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Pathways of risk, resilience, and recovery: Impact of stress and trauma on women and girls

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Pathways of risk, resilience, and recovery: Impact of stress and trauma on women and girls

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Editorial: Pathways of risk, resilience, and recovery: impact of stress and trauma on women and girls

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Editorial on the Research Topic
Pathways of risk, resilience, and recovery: impact of stress and trauma on women and girls

Introduction

Stress and trauma are ubiquitous experiences that have been identified as transdiagnostic factors associated with a higher risk for disproportionately detrimental physical and mental health outcomes for women and girls, including posttraumatic and affective disorders (1, 2). The underlying mechanisms of this increased risk likely involve complex biopsychosocial processes that have yet to be fully identified (3). Furthermore, the role of protective and resilience factors buffering these associations remain relatively unexamined. In this Research Topic, we aim to address this complexity from various interdisciplinary perspectives and discuss the biological, psychological, and social factors that may underpin both risk and resilience in the face of stressful and traumatic experiences.

This collection of research includes biological substrates of risk, such as neural (Eder-Moreau et al.), genetic (Carvalho et al.) and endocrine (Brouillard et al.) factors. It also addresses potential social determinants of poor health, such as economic precarity and social isolation (Pazderka et al.) as well as the co-occurrence among mental health, risky behavior, and infectious disease among women released from incarceration (Johnson et al.). Social determinants also hold the potential for buffering potentially negative impact, through resources accessed in the face of adversity (Zamir et al.). The psychological underpinnings that may help explain the associations between stressful experience and compromised outcomes are also explored. These include interpretation of stressors from a social perspective (Azoulay and Gilboa-Schechtman) as well as from a psychological perspective, such as mentalizing (Ensink et al.). Finally, this Research Topic considers potential mechanisms for familial, intergenerational effects of maternal stress, such as parenting (Ahmad et al.).

Biological substrates of stress-related disorders (SRDs) among women

A study investigating epigenetic changes in immune cells following trauma found that shortened leukocyte telomere length observed among women exposed to sexual assault was associated with re-experiencing post-trauma symptoms. However, this association between trauma and a marker of cellular aging did not persist over time, possibly indicating a temporary and reversible effect near the time of traumatic event (Carvalho et al.).

A systematic review of neural patterns among adult women exposed to trauma showed that the type of trauma (i.e., interpersonal violence, sexual trauma, and childhood trauma) is associated with specific neural regions. While the amygdala and frontal regions of the frontoparietal network were implicated in all trauma types, only childhood trauma was related to parietal regions of this network and with the hippocampus. Interpersonal violence was the only type of trauma consistently associated with the anterior cingulate cortex and medial prefrontal cortex and was also related to altered insula activity and structure, as was sexual trauma. The caudate was implicated only in sexual trauma (Eder-Moreau et al.).

Lastly, lifetime usage of hormonal contraceptives was identified as a risk factor for psychological distress during stressful experiences as it was associated with poor mental health during the COVID-19 pandemic: it was associated with both more severe and persistent symptoms (Brouillard et al.).

Taken together, these articles suggest that there are specific and enduring brain structural and functional alterations in adult women that are associated with specific timings and types of traumatic exposures, and that epigenetic changes may occur, albeit temporarily. Also, the utilization of oral contraceptives may be associated with risk for maladjustment following stress, thereby underscoring the potential role of gonadal hormones in stress response and subsequent adjustment.

Social determinants of SRDs among women

Social determinants of health encompass social variables that are associated with the risk of disease (4), its severity (5), access to care (6), and the recovery process (7). Such variables include social support, socioeconomic status, community factors, race, ethnicity among others (4, 8, 9). Social determinants of health have also been associated with SRDs. Within this collection, several studies have examined risk and resilience factors for women in high-risk, underserved populations.

In a survey of women living through the COVID-19 pandemic in a remote town considered to be inhospitable to women due to living in temporary accommodations, high crime rates, and a patriarchal reputation, the authors examined the impact of job loss, relationship status, access to mental health counseling or medication, and social support on probable diagnosis of PTSD (Pazderka et al.). Under these particularly harsh conditions, support from family and friends as well as negative stressors of job loss, but not access to mental health treatment or relationship status, predicted posttraumatic stress.

Women who have been released from incarceration constitute a vulnerable population as they have frequently been exposed to trauma prior to and during incarceration (Lynch and Heath (10) found that this marginalized group is particularly vulnerable to both SRDs and infections, in particular, sexually transmitted infections, including human immunodeficiency virus and hepatitis C (11, 12). As SRDs are associated with low adherence to healthcare treatment, increased infection risk is of particular concern. The WORTH Transitions is an intervention developed to reduce risk of additional trauma, prevent infection, and promote healthy behaviors among these high-risk women in a culturally appropriate treatment. The study of this intervention found that PTSD was negatively associated with session engagement and positively correlated with loss to follow up, but not with risk of infection. Being a black or indigenous woman of color was also associated with lower engagement, underscoring the need to tailor interventions to better meet the need of this marginalized population.

An additional study examined the association between stressors during pregnancy and mother and child's outcomes postpartum (Ahmad et al.). The study highlights the vulnerability of women from underserved communities of color with lower incomes who face a higher risk of experiencing prenatal stressors.

Social determinants of health have an impact on the general population as well. In one article (Zamir et al.) authors examine such impact for women contending with breast cancer a women with breast cancer. This study highlights the impact of family income level and partner support in parenting on maternal post-traumatic symptoms and parenting behaviors. Their findings suggest that partner support fully mediated the effects of income levels on maternal posttraumatic symptoms.

In summary, these studies underscore the importance of social determinants of health across several levels. On the community level, belonging to specific communities, such as minority or low socioeconomic status groups, constitutes a risk factor for traumatic exposure, as well as for low engagement with treatment programs, and requires community-level prevention and adherence support. On the interpersonal level, women benefit from the support of partners, family, and friends, which helps mitigate the effects of stressful and traumatic experiences, however the mere existence of partners appears not to be enough. Finally, economic disadvantage is a risk factor for the detrimental impact of stress and trauma, but its effect may also be explained, in some cases, by the availