully may make worse choices during a decision-making process compared to people with lower levels of nonplanning impulsiveness, who are more future-oriented and careful when making decisions.

Hypothesis 2 suggested that higher levels of nonplanning impulsiveness would lead people to less frequently manipulate data by performing calculations to answer the CRT questions. The results show that this hypothesis was not supported. People with higher levels of nonplanning impulsiveness would not necessarily perform fewer calculations to answer the CRT questions. That is, there is no difference between people with high levels of cognitive impulsiveness and people with low levels of cognitive impulsiveness in their strategies to answer CRT questions and make decisions.

Hypothesis 3 stated that higher levels of data manipulation, which entails a deeper development of structured reasoning and calculation to answer the CRT questions, would lead participants to perform better on CRT compared to those who did not use calculations. The hypothesis was supported ($\beta=0.33,p<0.001$). This suggests that the development of a complete thought may lead to better outcomes compared to only making notes and not expressing the reasoning and calculation behind them.

Finally, hypothesis 4 suggested that people who utilized erasures when answering the CRT questions– that is, people who gave an answer initially but then changed their mind and presented another answer– would show cognitive flexibility during rational decision making and therefore perform better in the CRT. The hypothesis was supported ($\beta=0.43,p<0.01$), revealing that those who are able to assess and reconsider immediate responses may make better decisions.

4. DISCUSSION

The ability to make advantageous and rational decisions has a critical impact on several daily decisions. Impulsiveness

TABLE 3 | Hypotheses tests.

		Ordinal Least Square (OLS)		l Logistic on (Ologit)
	CRT	Calculation	CRT	Calculation
Nonplanning	-0.05*	-0.01	-0.11**	-0.01
	(0.02)	(0.02)	(0.04)	(0.05)
Inhibition control	0.01	0.01	0.02	0.02
	(0.01)	(0.01)	(0.03)	(0.04)
Organization	0.13		0.29	
	(0.16)		(0.33)	
Calculation	0.33***		0.66***	
	(0.07)		(0.17)	
Erasure	0.44**		0.90**	
	(0.15)		(0.34)	
Gender (1 = female)	-0.38*	-0.11	-0.76*	-0.21
	(0.16)	(0.13)	(0.31)	(0.35)
Age (years)	-0.03**	-0.02*	-0.06**	-0.06*
	(0.01)	(0.01)	(0.02)	(0.03)
Occupation (1 = professional)	0.69*	-0.49*	1.37*	-1.70**
	(0.29)	(0.24)	(0.55)	(0.61)
Income (USD)	0.06	0.20**	0.08	0.58**
	(0.09)	(0.07)	(0.16)	(0.18)
N	180	183	180	183
R^2	0.283	0.081		
Adjusted R ²	0.245	0.050		
Pseudo R ²			0.125	0.051
F	13.41	2.73		
χ^2			60.21	16.79

Standard errors in parentheses.

 $^*p < 0.05, \ ^{**}p < 0.01, \ ^{***}p < 0.001.$

Inhibition control is a control variable for the effect of Nonplanning.

Organization is a control variable for the effect of Calculation

CRT = sum of right answers on CRT; Nonplanning = total nonplanning impulsiveness; Inhibition control = total inhibition control impulsiveness; Organization = sum of answers using Organizations;

 ${\it Calculation} = {\it sum}$ of answers using ${\it Calculations};$ ${\it Erasure} = {\it sum}$ of answers using ${\it Erasures}.$

may be one of the factors that could preclude development of this ability (Franken et al., 2008; Wittmann and Paulus, 2008). The goal of this study was to investigate the effect of impulsiveness on decision making and explore the strategies people use to solve problems. For this purpose, we applied two measures of impulsivity—BIS-11 (Patton et al., 1995) and CRT score (Frederick, 2005)—in a sample of 191 adults who were professionals or undergraduate students from the fields of business, accounting, or management.

Pen and paper were used to answer the questionnaire in order to evaluate which strategies participants used to answer the CRT questions, which were coded as *no expression*, *organization*, *calculation*, and *erasure*. **Table 4** summarizes the evidence collected in this study from all tested hypotheses.

 $^{^3}$ Table 2 in the Supplementary Material presents the analyzes of hypotheses tests without demographic variables in any of the models.

TABLE 4 | Summary of results.

Hypotheses	Supported
H1: High levels of the nonplanning impulsiveness trait negatively affect performance on rational decision making.	Yes
H2: High levels of the nonplanning impulsiveness trait negatively affect manipulation of apparent information to solve problems.	No
H3: The more participants manipulate data following structured reasoning, the better their performance on rational decision making will be.	Yes
H4: Cognitive flexibility positively affects rational decision making.	Yes

The results show some interesting findings. The outcome regarding the first hypothesis suggested that higher levels of nonplanning impulsiveness lead to worse performance on CRT. According to Klein (1999), experienced professionals present favorable performance while using the non-deliberative Type 1 cognitive style during decision making. The author suggests that this occurs because this cognitive process involves pattern matching and recognition of familiar and typical cases.

However, in unusual situations, planning has a key role in finding satisfactory solutions to a problem (Krikorian et al., 1994). Thus, in day-to-day life, nonplanning impulsiveness may appear in the form of frustration and stress, particularly in unusual situations, such as buying an apartment or car. It can lead people with higher levels of nonplanning impulsiveness to make disadvantageous choices since there may not be a logical reason for the choices made when logic is required. In turn, it may influence these people to erroneously experience feelings of incapability: they may think they are unable to make advantageous decisions, when the problem actually lies in the way they deal with the situation.

Another finding is that there was no difference between the strategies used by people with high levels of nonplanning impulsiveness and those who are nonimpulsive when it came to answering the CRT questions. Considering that the first hypothesis is supported, this second finding suggests that some people used an incorrect logical sequence of reasoning and gave wrong answers, which was confirmed by our analysis of the questionnaires. Thus, while participants with high or low levels of nonplanning impulsiveness might have followed a logical reasoning sequence while manipulating data to answer the CRT questions, this logical sequence was wrong.

An explanation for the second result may lie in the participants' difficulty in using their intuitive understanding to guide their numerical solutions as tested in a study by Ahl et al. (1992) with children. The authors evaluated the relationship between these different types of reasoning and showed how intuitive understanding influences the numerical solution. Another possibility is that in order to reduce their cognitive load, respondents used algorithmic reasoning based on superficial features of algorithms that are not related to inherent

characteristics of the problem at hand, leading to insufficient development of their mathematical skills (Jonsson et al., 2014). This finding is interesting, considering that one of the sample inclusion criteria was higher education completed or underway, which implies knowledge of basic math calculations.

The third hypothesis was supported: performing calculations positively affects CRT outcome. This suggests that when people persist in doing what they had planned their outcomes are better, assuming their plan was effective. This result seems to be intuitive, but it is important to highlight the relevance of adequate employment of executive functions. Calculating requires a plan of the necessary procedures to manipulate the given information; following up on this plan; and changing the plan when relevant circumstances have changed. Thus, it represents an adequate proxy for successful implementation of important executive functions, such as planning and inhibitory control during rational decision making, which is related to higher academic success in several fields and other success over the life course (Mischel et al., 2010; Bull and Lee, 2014).

The last hypothesis suggested that people who reevaluate their answers may perform better when making decisions. Even though some participants presented incorrect answers due to impulsive reasoning, if they had changed their mind they could have achieved better results. Thus, cognitive flexibility may play an important role in achieving the best results possible when it comes to rational decision making. In this study, participants were able to rethink their choices and change their minds without facing any negative consequences; however, this may not always be possible in their daily lives. Therefore, it is important to inhibit prompted thoughts, particularly in new situations, and to evaluate options carefully and then make the best possible choice. Finally, this finding could contribute to the literature on reasoning process conflicts, which investigates the dynamic between Type 1 and Type 2 processes and the factors that lead to Type 2 engagement (Pennycook et al., 2015). The action of reevaluating the given answer may represent the process of Type 2 monitoring of the Type 1 output.

Although the present study is not focused on the variables used as controls to test the hypotheses, such as gender, age, occupation, and income, the results in this regard present interesting and significant findings. Similarly to previous studies, this study identified that gender has a significant impact on CRT scores ($\beta = -0.40$, p < 0.05); i.e., men scored significantly higher than did women on CRT (Frederick, 2005; Oechssler et al., 2009; Hoppe and Kusterer, 2011; Barcellos et al., 2016). Literature has suggested that women are more risk averse compared to men when it comes to uncertain decision making (Francis et al., 2015; Jain, 2015). Moreover, Frederick (2005) found that women had lower performance on CRT compared to men: women presented more impulsive answers for each question on CRT (10, 100, and 24), while men presented more diverse wrong answers to these questions (20, 500, and 1). According to Frederick, this finding suggests that men are more reflective compared to women. However, the present study evidences that gender has no impact on the decision to engage in calculation. Considering that performing calculations is an important process related to the act of reflection and making choices, this is an interesting finding that raises a question about the concepts of reflection and reflective thinking used in the literature on decision making and cognitive ability. Moreover, studies on risk behavior and gender have considered the role of social learning in the difference between men and women regard making decisions (Booth and Nolen, 2012; Booth et al., 2014), and the type of test used to evaluate risk preferences (Filippin and Crosetto, 2016), rather than inherent gender traits.

With respect to age, the results show that older participants had poorer performance compared to younger respondents during decision making ($\beta=-0.03,p<0.01$), and calculated less frequently to answer the CRT ($\beta=-0.02,p<0.05$). In addition, professionals performed fewer calculations compared to students to answer the CRT ($\beta=-0.49,p<0.05$), but did not differ on their CRT scores. Lastly, people with higher incomes performed more calculations compared to their lower-income peers ($\beta=0.20,p<0.01$), but income did not have impact on rational decision making.

The main contributions of this study include a methodological advancement in literature on decision making and impulsiveness. Unlike extant studies on decision making that have emphasized only people's performance, this study complements such evidence by adding data about intrinsic characteristics, reasoning process, and performance. It also contributes to the literature on impulsivity by presenting evidence using BIS-11, based on the second-order sub-scale outcomes, unlike studies that have presented evidence based only on the total score.

An additional contribution of this study is its measurement of reasoning process based on the strategies participants used to answer the CRT questions. It provides an initial idea for the development of a tool to measure nonplanning impulsiveness, which is an important subtype of impulsivity that is difficult to evaluate, at least using self-report measures (Barratt, 1993). Even though there are several tests to measure motor impulsiveness, there are few tools to measure nonplanning impulsiveness (Malloy-Diniz et al., 2010). Moreover, our data-collection approach provides a different perspective on the evaluation of executive functions. Such data emerged from an individual and singular procedure with no explicit instructions, unlike in usual neuropsychological tasks (Heaton et al., 1993; Bechara et al., 1994; Krikorian et al., 1994). Thus, it provided more spontaneous and ecological data. Finally, to our knowledge, this is the first study to have used, simultaneously, BIS-11 and CRT as measures of cognitive impulsiveness.

This study presents a few limitations, such as the fact that while some people did not performed calculations or other reasoning expressions by hand on paper, they may have done so mentally or using other resources, such as the surface of the table or their own palm. Another limitation is that the sample is restricted to specific fields of study and professionals who have similar specialties.

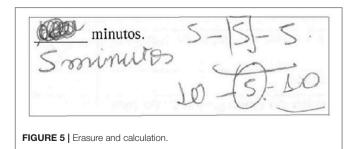
Moreover, we were unable to observe the relationship between *calculation* and *erasure* when participants presented both on their CRT answers. That is, we are not aware of the sequence performed by the participants, in terms of whether they first answered with no calculation, then rethought, then performed the calculation, and finally changed

their answer (*erasure*); or first performed the calculations and answered the questions, thought about it and performed more calculations, and then changed their answer (*erasure*), as shown in **Figure 5**. Finally, data collection was not performed in a standardized way, since some of the data was collected during a company event and some was collected in classrooms.

Future research could investigate the performance of reasoning tasks related to neuropsychological tools that evaluate inhibitory control, decision making, attention, and nonverbal fluency. Furthermore, it would be fruitful to evaluate people's cognitive effort and awareness of self-impulsiveness more deeply. Thus, it would be possible to investigate the issue of compensatory behavior and whether participants are presenting higher cognitive effort compared to the presence or absence of calculations in their answers.

Regarding sample analyses, replication of this study with different participants would be valuable. That is, it would be interesting to investigate the performance on CRT, cognitive processes, and impulsiveness traits with students from different fields and professionals with other specialties. Another suggestion is to measure the time a participant takes to answer each CRT question in order to investigate the relationship between time and impulsive decision making, and to collect information about the processes of reasoning for more detailed analyses. Osman (2013) pointed out that few studies have measured response time in tasks that assess dual processes. Time measurement could contribute to the reliability of findings regarding the differences between Type 1 and Type 2 processes of reasoning. Moreover, assessment of emotions and somatic markers could provide important insights about reasoning processes, and investigation of cognitive overload effects on CRT performances may also contribute to research in this field.

Another interesting future research possibility is the exploration of recent findings about a Type 3, together with Type 1 and Type 2 reasoning processes (Noël et al., 2013). Noël and colleagues suggested that a third neural system is responsible for craving sensations and, consequently, for addictions such as gambling and drug addiction. This third system is an insula-dependent system that is responsible for the reception of interoceptive signals and their translation into feeling states, presenting significant influence in decision making and impulse control related to risk, reward, and uncertainty. Thus, a study that tests and explores this theory using CRT, BIS-11, and other useful tools to measure the association between



insula, impulse control, and decision making would represent a significant contribution to both literature and the field. Finally, physiological measures such as brain activation using functional magnetic resonance imaging or electroencephalogram could be used to assess the coherence between neurophysiological activation, behavior, and feelings.

AUTHOR CONTRIBUTIONS

AJ: Contributed substantially to the conception and design of the work; conducted the survey and statistical analysis; and wrote the manuscript. RC: Contributed substantially to the conception and design of the work; conducted the recruitment of participants; contributed to the statistical analysis and wrote the manuscript. AL: Revised the manuscript critically for important intellectual content, and had an organizational role.

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Deficits in Response Inhibition in Patients with Attention-Deficit/ Hyperactivity Disorder: The Impaired Self-Protection System Hypothesis

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¹Laboratório de Investigações em Neurociência CLínica, Department of Mental Health, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil, ²ILumina Neurociências, Belo Horizonte, Brazil, ³Quantitative Methods and Predictive Psychometrics Laboratory, Department of Psychology, Universidade Federal da Bahia, Salvador, Brazil, ⁴Brazilian Association of Psychiatry, Rio de Janeiro, Brazil, ⁵Department of Pediatrics, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

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Coutinho TV, Reis SPS, Silva AG, Miranda DM and Malloy-Diniz LF (2018) Deficits in Response Inhibition in Patients with Attention-Deficit/ Hyperactivity Disorder: The Impaired Self-Protection System Hypothesis. Front. Psychiatry 8:299. doi: 10.3389/fpsyt.2017.00299 Problems in inhibitory control are regarded in Psychology as a key problem associated with attention-deficit/hyperactivity disorder (ADHD). They, however, might not be primary deficits, but instead a consequence of inattention. At least two components have been identified and dissociated in studies in regards to inhibitory control: interference suppression, responsible for controlling interference by resisting irrelevant or misleading information, and response inhibition, referring to withholding a response or overriding an ongoing behavior. Poor error awareness and self-monitoring undermine an individual's ability to inhibit inadequate responses and change course of action. In non-social contexts, an individual depends on his own cognition to regulate his mistakes. In social contexts, however, there are many social cues that should help that individual to perceive his mistakes and inhibit inadequate responses. The processes involved in perceiving and interpreting those social cues are arguably part of a self-protection system (SPS). Individuals with ADHD not only present impulsive behaviors in social contexts, but also have difficulty perceiving their inadequate responses and overriding ongoing actions toward more appropriate ones. In this paper, we discuss that those difficulties are arguably a consequence of an impaired SPS, due to visual attention deficits and subsequent failure in perceiving and recognizing accurately negative emotions in facial expressions, especially anger. We discuss evidence that children with ADHD exhibit problems in a series of components involved in the activation of that system and advocate that the inability to identify the anger expressed by others, and thus, not experiencing the fear response that should follow, is, ultimately, what prevents them from inhibiting the ongoing inappropriate behavior, since a potential threat is not registered. Getting involved in high-risk situations, such as reckless driving, could also be a consequence of not registering a threat and thus, not experiencing fear.

Keywords: attention-deficit disorder/hyperactivity disorder, anger recognition, theory of mind, visual attention, facial mimicry, alexithymia, error awareness, inhibitory control

The attention-deficit/hyperactivity disorder (ADHD) is traditionally characterized by intense and persistent difficulty in regulating attention and/or hyperactivity behaviors and/or impulsivity, thus producing a significant distress in many areas of the affected individual's life (1). According to the latest edition of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V), ADHD admits three different presentations: predominantly inattentive; predominantly hyperactive-impulsive; and combined. This disorder is highly heterogeneous due to different symptomatology, that includes inattention and hyperactivity/impulsivity, and can be classified according to the severity of symptoms and deficits related as "mild," "moderate," or "severe" (2).

Recent studies estimate that the prevalence of ADHD ranges from 6 to 7% among children and adolescents, 5% among young adults (3), and 3% among older adults (4). However, despite descriptive statistics found in literature, there is no real evidence of this disorder having increased significantly regarding the number of cases over the past three decades (5).

Since ADHD is considered a lifespan disorder, the impairments vary across age. In childhood, ADHD is related to learning disabilities (6), frequent conflicts in sibling relationships (7), and difficulty interacting with other children (8). In adolescence and/ or adulthood, individuals with ADHD have a higher chance of being involved in car accidents and reckless driving (9), especially for those with comorbidities (10); getting in trouble with the law (11, 12); presenting inconsequential sexual behavior (13, 14); as well as frequently changing jobs (15), which leads to the occupation of positions with lower social prestige (16), and lower income (17). Later in life, several burdens, such as impairments on financial and social well-being, may be identified (18). ADHD represents a greater risk for earlier mortality, regardless of age, mainly caused by unnatural events such as accidents (19).

Children with ADHD tend to be considered by their peers as intrusive, irritating, and generally aversive (20), which causes them to have problems maintaining friendships (21). These social deficits remain in adolescence (22). Due to the violation of behavioral norms and expectations, the externalizing behavior mediates the relationship between ADHD symptoms and peer rejection (23). Association between peer rejection and ADHD symptomatology goes both ways, since ADHD symptoms at age of 4 predicts more peer rejection at the age of 6, and also, peer rejection at the age of 4 predicts more hyperactivity symptoms at the age of 6 (24). Social exclusion and self-regulation are reciprocally regulated as well: the limited ability to suppress impulses in favor of reaching goals predicts social exclusion and vice versa (25). A common behavior associated with the negative peer evaluation of children with ADHD is excessively blaming peers for their inabilities, when dealing with negative outcomes (26). This condition results from a positive illusory bias, in which individuals with ADHD overestimate their competencies when feeling threatened in a competitive situation (27), which may lead to their own ostracism.

Studies support that inattention and hyperactivity/impulsivity symptoms in ADHD are distinguishable but substantially correlated (28). Recently, a study based on three different and independent data sets, collected among children, adolescents, and

adults, established that there is a causal path from inattention to hyperactivity/impulsivity, concluding that clinical interventions focused on the former will probably affect the latter, but not the other way around (29).

Inhibitory control is a key construct for understanding symptoms in ADHD (30). Several studies have pointed to remarkable impairment in inhibitory control in patients with ADHD (31, 32). Inhibitory control has been defined as the ability to deliberately suppress or interrupt the expression of cognitive, emotional, or behavioral responses (33–35). According to Barkley (30), such inhibition is composed of three separated and overlapping processes, responsible for: 1. inhibiting a certain unwanted behavior, creating a delay in the final answer; 2. stopping an answer in progress, being sensitive to error and changing the course of an answer which will prove unsatisfactory; 3. resisting the distraction that can occur during the delayed response, allowing oneself to carry the decision of changing the strategy until the end.

Some authors argue that inhibitory control might have an emotional foundation in which the conflict between two or more stimuli results in an aversive experience that provokes a negative emotion, leading the individual to exert control in order to resolve the conflict. In other words, the conflict-related emotion is a necessary precursor for control (36). In typical individuals, increasing negative emotions enhances cognitive control (37). Here, we will approach inhibitory control in this emotional perspective, applied to social contexts.

Recent studies have established that inhibitory control can be considered as a modular construct (38), with at least two different components that have different electrophysiological correlates (39). "Interference suppression" is the component related to resisting irrelevant or misleading information, whereas "response inhibition" refers to the capacity of withholding a response or overriding an ongoing action (40, 41).

In this paper, we will address problems regarding the "response inhibition" component in individuals with ADHD, especially in regards to the behavioral regulation in social contexts. Our purpose is to discuss how processes like visual attention and recognition of facial expressions are involved in a Self-Protection System (SPS), which enhances error awareness and inhibition of inadequate social behaviors. We argue that an impaired self-protection system (ISPS) is ultimately what causes perseverance of improper behaviors related to impulsivity/hyperactivity in individuals with ADHD.

EMOTION RECOGNITION IN ADHD

Human communication is multimodal, occurring through different channels of communication, such as facial and corporal expressions, speech, and prosody (42). The correct emotion recognition through facial expressions is critical to social adaptation because, among other things, it stimulates self-monitoring (43).

Individuals with ADHD have difficulty recognizing emotions in facial expressions (44, 45), an endophenotype shared with autistic patients (46). These difficulties are accentuated when negative emotions (such as anger) are concerned and may partially explain relationships problems with family members and peers (47, 48). Children with ADHD tend to take more time and

make more mistakes when trying to recognize emotions such as sadness, disgust, or anger (49).

According to a meta-analysis, deficits in recognition of anger and fear in facial expressions have been observed in children with ADHD (50). Highly hyperactive individuals are usually less likely to recognize fear, while individuals with the predominantly inattentive type of ADHD are less likely to identify anger (51). There seems to be a correlation between attention deficits and difficulty to identify anger in children with ADHD (52), and those problems with the recognition of emotions in facial expressions may actually result from visual attention deficits (53).

A neuroimaging study analyzed hemodynamic responses to expressions of happiness and anger in boys with ADHD, and it concluded that they have a lower hemodynamic response when facing the expression of anger (54). Young adults with ADHD also remained less sensitive to anger expressions (55), had impairments in recognizing anger in prosody (56) and had problems adequately responding to anger (57).

FEAR THE ANGER: THE SPS

Anger is one of the seven universal facial expressions of emotion (58) and, therefore, has very specific markers, mainly characterized by lowered and joined eyebrows, wide eyes, and upper eyelids pressed against the eyebrow —a kind of a "stare" look—along with tight and heavily strained lips (59). According to studies carried out in different cultures around the world, this pattern of facial contraction, despite the cultural influences (60), is quickly and easily identified by all subjects.

Evolutionary social psychology describes the mechanisms to detect any possible threat and properly respond to it (61–65). The "Self-Protection System" (SPS) (66) is one of them, and its function is to identify social cues that may indicate possible risk or intention of damage, responding to this threat perception with the activation of a cognitive and affective response, which facilitates escape (67).

An expression of anger is evaluated by that system as a possible signal of violent intent, and it leads to a fear response (68). At the cognitive level, the potential threat (in this case, anger expression) triggers an immediate response of "stop, look, and listen" (69), disrupting the ongoing action. And it is already known that the main category that elicits anger in a daily basis is, in return, "other people," which highlights that it is an emotion with an important social trigger (70).

An expression of anger can be a social sign of rejection of the other (71), disapproval, and/or intention of harm (72, 73). One person in a group expressing anger toward another immediately causes the targeted individual of that anger to feel excluded and motivated to act in a way so as to be accepted once again by the group (74). This happens because being rejected usually increases the motivation to reconnect to the group (75, 76).

An angry face can be tracked much faster in a crowd of neutral faces, in comparison to a happy face (77–82). This shows that, under normal circumstances, individuals tend to prioritize anger to the detriment of other emotions, and its identification triggers fear, which is critical to behavioral control (83). The probable cause for this is that anger is an emotion strongly associated with

the intention of causing harm to something or someone, and the sooner identified, the better it is concerning survival fitness. This phenomenon is called the "Anger Superiority Effect" and occurs both in children and adults (84).

Children in kindergarten seem to achieve a better performance in Go/No-Go tasks when they experience negative emotions, probably because those emotions lead to a more focused and attentive behavior, oriented toward problem-solving and reducing the chance of committing mistakes (85). Studies using emotional Go/No-Go tasks have concluded that emotional processing interferes with inhibitory control (86, 87).

Physiological studies indicate that the hypothalamic–pituitary–axis (HPA) plays a fundamental role in stress response by promoting behavioral and peripheral changes capable of maximizing the body's ability to adjust its homeostasis and increasing the chances of survival through the release of glucocorticoids, mainly cortisol (88). It has already been proved that fear is one of the main triggers for cortisol once the response of the HPA axis is more prominent whenever an individual experiences fear in response to a stressor (89).

It was reported that cortisol administration may improve inhibitory control in healthy adults on a Go/No-Go task (90). In another study, results indicated that the administration of a cortisol antagonist eliminated the positive effect of the hormone related to inhibitory control observed in healthy participants (91). A third study carried out with women, with and without borderline personality disorder, showed that a single cortisol administration improved inhibitory control for both groups (92).

Children with ADHD seem to present lower levels of diurnal cortisol, in comparison to those without the condition, and treatment with atomoxetine may help normalize these levels (93). Also, children and adolescents with ADHD, especially those with Defiant Oppositional Disorder or Conduct Disorder as comorbidities, presented low HPA responsiveness, having hyporesponsiveness to stressful situations, which may result in impulsive and/or defiant behaviors (94), as well as deficits in emotional regulation and aggressiveness inhibition (95). Pharmacological treatment with methylphenidate helps normalize the HPA alteration in children with ADHD (96).

THE ISPS HYPOTHESIS

Some authors emphasize the need to consider other processes for a more comprehensive understanding of ADHD, highlighting the importance of those related to emotion and social cognition (97). In an attempt to unify all of these aspects, we developed the "Impaired Self-Protection System" (ISPS) hypothesis, which explains response inhibition deficits in social contexts, more specifically, why individuals with ADHD seem unable to regulate their inadequate behavior even in the presence of disapproving social cues.

Children with ADHD have visual attention deficits (98), which compromises visual processing speed and sustained visual attention (99). We already know that visual attention deficits impair the ability to perceive facial expressions (100, 101). Emotional perception is often considered a low perceptual process necessary

to decode affective cues or identify outgoing emotional information in the environment (102). It is also the first step to Theory of Mind (103).

Theory of Mind refers to the natural ability to assertively infer other people's beliefs and desires, and to use this information to make assumptions and predict their behavior (104, 105). Several studies demonstrated that children with ADHD have a deficit in Theory of Mind (106–108). A recent meta-analysis considered the Theory of Mind impairments observed in patients with ADHD halfway between those observed in individuals with typical development and in individuals on the autism spectrum (50).

As mentioned before, Anger Recognition is the first step to activating the SPS, and Theory of Mind is responsible for properly interpreting that emotion (109). If there is impairment in Theory of Mind, an expression of anger may go unnoticed or be misjudged, and ultimately, the fear response that should have been triggered in that situation will not arise. Consequently, the improper behavior that induced that anger in the first place will persist instead of being discontinued.

A recent study partially corroborates this hypothesis by establishing that patients with ADHD, in addition to their difficulty recognizing anger, show a reduced ability to inhibit responses in the emotional Go/No-Go task, and this difficulty is more pronounced when the stimulus is a face expressing anger (110). This hypothesis aligns itself with the concept of Deficient Emotional Self-Regulation, characterized by deficits in the ability to inhibit inappropriate behavior in the face of certain emotional display (111), which, in the case of patients with ADHD, is anger.

Additionally, there are other processes indirectly involved in the activation of the SPS that seem to be impaired in patients with ADHD. Hereupon, we will present them and, subsequently, make an effort to unravel the possible connections between them and the other variables discussed so far.

FACIAL MIMICRY

"Mimicry" can be defined as the tendency to imitate facial, vocal, or postural expressions of the person who we are interacting with (112). There are four characteristics that define "emotional mimicry": 1. both people present the same emotional expression, although not necessarily through the same communication channel; 2. this expression occurs in a short window of time, usually within the first second; 3. the expression of the "mimic" is linked to the expression of the imitated person; 4. the mimetic expression consists of a sharing of the original expression, rather than a reaction to the original expression (113).

Facial mimicry favors the emotional experience in itself, which facilitates the recognition of the emotion of the other (114). It is an important tool for reconnecting with a group after social exclusion (115).

There is evidence that the corrugator supercilli muscle, fundamental to creating facial expressions of negative emotions, such as anger and fear, displays electrical activity after only 100 ms of the perception of a mistake. That reaction is associated to the concept of "error awareness," defined as the tendency to slow down responses after perceiving a committed mistake or a

received punishment, increasing self-monitoring and proceeding more cautiously in order not to commit further mistakes (116).

Some neuroimaging studies have already identified brain circuits involved in facial mimicry (117). Specifically for the anger mimicry, it is known that lesions in the right frontal cortex decrease its proper expression (118). It is also known that the right frontal cortex plays a key role in inhibiting unwanted behavior (119, 120). In children with ADHD, for example, abnormal functioning of the right frontal cortex has been associated with deficit in inhibitory control (121, 122). Among children, adolescents and adults a lower cortical thickness in the right upper frontal gyrus has been correlated to the severity of this disease (123).

Considering that one of the main regions involved in the inhibitory control is also responsible for anger mimicry, we could assume that individuals with ADHD present difficulties in facial mimicry, which would hamper their ability to simulate and infer emotions of others. But, so far, only one study has investigated the relationship between ADHD and facial mimicry (124), and it found no association between both. However, we must consider that the age group of participants were very limited (6–7 years old), and differences might have been undetectable due to their development stage, which highlights the need for further studies.

EMOTIONAL AWARENESS AND ALEXITHYMIA

The process of observing, identifying, discriminating, and evaluating one's emotions is called Emotional Awareness (125). In contrast, Alexithymia refers to the inability to access and nominate those emotions and thus, is associated with a deficit in the self-consciousness of the emotional state (126, 127), as well as in the recognition of other people's emotions (128, 129).

Alexithymia has also been associated to impairments in the processing of threat-related facial expressions, emotion recognition (130), and to reduced anticipation of negative emotional events (131). The difficulty in labeling the emotions of others in alexithymic individuals could be explained by a reduced neural activity in ventral striatum and in frontal, temporal, and occipital cortex in response to brief negative emotional facial expressions (132). Longer reaction times are presented when labeling angry and fearful faces, indicating that they were slower in labeling negative emotions (133). Interestingly, the practice of mindfulness focused on emotional awareness seems to enhance neural sensitivity to errors (134), which might also have an impact on behavioral regulation, leading the individual to be more cautious and avoid committing further mistakes.

There is evidence that children with ADHD show low levels of emotional self-awareness, and it is associated with externalizing behavior, in this case, opposition and challenging behavior in response to some perceived provocation (125). Alexithymia in children with ADHD has been correlated to hyperactivity and to impairments in inhibitory control (135). In adults with ADHD, it has been closely associated with difficulty in accepting their own emotions (136). A preliminary study held with adults that presented ADHD and alexithymia demonstrated that related symptoms improved significantly after pharmacotherapy with psychostimulants (137).

OVERVIEW

As shown in **Figure 1**, we began our argument by discussing how impulsive/hyperactive behaviors in ADHD might be a consequence of inattention. Even after committing a mistake, error awareness should help an individual to inhibit an ongoing action and override it. In simple Go/No-Go tasks, there are emotional processes that affect an individual's performance, but ultimately, he depends on his own cognition to regulate his responses. In social contexts, however, there is a series of social indicators that should help that individual to perceive his mistakes and inhibit inadequate behavior. Even in the presence of those cues, individuals with ADHD seem to persist on improper behavior, which causes them to be rejected by groups.

We continued by explaining how social disapproval of one's inadequate behavior is usually expressed as an angry expression and how visual attention is important in order to perceive that expression. That perception should be interpreted by the individual using Theory of Mind, in order to recognize that the perceived stimulus is an angry face, and that it is directed to him or her. Facial mimicry will help in the emotion recognition process, by internally simulating the observed expression.

Subsequently, anger recognition should be registered as a potential threat to the individual, allowing the SPS to take action, triggering a fear response. Emotional awareness, underpinned by social cues, will be a key to accurately experience and interpret those emotions, internally and externally. Ultimately, the SPS

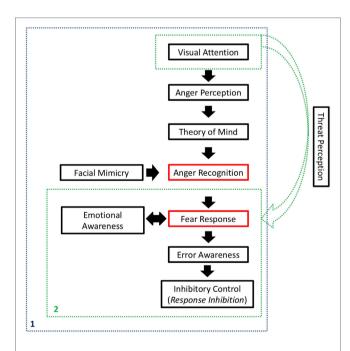


FIGURE 1 | Synthesis of the processes involved on the Self-Protection System (SPS). In blue (1), activation of the SPS in the presence of social inputs, related to anger expression. In green (2), possible activation of the SPS in non-social contexts, when a stimulus is registered as a potential threat. Red rectangles refer to the main components of the SPS, whereas black rectangles refer to processes that affect SPS activation and final response inhibition.

would lead that individual to inhibit his own behavior, discontinuing the action that had caused social disapproval in the first place. An adequate Theory of Mind and emotional awareness would be critical for interpreting the whole situation and establishing a cause and effect relationship, as well as regulating one's own emotions and evaluating the appropriate outcome.

All of that represents a whole cognitive circuitry that starts with visual attention and ends with inhibitory control. In individuals with ADHD, however, all of those functions seem to be impaired, impeding the SPS to be set in motion. As a consequence, social behavior is not properly regulated, resulting in social exclusion and worsening the patient's condition.

We argue that the link between the ISPS and the deficits in inhibitory control, specifically the "response inhibition" component, may be explained by reduced error awareness, since the ability to perceive their own mistakes is fundamental to individuals, in order to control their own behavior (138). Being aware of mistakes committed in a certain context enables the individual to adopt a more cautious behavior in the future, minimizing chances of recurrence (138).

According to a recent meta-analysis, patients with ADHD do not present adequate "post-error slowing," which is the natural reduction in response times after identifying one's error. In other words, these patients do not present the tendency to be cautious in order to avoid committing further mistakes (139). Another study indicated that children with ADHD not only committed more errors in Go/No-Go tasks but they were also less aware of the mistakes they committed (140). Some authors suggest that this reduced error awareness plays a key role in the behavioral regulation in individuals with ADHD, precisely because they cannot correctly identify when they are displaying inadequate postures in a particular context (141).

We argue that this reduced error awareness, specifically observed in social contexts in which a child with ADHD does not understand that he or she is behaving inadequately, happens because of problems in the SPS.

It is important to note that an inadequate social response might not only be related to an impulsive/hyperactive behavior but might also be a simply *faux pas* or an improper response due to not understanding a given social rule. Either way, an individual should perceive his mistake and override his action, even trying to compensate for it.

The SPS concept as proposed by evolutionary psychologists specifically designates anger recognition as the stimulus that put that system in motion. However, we theorize that in non-social contexts, other stimuli could be registered as a potential threat, triggering a fear response and leading to response inhibition as well. Other researchers have proposed the risk-as-feelings hypothesis, discussing that emotional reactions to risky situations often account more to decision-making than cognitive assessment of those risks, driving behavioral responses even if it means resisting cognitive interpretation of consequences (142). It is possible that inattention and SPS-related deficits prevent individuals with ADHD from perceiving other sorts of threat, and/or experiencing the fear response that should follow, making those individuals more likely to assume higher-risk conducts. In that perspective, our hypothesis might explain

response inhibition deficits in the absence of social inputs, in contexts where ADHD individuals seem to present problems as well, such as reckless driving, inconsequential sexual behavior, and breaking the law.

Interestingly, pharmacological treatment for those patients, particularly the use of methylphenidate, seems to improve Theory of Mind (143, 144) and emotion recognition (145), especially the ability to recognize anger (45). After 12 weeks of treatment with methylphenidate, there seems to be an improvement in the ability to recognize emotions of anger and sadness in children with ADHD (146). This may explain the prompt and effective decrease of dysfunctional behavior in patients with ADHD in response to that drug and corroborate to elucidate the role of emotion recognition in behavior regulation.

LIMITATIONS AND FUTURE RESEARCH

We must clarify that we do not intend to cover all the complexity of ADHD with the hypothesis here presented. It was outlined based on research and evidence available so far in literature. Therefore, we recognize and emphasize the need for empirical data that might support our hypothesis.

It is important to note that inhibitory control varies significantly depending on the context (147), which implies that this hypothesis does not explain all the possible alterations in inhibitory control in ADHD patients. We narrowed it down to the context of personal interactions, which are permeated by facial expressions of emotions, and we tried to explain the persistence dysfunctional behaviors that occur in those circumstances. In that perspective, a child with ADHD persists in a given behavior that displeases other people because he or she does not recognize anger properly and, therefore, does not realize he or she is being unpleasant or annoying.

Among the several aspects to be further investigated, the "Anger Superiority Effect" has already been analyzed in several psychiatric disorders, such as in Asperger Syndrome (148), generalized anxiety disorder and panic disorder (149) but never in any subtypes of ADHD. Studies in that direction will be important to assessing their ability to perceive anger in a crowd.

In addition to this, the degree of dependence between visual attention and emotional perception is still controversial (101), and so, it is important to develop paradigms capable of assessing that relation in children with ADHD.

As for the deficits in relation to Theory of Mind, most studies do not clarify whether they are related to the affective dimension (theorizing about the affections of others) or to the cognitive dimension (theorizing about thoughts and intentions of others) of that construct, as recently described (150). This type of study would not only refine our hypothesis but also give a foundation to more specific interventions.

There is also a need to clarify whether children with ADHD present a subjective response of fear when facing images of anger expression, which could demonstrate a more specific impairment of the SPS. It would also be important to analyze if there is evidence of alexithymia in patients with ADHD specifically related to fear. Furthermore, it would be interesting to verify if the

induction of fear could affect inhibitory control in patients with ADHD. In regards to facial mimicry, studies involving children of other age groups would be important in order to assess if there are any alterations involving anger mimicry or not.

We should investigate if the difficulty in recognizing anger in ADHD patients is restricted to facial expression, since anger can be communicated also through body muscle contraction (151), posture (152), gait (153), and voice (154). Studies focused on this will be necessary to verify if deficits in anger recognition are also present throughout other communication channels, thus suggesting a much more difficulty in emotional recognition.

Clinically, it will be important to investigate whether psychological interventions focused on training recognition and adequate response to anger expressions would significantly improve inhibitory control. It creates a promising field to further investigate ADHD and possibly characterize differences and similarities between gender, age, and subtype of ADHD. Even though our hypothesis has been developed to approach ADHD deficits, it is possible that it might apply to other psychiatric disorders. For instance, response inhibition deficits have been also observed in patients with schizophrenia (155, 156), as have been difficulty in emotion recognition (157, 158). Further research would be necessary in order to analyze if other processes involved in the SPS are also impaired in these patients.

Since we are presenting a novel hypothesis, alternative explanations should be assessed experimentally. Some core deficits in ADHD, as the primary attentional deficit, sensation seeking behavior, and general impulsiveness traits could also explain the lack of ability in perceiving inappropriate social responses. Future studies controlling for inattention and inhibition problems should be carried out using experimental design. The emotional Go/No-Go task (110) may be used with a bigger sample contemplating all three ADHD's subtypes, and all basic emotions. That might better demonstrate the deficits in inhibitory control specifically when faced with an angry expression.

Our hypothesis might also lead to a better understanding of the inhibitory control mechanism in typical individuals. Individual differences in regards to emotion recognition have been observed in healthy individuals, both in children (159) and adults (160). Those differences are associated with anatomical and physiological differences (161–163). It is possible that different activation of the SPS in typical individuals also explain individual differences in response inhibition, but that it just a possibility not yet supported by empirical evidence, since we are discussing a novel hypothesis.

The purpose of this paper was to present and discuss a plausible theoretical explanation for the problems in inhibitory control, specifically in the "response inhibition" component, observed in patients with ADHD, addressing them as a consequence of an ISPS which does not function properly because of primary visual attention deficits.

We have made an effort to take social, clinical psychology, and evolutionary perspectives into account. Empirical investigation, however, is necessary in order to find evidence that supports the ISPS hypothesis. Ultimately, we hope we have contributed to the efforts of better understanding ADHD and connecting the knowledge gathered so far by the scientific community.

AUTHOR CONTRIBUTIONS

TC carried out the literature review and elaborated the initial review that gave rise to the basic structure of the hypothesis. SR contributed to the theoretical basis and discussion of the proposal, besides the semantic and grammatical revision. DM guided the article, contributing to the theoretical basis and discussion of the proposal. AS contributed to the theoretical basis and discussion

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Psychometric Properties of a Short Version of the Impulsiveness Questionnaire UPPS-P in a Brazilian Adult Sample: Invariance for Effects of Age, Sex and Socioeconomic Status and Subscales Viability

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Five different facets or domains of impulsivity (lack of Perseverance, lack of Premeditation, Sensation Seeking, Positive and Negative Urgency) have been detected in undergraduate students by means of a short, 20-item version of the Impulsive Behavior Scale UPPS-P. The present cross-sectional study examined the psychometric properties of a Brazilian version of this short scale (SUPPS-P) in a non-clinical sample of 510 individuals with a larger age range (10-72 years) and from varying socioeconomic strata (SES). We also investigated: (a) differential item functioning according to age, sex and socioeconomic status; (b) whether these demographic factors affected participants' responses (population heterogeneity); and (c) if using scores directly derived from respondents' answers (raw scores) reflected the 5 distinguishable impulsiveness domains out of the structural equation modeling environment (bifactor model). We showed that the short UPPS-P version replicated factor structures, internal consistency across domains and inter-scale correlations found in prior studies, and confirmed the psychometric separability of the 5 impulsiveness domains. Only three out of the 20 items showed differential item functioning. Higher Positive and Negative Urgency and lack of Premeditation were reported by men and impulsiveness decreases with age in all domains except lack of Premeditation. SES did not influence results. The viability of using raw scores to assess the five domains was not confirmed via bifactor modeling. The use of a general composite score was psychometrically acceptable. We conclude that, in the structural equation modeling environment, the SUPPS-P is a reliable instrument to assess multiple impulsivity domains in non-clinical community samples in different cultural settings. However, out of this statistical environment, viability was only found for a general factor of impulsivity.

Keywords: impulsive behavior, self-control, affect, attention, risk-taking, sex factors, socioeconomic factors, age factors

INTRODUCTION

Impulsive behavior involves acting without delay, reflection, voluntary direction or control in response to stimuli (Medical Subject Headings, MeSH Unique ID: D007175¹). Although impulsivity (or impulsiveness) is considered by some as a unitary construct, it has been proposed that it encompass various facets or domains which vary among non-clinical populations (e.g., Whiteside and Lynam, 2001; Whiteside et al., 2005; Smith et al., 2007) and individuals with psychopathologies (see Berg et al., 2015).

A widely used (see Berg et al., 2015) instrument that assesses overlapping but distinguishable impulsive domains is the self-report Impulsive Behavior scale UPPS (Whiteside and Lynam, 2001; Whiteside et al., 2005). The domains that this scale reflected factors, obtained in exploratory factor analysis, that aggregated items/questions from various valid and reliable questionnaires that measure traits associated to impulsivity (Whiteside and Lynam, 2001; Whiteside et al., 2005). Each domain has been found to be differently associated to behavior in several psychopathological conditions such as alcohol/substance abuse, attention deficit hyperactivity disorder, eating disorders, as well as traits found in non-clinical samples, such as variations in aggressiveness, self-discipline, academic performance, anxiety and depressive symptoms, and risk taking (e.g., gambling, engaging in antisocial and illegal activities) (e.g., see Whiteside et al., 2005; Cyders and Smith, 2007; Smith et al., 2007; Berg et al., 2015).

UPPS is an acronym composed of letters that represent each of its impulsiveness domains: (1) Negative <u>Urgency</u>, the tendency to commit rash or regrettable actions as a result of negative affect; (2) (lack of) <u>Premeditation</u>, the tendency not to reflect on the consequences of one's actions; (3) (lack of) <u>Perseverance</u>, or difficulty in staying focused on hard of tedious tasks; and (4) <u>Sensations Seeking</u>, the tendency to seek new and exciting experiences. A fifth domain, <u>Positive Urgency</u> ("—P"), or the tendency to experience strong impulses when in unusually positive mood (see Cyders and Smith, 2007; Berg et al., 2015), was later added to the scale, forming an instrument named UPPS-P.

The UPPS-P is a relatively long scale containing 59 items, a somewhat inappropriate characteristic if testing time is short and for populations who tire and become easily distracted, such as youngsters and people with low socioeconomic status/schooling. To circumvent these limitations, reduced versions of the scale have been proposed, such as the one by Cyders et al. (2014), called short UPPS-P (SUPPS-P). To build this scale, items with highest corrected item-total correlation for each domain in the full UPPS-P version were initially selected. Redundant items (i.e., those with inter-item correlations greater than 0.50 with the already selected item) were discarded and then the next most correlated item within the domain was selected. The procedure was repeated until four items per domain were selected, totaling 20 items (Cyders et al., 2014).

Compared to the full UPPS-P, the SUPPS-P of Cyders et al. (2014) was completed much faster and maintained

comparable factor structure, internal consistency and subscale inter-correlations, with only a minimal loss of shared variance (Cyders et al., 2014). Such a short scale that allows the identification of separable impulsivity traits is of great interest for research and clinical purposes worldwide.

There is another short, 20-item version of the UPPS-P that was proposed by Billieux et al. (2012) (translated into Spanish: Cándido et al., 2012; Italian: D'Orta et al., 2015; and Arabic: Bteich et al., 2017). To build this short scale the authors followed a different approach to that used by Cyders et al. (2014): they chose the four items with the highest factorial loads in their respective domains. As explained in Cyders et al. (2014), although this may preserve the reliability of the reduced scale by eliminating items with more error variance, it can increase redundancy and in this way may reduce content validity.

The SUPPS-P (Cyders et al., 2014) and the publications derived from Billieux et al.'s (2012) work studied the psychometric properties of the scales mostly in highly educated young adults from developed nations. It would be of interest to determine whether this type of scale could be used in populations with different cultural and demographic characteristics. After all, various facets of impulsiveness are affected by respondents' age, sex, socioeconomic status (e.g., Costa et al., 2001; Steinberg et al., 2008; Reimers et al., 2009; Cross et al., 2011; Chamorro et al., 2012; Cyders, 2013) and, possibly reflect differences in culture, genetics, biological and environmental backgrounds (Kacen and Lee, 2002; Bezdjian et al., 2011; Cross et al., 2011; Chamorro et al., 2012). For example, in the United States, higher impulsiveness is associated with being born in that country, non-Hispanic white, never married and aged 18-29, while lower impulsiveness is found in people with high educational attainment and income (Chamorro et al., 2012). It is therefore not unreasonable to suppose that varying demographic characteristics could influence the factor structure of the SUPPS-P, possibly making it inadequate in samples other than undergraduate students from high-income industrial countries. In effect, the factor structure of the SUPPS-P in undergraduate students from Iran (Shokri and Sanaeepour, 2016), a country with different demographics to those in the United States, needed some corrections to be comparable to the 5 factor model solution found by Cyders et al. (2014).

Hence, in order to determine the extent to which Cyders et al.'s (2014) SUPPS-P is useful in populations that are not highly educated young adults from fully developed nations, the present study investigated whether a translated version of the SUPPS-P into Portuguese would have adequate psychometric properties in a Brazilian non-clinical community sample. We also investigated the effects of age, sex and socioeconomic status on the way participants responded to the scale items (invariance testing) and on the latent traces in the 5 domains of impulsivity.

Because we included in our sample many under-aged individuals who had not reached their maximum schooling levels, participants' schooling was not controlled for. Instead, we used parental education as a proxy for socioeconomic status (see Sirin, 2005) because it reflects home and school environments while their progeny is growing up, which influences biopsychosocial trajectories of development (see Cohen et al., 2010). In adults

¹ https://www.ncbi.nlm.nih.gov/mesh/?term=impulsivity

worldwide, schooling tends to remain stable over time, as do income and occupation (see Sirin, 2005), so parental schooling is unlikely to change. Furthermore, as there is not much intergenerational social mobility in Brazil (Ribeiro, 2014), this measure can indicate indirectly, to some extent, participants' present socio class.

Lastly, we assessed the practical utility of raw scores (directly derived from participants' responses, and not latent variables) to indicate the separability of the 5 domains of the UPPS-P. In other words, we studied if it is reliable and viable to use such scores out of the structural equation modeling environment (bifactor modeling).

MATERIALS AND METHODS

Participants

This study involved a Portuguese-speaking non-clinical community sample that either responded to a translated version of the SUPPS-P available online or provided responses in person (young population over the age of 9 years, with legal guardian agreement).

Procedure

This cross-sectional study was conducted according to international ethical guidelines and the Brazilian National Heath Council ethical resolution (Resolução 466/12). It was approved by the Ethic Committee of the Universidade Federal de São Paulo (UNIFESP) (#1.976.055; #2.001.042). All participants and legal guardians, when applicable, provided informed consent and/or assent. A demographic questionnaire and the SUPPS-P (see below) were made available online in the platform Google Forms for 5 months. Recruitment of respondents was made through social media. For the under-aged participants, the same questionnaires were printed out and handed to minors in a waiting room at an adolescent clinic at UNIFESP during the same period. Data other than cited below were also collected and results pertaining to them will be reported elsewhere.

Demographic Questionnaire

We enquired about participants' age, sex, and schooling of their male and female parents (or corresponding guardians with these roles) in seven strata (ordinal variable) according to the Brazilian educational system: 1 (incomplete basic schooling, which lasts 8 or 9 years depending on participants' age); 2 (complete basic schooling); 3 (incomplete high school, which lasts 3 years); 4 (complete high school); 5 (incomplete tertiary education, which usually lasts 4 years); 6 (complete tertiary education); or 7 (any sort of post-graduate training).

SUPPS-P

The items from the SUPPS-P (Cyders et al., 2014) in Portuguese pertaining to all impulsiveness domains except Positive Urgency were obtained from the research team that adapted the UPPS for use in Brazil, which was shown to display adequate psychometric properties (Nogueira et al., 2013; Sediyama et al., 2017). These researchers also provided translations of the Positive Urgency

items, which are currently under validation. Items of the scale are affirmations. Respondents are asked to report the extent to which they agree with each statement on four-point Likert scales ranging from 1 (agree strongly) to 4 (disagree strongly). In our version, higher scores in the domains Perseverance and Premeditation indicated higher impulsivity, while for the domains Sensation Seeking, Positive and Negative Urgency, lower scores indicated more impulsivity.

Statistical Analysis

The analysis was undertaken in various steps, using Mplus 8.0 (Muthén and Muthén, 1998–2017).

Firstly, we tested three models specified by Cyders et al. (2014) using Confirmatory factor analyses (CFA) under weighted least squared mean-variance estimator (WLSMV) due to the fourpoint Likert structure of SUPPS-P. The following models were investigated: Model 1 included all 20 SUPPS-P items loading onto a single general impulsivity factor. Model 2 included five latent traits corresponding to the five SUPPS-P domains, each with four items. Model 3 is specified in a second-order, hierarchical structure, having two higher order latent variables (see Cyders and Smith, 2007): 1) Emotion-based Rash Action (formed by Negative and Positive Urgency first order factors); 2) Deficits in Conscientiousness (formed by lack of Perseverance and of Premeditation first order factors). Sensation seeking was kept as a first order factor. To compare the nested models 2 and 3 we used the Delta CFI (Cheung and Rensvold, 2002), which indicates worsening in model fits when values are greater than 0.002 (Meade et al., 2008). This is a more stringent approach to compare models than the use of $\chi 2$ (Meade et al., 2008) applied by Cyders et al. (2014).

We tested model invariance through the Multiple Indicators Multiple Causes (MIMIC) method for the covariates sex, age, mother and father's level of education. This was done under Model 2, which had a good fit and informs on the separability of all 5 domains (see Results and Discussion for details on the reasons for this selection). We followed the two basic steps for MIMIC modeling (Brown, 2015). First, a measurement model was established using the full sample (in our case, in Model 2). Then, the direct effects of the covariates on the factors and the indicators (items) were evaluated. When a significant direct effect of the covariate on the factor is found, it indicates population differences or heterogeneity (i.e., the factor means are different at different levels of the covariates). On the other hand, a significant direct effect (i.e., modification indices > 4) of the covariate on an indicator of a factor (i.e., the UPPS-P items) represents Differential Item Functioning (DIF). This means that responses to specific item are different at different levels of the covariate. As described in Brown (2015, p.282) and here tested "[MIMIC] is frequently evaluated in an exploratory fashion." We fixed all direct effects between sex, age, mother and father's schooling and the fivefactors correlated solution indicators to zero. We then inspected modification indices to determine whether relevant direct effects were present. To evaluate the reliability (called rho, ρ) of the five factors under the specifications of Model 2, we used the factor loadings and residual variances from the CFA's Model 2

as described by Joreskog (1971) and Dillon and Goldstein (1984).

To assess the reliability and viability of SUPPS-P's subscales using raw scores derived directly from participants' answers, and not from latent traces in the structural equation modeling environment, we ran another model (Model 4). This bifactor structural model (also called general-specific model) specifies that the covariance among a set of item responses can be accounted for by two main sources of information. The first is a single general factor that reflects the common variance to all scale items (in our case, the general concept of impulsivity); the second source of information derives from group factors (the five domains of impulsivity) that reflect additional common variance among clusters of items with similar content. It is assumed that the general and group factors are all orthogonal (i.e., not correlated) (Figure 4). Under a bifactor model, different indices can be computed: (a) Coefficient omega (Lucke'sω) (Revelle and Zinbarg, 2009; Reise, 2012; McDonald, 2013), which is a reliability estimate based on factorial model that estimates the proportion of the observed variance in the total score attributed to all sources of common variances; (b) Coefficient omega hierarchical (ω_h) (Reise et al., 2011; Rodriguez et al., 2016a), which is a reliability index that judges the degree to which the composite scale scores are interpretable as a measure of a single common factor. -The coefficient omega hierarchical is computed by dividing the squared sum of the factor loadings on the general factor (model estimated) by the variance of total scores -; (c) Coefficient omega subscale (ω_s) (Reise et al., 2011; Rodriguez et al., 2016a) reliability and viability estimate for a residualized subscale, controlling for that part of the reliability due to the general factor (i.e., the percentage of the subscale score variance attributable to a specific group factor of items after removing the reliable variance due to the general factor). - This index reflects the reliability of a subscale score after controlling for the variance due to the general factor -; and (d) Explained common variance (ECV), which is the percentage of common variance explained by the general factor. This is a type of unidimensionality index which is directly related to the relative strength of the general factor. It can be defined as the ratio of the explained variance by the general factor divided by the variance of the general and specific factors. Details of these calculations can be found in (Rodriguez et al., 2016a,b).

For Lucke's omega (ω) , Coefficient omega hierarchical (ω_h) , and Coefficient omega subscale (ω_s) , scores higher than 0.8 indicate a strong relationship between the latent variable and item scores. An ECV higher than 0.70 indicates that the instruments should be treated as essentially unidimensional, as a single common factor (Rodriguez et al., 2016a,b).

RESULTS

The sample was composed of 528 participants. There were incomplete SUPPS-P data from 9 under-aged and 9 adult volunteers so their data were excluded from the analyses. The sample used in the models was thus of 510 individuals (27% of whom were male) aged 10-72 years (mean age = 25.4, SD = 12.3 years). There were 160 participants under the age of 18,

210 between the ages of 18 and 29 years, 105 aged 30–49 years, and 35 were aged 50 or older. Schooling of parents (the measure of socioeconomic status) ranged from strata 1 to 7, with a mean score (mean = 4.3 years, SD \pm 2.0) that corresponds to having completed high school. The sample was varied in this respect as there was a minimum of 23 cases in each of the 7 mother or father schooling stratifications. Ten participants reported not having had a person who acted as a mother and 39, as a father.

Structural Equation Modeling Following Cyders et al. (2014)

Regarding the models proposed by Cyders et al. (2014), with no correction for demographic characteristics, we found that Model 1 (one-factor model), with all 20 SUPPS-P items loading onto a single "impulsivity" factor, fit data poorly $[\chi^2_{(170)} = 2884.743,$ p-value < 0.001, RMSEA = 0.176 (90%CI = 0.171 to 0.182), CFI = 0.567, TLI = 0.516] (Figure 1). In contrast, adequate fits were obtained for Model 2 (Figure 2), with five first-order correlated latent factors corresponding to the five SUPPS-P domains $[\chi^2_{(160)} = 536.059, p$ -value < 0.001, RMSEA = 0.068 (90%CI = 0.061-0.074); CFI = 0.940; TLI = 0.929], and Model 3 (Figure 3), the second order factor model with 2 s order factors (emotion-based rash action and deficits in conscientiousness, and Sensation Seeking as a first order factor) $[\chi^2_{(163)} = 527.974,$ p-value < 0.001, RMSEA = 0.066 (90%CI = 0.060-0.072), CFI = 0.942, TLI = 0.932]. Low inter-correlations between the majority of the domains were found in Models 2. The two pairs of domains with the highest correlations formed the 2 s order factors in model 3. Adding this restriction (e.g., second order factor) in Model 3, when compared to model 2, did not worsen the fit indices ($\Delta CFI = 0.942$ minus 0.940 = 0.002). Under Model 2 structure, the reliability of the five factors (ρ) were: ρ of Negative Urgency = 0.820; ρ of Perseverance = 0.794; ρ of Premeditation = 0.825; ρ of Sensation Seeking = 0.824; ρ of Positive Urgency = 0.866. ρ were not assessed for Model 3 as they are not appropriate for hierarchical models.

Measurement Invariance (MIMIC model)

Here, again we focused on Model 2 (see more details about this in the Discussion section). We identified only three items with DIF related to sex. Males had a higher probability of disagreeing with the statement "Unfinished tasks really bother me" (Premeditation) and agreeing with "I would like to learn to fly an airplane" (Sensation Seeking) and "Others are shocked or worried about the things I do when I am feeling very excited" (Positive Urgency) than females. Moreover, the latter item also exhibited a DIF in terms of age (i.e., the older the participant, the higher the probability of disagreeing with this statement). No items with DIF were associated to parental schooling (measure of socioeconomic status).

Population Heterogeneity

Regarding latent outcomes using Model 2, we found an effect of sex on Premeditation (beta = -0.134; p = 0.01), Positive (beta = 0.115; p = 0.02) and Negative (beta = 0.123; p = 0.02) Urgency, indicating that males were more impulsive on these

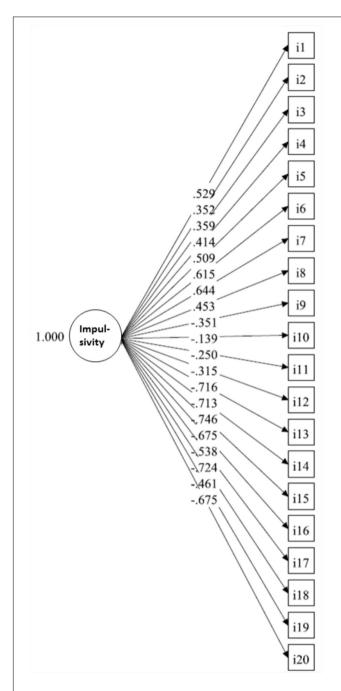


FIGURE 1 | Model 1, including all 20 items of the Short Impulsive Behavior Scale SUPPS-P loading onto a single "impulsivity" factor. N.B. Individual items (i1–i20) from Cyders et al. (2014) are identified in boxes. The first 8 items correspond to the domains Perseverance and Premeditation (4 items each, in order) for which lower scores indicated higher impulsivity. The following items refer to Sensation Seeking, Positive Urgency and Negative Urgency (Neg), for which higher scores indicate more impulsiveness. Values on single headed arrows indicate factor loadings.

domains. Older ages were associated with lower impulsiveness in all domains except Premeditation [Perseverance (beta = -0.185, p < 0.001); Sensation Seeking (beta = 0.178, p < 0.001); Positive Urgency (beta = 0.178, p < 0.001); and Negative Urgency

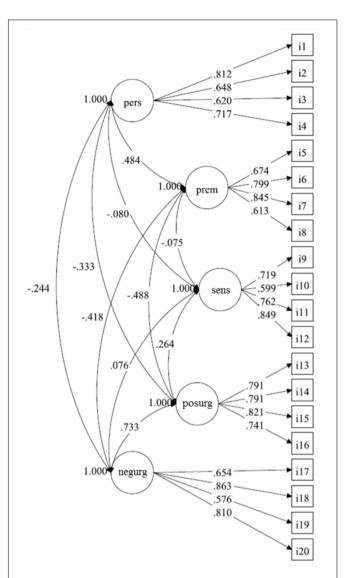


FIGURE 2 | Five-factor model (Model 2) of the Short Impulsive Behavior Scale (SUPPS-P), in which groups of four items (i) load onto their specific domains. N.B. individual items (i1–i20) are identified in boxes and impulsive domains, in circles. Higher scores in the domains Perseverance (pers) and Premeditation (prem) indicate lower impulsivity, while higher scores indicate more impulsiveness in Sensation Seeking (sens), Positive Urgency (posurg), and Negative Urgency (negurg). Values on double headed arrows indicate correlations among domains (those with r > 0.09 had p < 0.05); values on single headed arrows indicate factor loadings.

(beta = 0.201, p < 0.001)]. Parental schooling had no effects (p-values > 0.17).

Bifactor Model and Scale Reliability and Viability When Using Scores Directly Obtained From Participants' Answers

Model 4 (**Figure 4**), the less restrictive model (the bifactor solution), returned the following fit indices: $[\chi^2_{(150)} =$, p-value < 0.001, RMSEA = 0.062 (90%CI = 0.055 to 0.068), CFI = 0.953, TLI = 0.941]. Based on this model, we

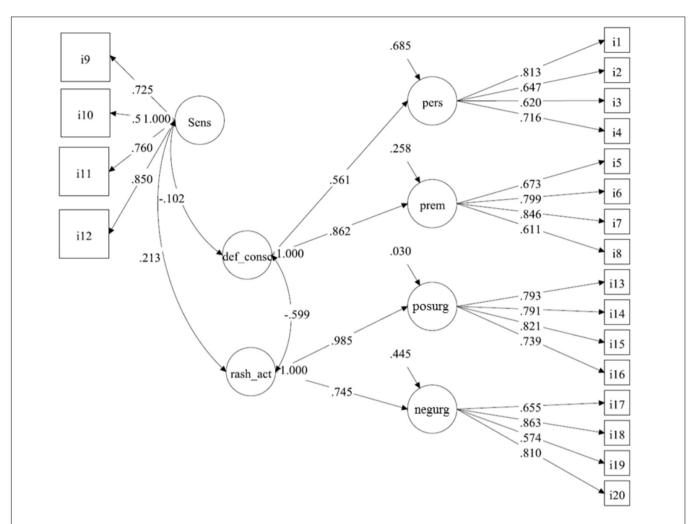


FIGURE 3 | Model 3 on data from the Short Impulsive Behavior Scale (SUPPS-P), with a second-order hierarchical structure with two higher order latent variables (see Cyders and Smith, 2007): (1) Emotion-based Rash Action (formed by Negative and Positive Urgency first order factors; rash_act); (2) Deficits in Conscientiousness (formed by lack of Perseverance and of Premeditation first order factors; def_consc). Sensation seeking (Sens) was kept as a first order factor. N.B. individual items (i1–i20) are identified in boxes and impulsive domains, in circles. Lower scores in the domains Perseverance (pers) and Premeditation (prem) indicate higher impulsivity, while higher scores indicate more impulsiveness in Sensation Seeking (Sens), Positive Urgency (posurg) and Negative Urgency (negurg). Values on double headed arrows indicate correlations among domains; values on single headed long arrows indicate factor loadings. Short arrows indicate residual variance.

computed a model-based reliability estimate for each of the SUPPS-P subscales using Lucke's omega, applying it to one domain at a time: ω of Negative Urgency = 0.828; ω of Perseverance = 0.797; ω of Premeditation = 0.824; ω of Sensation Seeking = 0.829; ω of Positive Urgency = 0.875. Although these reliabilities were good, they were considerably lowered when the effects of the general impulsivity factor was removed in Model 4, with the exception of the domain Sensation Seeking [this evaluation was conducted via Coefficient omega subscale [ω_s]: $\omega(s)_{Perseverance} = 0.659$, $\omega(s)_{Premeditation} = 0.533$, $\omega(s)_{Sensation Seeking} = 0.801$, $\omega(s)_{Positive Urgency} = 0.169$, and $\omega(s)_{Negative\ Urgency} = 0.363$]. Other indices derived from the bifactor model were: EVC = 0.404, ωH = 0.673, Lucke's ω for the whole scale = 0.917. From ω_H , we found that 67.3% the variance in the unit-weighted total scores could be attributed to the differences between participants in the general

impulsivity factor. The square root of ω_H (82.03%) indicated a very strong correlation between the general impulsivity factor and the observed raw scores. Only 8.3% of variance was due to random error (i.e., the difference between 1.000 and 0.917).

DISCUSSION

Our data replicated Cyders et al.'s. (2014) in terms of factor structure and reliability of the SUPPS-P, in spite of having involved a sample from a different culture that varied more in terms of age and socioeconomic status. As found by Cyders et al. (2014), the model with all SUPPS-P items loading onto a single "impulsivity" factor (Model 1) fit the data poorly, whilst the solution with five distinguishable impulsivity

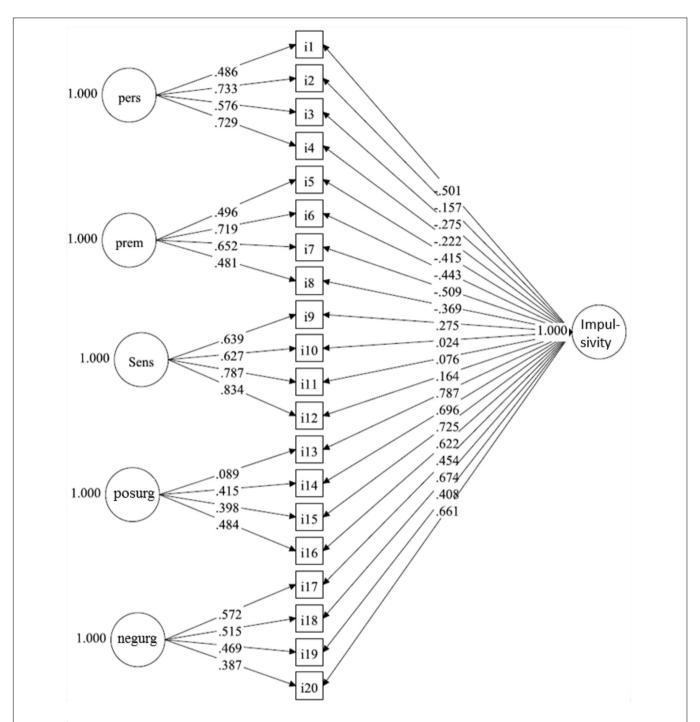


FIGURE 4 | Bifactor structural model (Model 4) on data of the Short Impulsive Behavior Scale (SUPPS-P), which specifies that the covariance among a set of item responses can be accounted for by two main sources of information: (1) a single general factor of impulsivity that reflects the common variance among all scale items; (2) group factors (the five domains of impulsivity) that reflect additional common variance among clusters of items with similar content. N.B. Individual items (i1–i20) are identified in boxes and impulsive domains, in circles. Lower scores in the domains Perseverance (pers) and Premeditation (prem) indicate higher impulsivity, while higher scores indicate more impulsiveness in Sensation Seeking (Sens), Positive Urgency (posurg), and Negative Urgency (negurg). Values on single headed arrows indicate factor loadings.

domains (Model 2) and the hierarchical Model 3 had adequate psychometric properties. Additionally, the restrictions imposed from Model 2 to Model 3 did not worsen fits here, nor in Cyders et al.'s. (2014) publication, even when we used a more

stringent approach to compare these models (Meade et al., 2008). Hence, regarding Model 3, we confirm (Cyders and Smith, 2007; Cyders, 2013; Berg et al., 2015) that there is a particular association between Positive and Negative Urgency,

and Premeditation and Perseverance (see also Billieux et al., 2012).

We used Model 2 instead of Model 3 to analyze if there were any items that were answered differently (DIF) according to age, sex and socioeconomic status and to assess population heterogeneity according to these demographic variables. This choice was based on the following reasoning: (1) Model 2 exhibits direct association between the items and their respective domains (reflected via factor loadings), whereas these relationships cannot be directly tested in the second-order model because the specific factors of each domain are represented by disturbances of the first-order factors (Chen et al., 2006); (2) Model 2 informs in more detail on factors that influence more dissociable impulsiveness domains; 3) Model 2 has also been found in other studies using the full UPPS-P scale with adolescents (Gunn and Smith, 2010) and the UPPS without considering Positive Urgency (e.g., Whiteside and Lynam, 2001; Smith et al., 2007).

In our sample, we found that when five different facets of impulsiveness are considered separately (Model 2), the majority of SUPPS-P items functioned comparably across ages, sexes and different socioeconomic backgrounds. Such inspection is fundamental to assert about the usefulness of comparing groups of individuals with different demographic characteristics in simple statistical analyses such as correlations and t-tests. Only three items were answered differently by men and women, reflecting intuitive sex differences: men wanted to fly airplanes to a greater extent, were less bothered by unfinished tasks and reported worrying people more over impulsive behaviors when in unusually positive states. The latter item was also reported more often by younger individuals, which makes sense as they have adult guardians who are responsible for their wellbeing. These effects may be culturally driven or might be found irrespective of respondents' origins (biological based) (see Cross et al., 2011). Because this type of analyses has not been previously done in the SUPPS-P literature, we have no data do compare our results with.

The finding that sex influences responses in some items is in accord with the sensitivity of Model 2 to population heterogeneity. Males reported lower levels of Premeditation, Positive and Negative Urgency, effects that are not in total agreement with data from Cyders (2013), who found that, among undergraduate North Americans, males indicated higher positive urgency and sensation seeking than females. This may be accounted for by the demographic and/or cultural differences in our and their samples. Another possibility is that our samples varied in terms of genetics and the environment, both of which influence impulsivity (Bezdjian et al., 2011). In fact, meta-analytic and nation-wide surveys often report that sex effects are variable and not always found (Cross et al., 2011; Chamorro et al., 2012; Sharma et al., 2014). Furthermore, some impulsive traits are systematically influenced by regional (individualism-collectivism) and individual cultural differences (independent –interdependent self-concept) (e.g., Kacen and Lee, 2002). Factors that determine an internationally found bias in female volunteering (e.g., Wilson, 2012) must also be considered, as most of our sample was composed of women.

The present study was not designed to investigate factors that could account for possible sex effect and there is little information

on how culture affects the SUPPS-P, which is a relatively new scale. Rather, we focused on showing whether this short scale was adequate for use in populations with varied demographic characteristics from non-developed cultures. This was confirmed.

The finding that increases in age were associated to a fall in impulsiveness in all domains except Premeditation corroborates that most aspects of impulsivity decrease throughout adulthood (Reimers et al., 2009; Chamorro et al., 2012), irrespectively, it seems, to country of origin. However, there are exceptions. In the cross-cultural study by Adrianson et al. (2013), despite similar levels of impulsivity (Barratt Impulsivity Scale) in samples from Indonesia and Sweden and higher overall impulsiveness in younger individuals, younger Indonesians had higher impulsivity than older individuals from their culture, while the opposite pattern was found in the Swedish sample. A myriad of sociocultural differences can be used to explain these differences (see Adrianson et al., 2013) and indicate that age-effects in impulsiveness are influenced by the environment in which people are raised.

The lack of effects of socioeconomic background is of interest, especially as Brazil has a much wider range of social strata than most countries in which the UPPS-P was tested. Low socioeconomic status has been found to be associated to higher impulsivity (e.g., Reimers et al., 2009; Chamorro et al., 2012), but this is difficult to tease apart from biological, environmental and/or cultural differences among samples of different nations, as outlined above. The self-report nature of the SUPPS-P might also explain these results, because socioeconomic status-induced effects on impulsive-like traits are higher when impulsiveness is assessed by others, such as parents or teachers (see Piotrowska et al., 2015).

Overall, we found that, in terms of factor structure, the SUPPS-P behaved very much as it did in the North American undergraduate sample of Cyders et al. (2014). Nevertheless, Shokri and Sanaeepour (2016), who applied this scale in a sample of Farsi speaking undergraduates, only found a 5 domain factor solution after some adjustments to their statitical model. It is possible that this occurred because their study was underpowered due to a small sample or that the adaptation of the scale was not adequate. Given our data, it is unlikely that the necessity of this adjustment stemmed from different socioeconomic status between the North American and Iranian samples. However, other genetic, environmental and/or cultural differences that are not observed when comparing Brazil and the United States, both Western cultures, might be to blame (see Kacen and Lee, 2002). Understanding the reasons why the SUPPS-P behaved differently in Shokri and Sanaeepour's (2016) study may be possible when further cross-cultural studies on the SUPPS-P are carried out.

The structural similarity of impulsiveness as measured by the SUPPS-P in prior and the present study suggests that these traits reflect expressions of biology, such as genetic predisposition (see Kreek et al., 2005; Fineberg et al., 2014), as observed for personality (see McCrae et al., 2000). However,

these characteristics can be modulated and moderated by culture, in that they can result from varying expectations from distinct environmental settings. This can explain part of the different patterns of effects of sex (Cross et al., 2011)

and age (e.g., Adrianson et al., 2013) in different samples. The present study, however, was not a cross-cultural investigation in the sense that it did not compare data of different cultures directly. Rather, it descriptively compared the factor structure of the SUPPS-P in a Brazilian and North-American sample. To confirm the extent to which the 5 types of impulsiveness proposed in the SUPPS-P are due to biology and how other sociocultural factors influence them, cross-cultural investigations must be carried out, ideally investigating genetic and longitudinal maturational changes in the factor structure of the SUPPS-P as done when analyzing personality traits (e.g., McCrae et al., 2000).

In the present study, despite the good reliability of the 5 factor solution and the sensitivity of the different domains to age and sex, under the bifactor model the viability and reliability of using raw scores (participants responses, and not latent traces) on the 5 subscales were poor (with exception of the subscale Sensation Seeking). Moreover, when ω_H was compared with Lucke's ω, around two thirds of the reliable variance in raw scores could be attributed to a general impulsiveness factor determined by adding scores of all items, which reflects individual differences in impulsivity considered only as a broad concept. Importantly, in this case, there was only 8.3% of variance due to random error, which shows that the items adequately captured the intended construct when considering the general concept of impulsivity. Therefore, only around one third of the reliable variance in the raw scores could be associated to the dimensionality of the 5 specific domains. This means that the raw scores obtained in the 5 domains of the SUPPS-P should not be used out of the structural equation modeling environment to indicate different aspects of impulsiveness.

Many factors lead us to believe that the SUPPS-P is a reliable instrument that can be used in different cultural settings: (a) its psychometric properties in a North American (Cyders et al., 2014) and Brazilian samples were similar to each other and to the full UPPS-P scale in a young sample (see Gunn and Smith, 2010) regarding the existence of 5 distinguishable impulsivity dimensions; - like others (Cyders and Smith, 2007; Cyders, 2013; Berg et al., 2015) we also found an association between Positive and Negative Urgency, and Premeditation and Perseverance in a hierarchical model-; (b) it allows a quick characterization of different types of impulsiveness because it involves a significant gain in time of response compared to the full scale (Cyders et al., 2014); (c) sex and variable ages differently influenced distinct domains, making the scale useful to differentiate traits associated to impulsiveness in various cultures, especially as socioeconomic status did not influence results. However, the above mentioned issues regarding the separability of the 5 domains should be considered only in structural equation modeling environments

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and do not hold true when using raw scores, directly derived from respondents' answers in each domains. This is so because only one third of the reliable variance in the bifactor model could be attributed to the dimensionality associated with the 5 impulsivity dimensions. In contrast, using measures obtained from all items considered jointly (such as adding the raw scores) reliably reflected a general factor of impulsiveness.

We conclude that the SUPPS-P has good psychometric potential and can be useful, in structural equation modeling environments, to investigate 5 distinct impulsiveness domains in populations other than young, highly educated adults from developed countries. However, using raw scores only provides reliable information on a general impulsiveness trait. Future studies must analyze the psychometric properties of the SUPPS-P in clinical populations and elderly individuals. A comparison of the psychometric properties of the short version used here to that proposed by Billieux et al. (2012), despite the shortcomings of the latter (explained in Cyders et al., 2014), would also be of use to the international literature to inform on which short scale best reflects the full UPPS-P factor structure.

AUTHOR CONTRIBUTIONS

SP conceived the study, performed the formal analysis, wrote the initial draft, supervised, administrated the project, and acquired the funding. LI, GZ, and RdF performed the experiment and collected data, prepared visualization/data and manuscript presentation, and reviewed the manuscript. LM-D critically reviewed, commented, and revised the manuscript. HC-M performed formal analysis, critically reviewed, commented, and revised the manuscript.

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Bad Choices Make Good Stories: The Impaired Decision-Making Process and Skin Conductance Response in Subjects With Smartphone Addiction

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Introduction: Smartphone Addiction (SA) has caused negative consequences and functional impairments in college students, such as reduction of academic performance and impairment in sleep quality. Studies have shown that individuals with chemical and behavioral dependencies have a bias in decision-making process, which leads to short-term advantageous choices even if they cause long-term harm. This bias in decision-making process is accompanied by a change in somatic markers and is associated with the development and maintenance of addictive behavior. The decision-making process and the measurement of physiological parameters have not yet been analyzed in SA. The neuropsychological and physiological characterization of the SA can contribute to its approach with the other dependency syndromes and to its recognition as a disease.

Objective: we aimed to evaluate the decision-making process under risk and under ambiguity in individuals with SA and to measure the physiological parameters that accompany this process.

Method: We compared the performance in the lowa Gambling Task (IGT), Game of Dice Task (GDT) and skin conductance response (SCR) between 50 individuals with SA and 50 controls.

Results: Smartphone dependents presented a profile of impairment in decision-making under ambiguity, without impairment in decision-making under risk. They demonstrated lower SCR before disadvantageous choices, higher SCR after rewards and lower SCR after punishments during decision-making, which suggests difficulty in recognizing disadvantageous alternatives, high sensitivity to rewards, and low sensitivity to punishments.

Conclusion: The impairment in the decision-making process in smartphone dependents is similar to that found in other chemical and behavioral addictions, such as alcohol addiction, gambling disorders and pathological buy. The impairment in decision under ambiguity with preservation of decision under risk may reflect dysfunction of implicit emotional processes without dysfunction of explicit cognitive process. This profile can contribute to the recognition of SA as a behavioral dependence and to guide specific preventive and therapeutic strategies.

Keywords: decision-making, game of dice task, Iowa gambling test, skin conductance, smartphone addiction, somatic markers

INTRODUCTION

Smartphone Addiction (SA) is a new construct that has been associated with morbidity, such as reduction in academic and labor performances (1–9), sleep disorders (10, 11), impairments in interpersonal relationships (12–14), and an increased risk for in traffic accidents (12–14). The screening prevalence of SA ranges from 25% in the USA (15), 27% in Hong Kong (16), and 38% in Spain (17), to 43% in Brazil (18).

The key features of SA are the interruption or reduction of important social, occupational, or recreational activities due to smartphone use (19–24); constant preoccupations with the possibility of device absence (13, 21, 24, 25); an increased frequency and intensity of use despite negative consequences (19–21, 24); a difficulty in controlling use (12, 19, 23, 25–27); and the presence of dysphoric symptoms when the contact with the smartphone is precluded (17, 19–21, 24, 25, 27, 28). SA has not been included in the diagnostic and statistical manuals of mental disorders (DSM) (29) despite the large range of data already available.

Similar to what occur in other dependence syndromes (30–37), decision making may be impaired in SA. This impairment in decision making process may predispose subjects to become addict to smartphones and increase the negative consequences of SA. For example, preferring smartphone use, as a short-term reward, may be a risk factor for the development of addiction, and may result in long-term impairments such as reduction of interpersonal relationships quality.

Decision making can be divided in two subtypes, accordingly to probability of its results: (1) decision making under ambiguity; and (2) decision making under risk (38). In decision-making under ambiguity, the consequences of decision and probability of outcomes are implicit in the decision. The subject must initially infer about the quality of the options available by the memory processing of previous decisions (cognitive feedback and emotional feedback). Decision-making under ambiguity reflects more strongly the reality of daily decisions, which are made without prior certainty of the probability of each outcome (39). In decision making under risk, the subject receives explicit rules and can choose through the risk calculation of the options before making any choice. Decision making under risk is more frequently observed in situations where there is certainty of the probability of each outcome (40). Previous studies have demonstrated impairment in performance in decision-making in behavioral addictions (33, 41–44). Most studies that investigated the two types of decision making concomitantly in these patients demonstrated impairment in decision making under ambiguity, with preservation of decision-making under risk, as suggested in studies with pathological buyers (44) and pathological gamblers (45, 46). We present, in **Supplemental Material**, a compilation of studies that have evaluated the decision-making process in individuals with behavioral dependencies.

Physiological parameters and somatic markers contribute to decision making process (47). Skin conductance response (SCR), is one of the physiological parameters modified during decision making process (47). Accordingly to somatic marker hypothesis, the modification of SCR after losses and gains reflects the appraisal of decision outcome and the sensibility to punishments and rewards (47). Anticipatory SCR, in face of a decision process, is a somatic marker, that may be interpreted as warning signal, helping the subject to choose advantageous alternatives and to avoid disadvantageous alternatives in future decisions (47). In real life, the increase of SCR before disadvantageous choices and after losses during decision-making help to postpone rewards and to guide choices based on long term benefits, helping achieve goals and objectives. Subjects with addictions present a decreased SCR when confronted with disadvantageous choices and after losses. They also present an increased SCR after wins on decision-making tests (31, 35, 48). These findings suggest that subjects with addictions present impairment in recognizing disadvantageous alternatives, hypersensitivity to rewards and hyposensitivity to punishments. These pattern of decision making process contribute to the onset and maintenance of addictive disorders (49, 50).

Three studies assessed decision making under risk in subjects with SA. They used the "Intertemporal Choice Test" (ICT) to access decision under risk and do not measured physiological parameters (51–53). As far as we know, until know, no study has evaluated decision-making under ambiguity in SA. However, the study of the two types of decision making is important so that we can compare the neuropsychological profile of individuals with SA with individuals with other dependency syndromes. Individuals with SA are more likely to present a decision-making profile similar to that presented by the majority of individuals with other behavioral dependencies (preservation of the decision under risk with impairment of the decision under ambiguity) and slightly different from that presented by the majority of individuals with chemical dependencies (impairment

in the two types of decision-making). If this is true, it will be another fact that suggests the inclusion of SA within the behavioral dependency syndromes, thus increasing the validity of this new construct.

Furthermore, no studies have measured alterations in SCR during decision making process in subjects presenting SA, which makes it difficult to interpret the impairments found in the performances in the tests that measure decision making.

We hypothesize that smartphone dependents make more disadvantageous decisions on tests that measure decision-making under ambiguity and have no impairments in decision-making under risk when compared to control subjects. Moreover, we hypothesize that higher scores on the screening scale for SA are correlated with worse performances in both decision-making under ambiguity test. Finally, we expect that smartphone dependents present a lower anticipatory SCR before disadvantageous choices compared to SCR before advantageous choices; and higher SCR after wins compared to SCR after losses during both decision-making tests. Therefore, in this study we assessed decision-making under risk and under ambiguity in subjects at risk for SA and measured alterations in SCR that accompanied this process.

MATERIALS AND METHODS

Participants and Sample

For this study we randomly selected 100 graduate students aged between 18 and 25 years, from the sample of our previous study for the validation of the Brazilian version of the "Smartphone Addiction Inventory (SPAI-BR)" (18). For this study we divided the selected subjects in two groups of 50 subjects each, accordingly to the SPAI-BR results. We included, in the positive screening group, subjects presenting positive screening for SA; and not presenting other psychiatric disorders accordingly to Brazilian version of the "Mini-International Neuropsychiatric Interview" (MINI). In the control group we included subjects with negative screening for SA; and not presenting other psychiatric disorders accordingly to MINI. We excluded subjects presenting past history of traumatic brain injury; current or past history of neurological disorder; current or past history of psychiatric disorder/substance use disorder; current use of psychiatric and/or neurological drugs; an intelligence quotient inferior to 80.

Instruments

• Brazilian Smartphone Addiction Inventory (SPAI-BR): the SPAI is a screening scale for SA, which was constructed and validated in Taiwan in 2014 (54). It has 26 items and four factors: "compulsive behavior," "functional impairment," "withdrawal syndrome," and "tolerance." In 2017, we translated and validated the SPAI for use in Brazil (18). The SPAI-BR is positive for SA screening if there is at least seven positive answers (18). We chose the SPAI-BR as the measure for SA because no established diagnostic criteria for the construct currently exist. Also, SPAI-BR has good psychometric characteristics, and it is the only scale for SA screening that has been validated for use in Brazil.

- Raven Progressive Matrices Test–General Scale: it assess non-verbal intellectual performance of all age individuals (55). The test checks a person's ability to grasp meaningless figures, establish relationships between them, make inference about the nature of the figure that would complete the system of implicit relationships, and develop a systematic method of reasoning. The test consists of 60 items, each successful one scores at one point. The total score is transformed into intelligence quotient (IQ) by a mathematical formula. The instrument was validated for use in Brazil in 2003 (56).
- Game of Dice Task (GDT): In this study, we used a computerized version of GDT, which was developed by Brand et al. (57) and validated for Brazilian use by Rzezak et al. (58). In GDT the rules are explicit and stable for gains and losses as well as for the probabilities of winning throughout the test. Individuals are required to predict the outcomes of a dice throw. They must decide between different alternatives (a single number or a combination of numbers) that are explicitly related to a specific amount of gain and loss and which have obvious probabilities of an advantageous result (1: 6-4: 6). Because rules for profit and loss are explicitly provided, individuals can calculate the risk associated with each alternative from the beginning of the test and can use strategies to maximize profit. Each choice is related to a specific gain and loss that depends on the probability of occurrence of the choice (one number: U\$1,000 loss/gain; combination of two numbers: U\$500 loss/gain; combination of three numbers: U\$200 loss/combination of four numbers: U\$100 loss/gain). Participants are also informed that they are expected to make a total of 18 throws. To analyze decisionmaking under risk, authors ranked the choices of one or two numbers as risky or disadvantageous, and the choices of three or four numbers as non-risky or advantageous. A total score is calculated by the sum of advantageous choices (three and four numbers) minus the sum of disadvantageous choices (one and two numbers). Therefore, a positive overall score indicates a better test performance and a lower propensity to make risky choices.
- Iowa Gambling Task (IGT): In this study, we used a computerized version of IGT, which was developed by Bechara et al. (59) based on the original test (60) and validated for Brazilian use by Malloy-Diniz et al. (61). In the computerized version of IGT, participants see four decks of cards on the computer screen (A, B, C, and D) and must choose one card at a time, which can generate a gain or a gain followed by a loss. After choosing 100 cards, the test ends automatically. For each 10 cards from the deck "A," the participant earns U\$ 1,000, but there are 5 unpredictable losses of U\$250, causing a total loss of U\$250. For each 10 cards from the deck "B," the participant earns U\$1,000, but there is also a large loss of U\$1,250, causing a total loss of U\$250. On the other hand, for every 10 cards in decks C and D, the patients earn only U\$500, but the losses are also smaller (ranging from U\$25 to U\$75 on deck C and U\$250 on deck D), leading to a total gain of U\$250. In sum, mounts A and B are equivalent in terms of total loss and mounts C and D are equivalent in terms of total gain. In long

term, decks A and B are disadvantageous and decks C and D are advantageous.

Skin Conductance Response (SCR): SCR was measured using the NeXus4[®] physiological data meter and obtained by applying a 0.5 V voltage current to electrodes positioned on the index and middle fingers of each participant's nondominant hand. SCR was measured in Micro-Siemens (µS) and the fluctuation of SCR was considered significant if $>0.1 \mu S$ (62, 63). The following SCR measures were carried out: post-rewards SCR (measured after money wins), post-punishment SCR (measured after money losses), advantageous anticipatory SCR (measured before advantageous choices), and disadvantageous anticipatory SCR (measured before disadvantageous choices). In accordance to the recommendations of Nikolaidou et al. (37), the time window for the measurement of SCR in rewards and punishments began in the 2nd s after the result of the choice until the 5th s. For the anticipatory SCR, the measurement began in the 6th s after the result of the previous choice until the 9th s. SCR was quantified dividing the area under the SCR curve by the time determined in seconds (μ S/s). The interval between the choices in both tests was set at 10 s to ensure non-overlap between SCRs and to allow skin conductance to return to the baseline level between the choices.

Procedures

Participants were submitted to a self-filled questionnaire composed of the following parts: (1) sociodemographic questions (i.e., biological gender; self-declared race/skin color; date of birth; marital status; monthly family income); (2) questions about health conditions (current or past history of cranioencephalic trauma; current or past history of neurological disorder; current or past history of psychiatric disorder; current use of psychiatric and/or neurological medication; current use of licit or illicit drugs); (3) Raven Progressive Matrix Test; and 4-SPAI-BR. After completing the questionnaires, participants performed the GDT and the IGT, concomitantly with the measurement of the SCR. Procedures were performed under the supervision of a psychiatrist and two trained students.

Statistical Analysis

The sample size was calculated using G Power 3.1.0 software. The parameters used were: F-test, two-tailed, hypothetical effect size of 0.29 [according to the study of Tang et al. for the assessment of decision-making under risk in smartphone dependents (53)], p < 0.05, and test power of 0.80. For these parameters, the sample size should be of 80 individuals (40 in each group). Considering a possible loss of 20%, 100 individuals were recruited to participate in the study (50 for the case group and 50 for the control group).

The results were submitted to statistical analysis using the statistical package SPSS version 23 (IBM Corporation, Rochester, MN), and "p" was set at < 0.05 as significance level. The normality of the data was analyzed by the Kolmogorov- Smirnov test.

For descriptive analyses, means, standard deviations, medians, quartiles, and intervals for the continuous variables were calculated. For the categorical variables, absolute, and relative frequencies and proportions were calculated. As the data had

a non-normal distribution, we used the Mann-Whitney test to compare means of independent samples and the Wicoxon test to compare means of dependent samples. The Spearman Correlation Coefficient was used to calculate the correlation between SPAI-BR, IGT, and GDT scores. Effect sizes were calculated as suggested by Field (64).

RESULTS

At the endpoint, 10 subjects were excluded from the sample: four individuals interrupted the questionnaire during the procedure, and six failed to measure SCR. Of the 90 individuals composing the final sample, 47 (52.22%) were female and 43 (47.77%) were male. In addition, 47 (52.22%) individuals were smartphone dependents and 43 (47.77%) were controls. Regarding sex, there were 25 (27.77%) women and 22 (24.44%) men in the SA group; and 22 (24.44%) women and 21 (23.33%) men in the control group. The mean age was 22.39 (\pm 1.67) years. The average monthly family income was U\$ 1,762 (\pm 712). The mean IQ was 115.89 (\pm 6.18). The sociodemographic characteristics of the sample can be seen in **Table 1**.

Decision Making Process Under Ambiguity and Under Risk in SA and Controls

The variables presented a non-normal distribution in the Kolmogorov-Smirnov test (p < 0.001). The control group presented higher total score in the IGT, with a large effect size, when compared to the smartphone dependents group (z = -6.094, p < 0.001, ES = 0.64). The score in Block 1 of the IGT did not differ between the two groups (z = -0.057, p = 0.955). The score in Block 2 was higher, with an average effect size, in the control group when compared to the smartphone dependents group (z = -3.308, p = 0.001, ES = 0.35). The scores in Blocks 3, 4, and 5 were higher, with a large effect size, in the control group

TABLE 1 | Sociodemographic characteristics of the sample.

Characteristics		N	%
Gender	Female	47	52.2
	Male	43	47.8
Marital status	Married	5	5.6
	Not-married	85	94.4
Race/skin color	White	55	61.1
	Not-white	35	38.9
IQ range	Average average	15	16.7
	High average	47	52.2
	Superior	27	30
	High superior	1	1.1
Monthly family income	Up to \$814	5	5.6
	From U\$814 to U\$1,628	13	14.4
	From U\$1,628 to U\$2,442	8	8.9
	From U\$2,442 to U\$3,257	8	8.9
	From U\$3,257 to U\$4,071	8	8.9
	From U\$4,071 to U\$5,428	5	5.6
	Above U\$5,428	25	27.8
	Do not know/did not answer	18	20

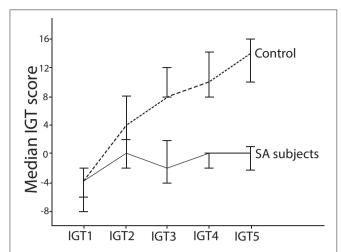


FIGURE 1 | Median score per block in IGT in individuals of the smartphone dependents group and control group. This figure shows that smartphone dependents score lower than controls in the IGT as they progress through the test. This figure also shows that only in Block 1 the control subjects had negative scores (more disadvantageous than advantageous choices), while in blocks 2, 3, 4, and 5 they had positive scores (more advantageous than disadvantageous choices). On the other hand, smartphone dependents do not show tendency of overall increase on scores throughout the test. In addition, in all blocks the scores were negative (i.e., more disadvantageous than advantageous choices) or equal to zero (the same amount of advantageous and disadvantageous choices). Throughout all the game, the scores of the control group were higher than the scores of the smartphone dependents group.

when compared to the smartphone dependents group (z = -5.250, p < 0.001, ES = 0.55; z = -5.216, p < 0.001, ES = 0.55; and z = -5.381, p < 0.001, TE = 0.57, respectively). **Figure 1** shows the median scores by blocks on the IGT in the control group and in the smartphone dependents group.

There was no significant difference in the GDT score between the smartphone dependents group and the control group (z = -0.831; p = 0.416). This data can be seen in **Table 2**.

Correlations

As shown in **Table 3**, we found a positive weak correlation between the IGT score and the GDT score (rho = 0.288, p = 0.006). In addition, we found negative and moderate correlation between the IGT score and the SPAI-BR score (rho = -0.516, p < 0.001). No significant correlations were found between the GDT score and the SPAI-BR score (rho = -0.056; p = 0.602).

Skin Conductance

The skin conductance values presented a non-normal distribution in the Kolmogorov-Smirnov test (p < 0.05). Therefore, the Wilcoxon test was performed for the paired skin conductance analysis.

In the control group, we found a higher SCR anticipatory to the disadvantageous choices in relation to the advantageous choices in the IGT (z=-4.069; p<0.001; ES =0.62). On the other hand, the smartphone dependents group presented a higher SCR anticipatory to the advantageous choices in relation to the

TABLE 2 Comparison between the smartphone dependents and the controls with respect to the medians of the scores in the total IGT. IGT by blocks, and GDT.

	Smartphone dependents		Controls		Z	p	ES
	М	IQ	М	IQ			
IGT total score	-6	22	30	22	-6.094	<0.001*	0.64
IGT block 1 score	-4	6	-4	8	-0.057	0.955	NA
IGT block 2 score	0	8	4	10	-3.308	0.001*	0.35
IGT block 3 score	-2	10	8	10	-5.250	<0.001*	0.55
IGT block 4 score	0	8	10	10	-5.216	<0.001*	0.55
IGT block 5 score	0	8	14	10	-5.381	<0.001*	0.57
GDT	12	12	14	10	-0.831	0.416	NA

ES, effect size; IQ, interquartil interval; M, median.

*p < 0.05; NA, not applicable.

TABLE 3 | Spearman coefficient correlation between variables.

	SPAI-BR	IGT
SPAI-BR		
IGT	-0.516*	
GDT	-0.056	0.288*

*p < 0.05.

disadvantageous choices in the IGT (z=-5.037; p<0.001; ES = 0.73) (**Table 4**).

In the control group, there was a higher SCR after punishments compared to the SCR after rewards in the IGT (z=-3.595, p<0.001, ES = 0.55). However, in the smartphone dependents group, there was a higher SCR after rewards compared to SCR after punishments in the IGT (z=-3.810, p<0.001, ES = 0.56). These data can be visualized in **Table 5**.

In the control group, there was a higher SCR anticipatory to disadvantageous choices in relation to the SCR anticipatory to advantageous choices in the GDT (z=-3.968; p<0.001; ES = 0.61). However, in smartphone dependents group, there was a higher SCR anticipatory to advantageous choices in relation to the SCR anticipatory to disadvantageous choices in the GDT (z=-4.996; p<0.001; ES = 0.73). These data can be visualized in **Table 6**.

In the control group, there was a higher SCR after punishments compared to the SCR after rewards in the GDT (z=-3.212, p=0.001, ES=0.49). However, in the smartphone dependents group, there was a higher SCR after rewards in relation to the SCR after punishments (z=-4.318, p<0.001, ES=0.63). These data can be seen in **Table 7**.

DISCUSSION

According to our initial hypothesis, smartphone dependents presented impairment in the decision-making under ambiguity with preservation of decision-making under risk. Our sample presented a negative correlation between the severity of SA in the SPAI-BR questionnaire and the performance in decision making under ambiguity in the IGT. Regarding the physiological

TABLE 4 | Comparison between SCR anticipatory to advantageous choices and SCR anticipatory to disadvantageous choices in the smartphone dependents group and in control group during IGT performance.

	SCR anticipatory to advantageous choices		SCR anticipatory to disa	Z	р	ES	
	Median	IQ	Median	IQ			
SD	1.1122	1.2656	1.0709	1.0053	-5.037	<0.001*	0.73
Controls	0.7667	0.9220	0.8582	0.9876	-4.069	<0.001*	0.62

ES, effect size; IQ, interquartil interval; SD, smartphone dependents.

TABLE 5 | Comparison between SCR after rewards and SCR after punishments in the smartphone dependents group and in control group during IGT performance.

	SCR after rewards		SCR after	SCR after punishments		p	ES
	Median	IQ	Median	IQ			
SD	1.1326	1.0969	1.0072	0.9953	-3.810	<0.001*	0.56
Controls	0.8173	1.1218	0.8622	1.1758	-3.595	<0.001*	0.55

ES, effect size; IQ, interquartil interval; SD, smartphone dependents.

parameters, smartphone dependents presented, in both decision-making tests, a decrease in SCR before disadvantageous choices, an increase in SCR after rewards, and a decrease in SCR after punishments, which also corroborated our initial hypothesis. To the best of our knowledge, this is the first study investigating decision-making performance under risk and ambiguity in smartphone dependents both in behavioral and physiological levels.

Except for the performance in the first block of the IGT, smartphone dependents presented a worse performance in all IGT blocks and total IGT when compared to controls. These findings strongly suggest that smartphone dependents chose more disadvantageous alternatives than advantageous alternatives during almost the whole test. We suggest that smartphone dependents present an impaired decision-making under ambiguity. When the rules of the game are not explicit and the outcomes are uncertain, smartphone dependents presented a difficulty making advantageous long-term choices. They tend to prefer advantageous alternatives in the short term, even when they bring greater future losses. Their decision-making pattern is in parallel to the physiological modifications found in smartphone dependents during decisionmaking under ambiguity. The lower anticipatory SCR before disadvantageous choices indicates a possible deficit in generating somatic markers that usually work as warning signals against disadvantageous decisions (47). Consequently, it is possible that smartphone dependents have deficits in transferring their emotional reactions to create anticipatory warning signals that would guide future decisions (48, 65). Moreover, the increase in SCR after rewards, associated with the decrease in SCR after punishments, suggests that smartphone dependents appraise decision outcome differently from control subjects. Smartphone dependents presented a greater sensitivity to rewards and a lower sensitivity to punishments. Their decisions are guided preferably by the search for rewards rather than the avoidance of punishments. Therefore, when an alternative generates high reward, it is chosen even if it generates greater punishment in long term.

The same profile of decision-making under ambiguity in smartphone dependents has been described in subjects presenting substance and gambling addictions (33, 41, 66-69), suggesting that SA is part of the addictive syndromes. This "myopia for the future" profile at decisive moments can contribute to the initiation and maintenance of addictive behaviors, as individuals perform the behavior because they are more sensitive to the immediate reward caused by it and less sensitivity to the damage they can cause in various areas of life (47). Therefore, the greater sensitivity to "likes" and "comments" on social networks for example may be a vulnerability factor for the development of SA and for the maintenance of dysfunctional use of smartphones, even when there are losses or possibility of damages in several areas of life, such as reduction of academic and work performance and impairments in interpersonal relationships. This can contribute to the reduction of functionality and to the generation of suffering to self and / or others, essential characteristics to consider a set of signs and symptoms as a psychiatric disease.

Although in the GDT the smartphone dependents presented the same changes in the SCR as in the IGT, there was no impairment in the GDT performance in these individuals. This finding can be explained by the fact that cold executive functions can contribute to GDT performance, independently of emotional feedback processing (32, 38, 39). In other words, when smartphone dependents have doubts about the probability of winning or losing, biased implicit emotional processing can influence the choice of disadvantageous alternatives, but when they know exactly the likelihood of winning or losing, explicit knowledge influences the decision of advantageous options. These results were similar to those found in one study with pathological buyers (44), and in two studies with pathological gamblers (45, 46). In these studies, individuals of case group presented a worse performance in the IGT when compared to controls, but there was no difference in the performance in the GDT between groups (44-46). As postulated by Damasio, impairment in decision-making under ambiguity is probably

p < 0.05

p < 0.05.

TABLE 6 | Comparison between SCR anticipatory to advantageous choices and SCR anticipatory to disadvantageous choices in the smartphone dependents group and in control group during GDT performance.

	SCR anticipatory to advantageous choices		SCR anticipatory to dis	Z	p	ES	
	Median	IQ	Median	IQ			
SD	0.6185	0.6179	0.4388	0.7342	-4.996	<0.001*	0.73
Controls	0.3369	0.7786	0.5143	0.6337	-3.968	<0.001*	0.61

ES, effect size; IQ, interquartil interval; SD, smartphone dependents. $^*p < 0.05$.

TABLE 7 | Comparison between SCR after rewards and SCR after punishments in the smartphone dependents group and in control group during GDT performance.

	SCR after rewards		SCR after punishments		z	p	ES
	Median	IQ	Median	IQ			
SD	0.5533	0.7072	0.4567	0.6505	-4.318	<0.001*	0.63
Controls	0.4633	0.6478	0.5267	0.6830	-3.212	0.001*	0.49

ES, effect size; IQ, interquartil interval; SD, smartphone dependents.

*p < 0.05.

more detrimental to real life than impairment in decision making under risk (39).

Three studies found impairment in decision-making under risk in smartphone dependents (51–53). However, they used the Intertemporal Choice Test (ICT) to evaluate decision making. In the ICT individuals have to react to changing winning probabilities, while the probabilities in GDT are stable, allowing the establishment of long-term strategies (38). Therefore, the tests may measure different aspects of executive functions and, consequently, different aspects of decision-making under risk.

In the analysis of decision-making process in Internet dependents, most of the studies demonstrated that these individuals do not show impairment in the performance in the IGT (36, 37, 70). In addition, during the IGT performance, Nikolaidou et al. (37), demonstrated that Internet dependents had higher SCR after punishments and lower SCR after rewards, indicating a profile of hypersensitivity to punishments and hyposensitivity to rewards in these individuals. This profile is just the opposite of that presented by smartphone dependents. Therefore, the neuropsychological profile of Internet dependents may be different from that of smartphone dependents. Internet dependents (who use Internet preferably for online games on desktop computers) (71-73) are more introverted, have more social phobia, and are more sensitive to punishments (74-76). Therefore, they can use the Internet as a way to escape from punitive reality, as if they wanted to "escape from real life" and from social exposure. On the other hand, smartphone dependents (who use smartphone preferably for social networks engagement) (77, 78) are more extroverted, more impulsive and more likely to novelty-seeking (12, 15, 16, 76, 79-82). Therefore, they can use the smartphone as a way to broaden social contacts, seek new sensations and receive rewards. This difference in the profile may be another evidence to distinguish the constructs "Internet Addiction" and "Smartphone Addiction."

The decision-making profile of smartphone dependents may reflect a dysfunction of the ventromedial pre-frontal cortex (VMPFC), and limbic system, with preserved functionality of the dorsolateral pre-frontal cortex (DLPFC) (83). More specifically, alterations in the functioning of the amygdala and other structures of the limbic system may cause less sensitivity to punishment and greater sensitivity to rewards (primary emotions). Some authors have suggested that, in substance addictions, there is initially a functional impairment of the VMPFC and the limbic system that favors the beginning and continuation of psychoactive substances use, even in face of possible future damages. On the other hand, the DLPFC impairment would occur lately in chemical addictions and would be caused by the direct neurotoxic effect of the drugs in this region. Therefore, it is plausible that in SA there is only impairment in decision making under ambiguity with preservation of decision under risk, since there is no direct effect of a chemical substance in the central nervous system (84–86).

The impairment in decision-making under ambiguity in smartphone dependents can be analyzed through the triadic model of decision-making (87). The impulsive system, represented mainly by the amygdala-striatum, contributes to automatic behaviors and habits (87). Its hyperactivation in SA may contribute to the compulsive ritual of regular checking of smartphones due to hypersensitivity to rewards (e.g., likes and comments on social networks) and hyposensitivity to punishments (e.g., traffic accidents, relationships problems). In addition, the influence of external stimuli (such as smartphone vibration, emission of sounds and lights, or even the visualization of people using the device) can contribute to the hyperactivation of the impulsive system, contributing to increase the smartphone use behavior. The reflexive system, represented mainly by the VMPFC, contributes to self-regulation and prediction of future consequences of the behavior (87). Its hypoactivation in SA may contribute to the difficulty to control the intensity and frequency of smartphone use, and to the difficult in

recognizing its long-term disadvantages, such as academic and labor impairments. Finally, the insula system, which detects homeostatic perturbations translating internal signals into feelings of craving, increases the activation of the impulsive system and reduces the activation of the reflexive system. In SA, the hyperactivation of the insula may contribute to the identification of insight feelings and thoughts that trigger the search for the smartphone, increases impulsivity and reduces selfcontrol. Therefore, the possible hyperactivation of the impulsive and insula system and the hypoactivation of the reflexive system in SA can impair the decision making under ambiguity, favoring abusive use of smartphones even in face of negative consequences or possibility of future negative consequences caused by this behavior. However, these assumptions are hypothetical, since the correlation between the impairment in decision-making and the functional alterations in brain circuits in SA can only be established by studies with functional imaging.

Decision-making under ambiguity reflects more strongly the reality of daily decisions, since most decisions in real life are made without the prior certainty of the probability of each outcome (39). In addition, it has already been shown that impairment in decision-making under ambiguity is more detrimental to daily life than impairment in decision-making under risk (39). Therefore, the functional decline in smartphone dependents daily lives can be consequent of the impairment in decision-making under ambiguity. The current findings have clinical implications as preventive strategies can focus on the development of emotional regulation, awareness of bodily signs / symptoms, and postponement of rewards. It has already been shown that these strategies can be achieved by physical exercises, focus attention training, mindfulness, biofeedback, interoceptive exposure therapy, and Cognitive-Behavioral Therapy (CBT) (87).

Our findings should be regarded considering some limitations. This study has a cross-sectional design and do not allow the establishment of cause and effect relationships. In addition, the only physiological parameter measured was skin conductance, which may have reduced the sensitivity and specificity of these measures. The use of fake money during decision-making tests may have induced a less cautious behavior of the individuals who participated in the study. Finally, the use of a sample without psychiatric comorbidities in the experimental group does not reflect the clinical presentation of the majority of the subjects with smartphone dependents, according to previous studies. However, we preferred to exclude subjects with psychiatric disorders from the experimental group to avoid the effects of mood in the performance in the decision-making process. Therefore, the creation of a homogenous experimental

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group made possible the evaluation of the exclusive influence of the dependence of smartphone on the modification of the decision-making process.

Therefore, we can assume that technology is not only a source of benefits. Our results suggest that some technologies, as smartphone use, may trigger patterns of mental dysfunctions in vulnerable subjects, similar to additive disorders. SA seems to be the same disease with another face, the dimensional syndrome of addiction that share biological and cognitive vulnerabilities. More studies are warranted to assess the cognitive dysfunction in a longitudinal design using neuroimaging approach in SA.

ETHICS STATEMENT

All participants were informed about the voluntary nature of the study and its implications, and signed the Informed Consent Term. The study was submitted and approved by the Research Ethics Committee of the Federal University of Minas Gerais (UFMG) with the number C.A.A.E. number 54066516.0.0000.5149 and carried out according to the latest version of the Declaration of Helsinki.

AUTHOR CONTRIBUTIONS

All authors participated in the whole study process in an egalitarian way. All authors had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt. 2019.00073/full#supplementary-material

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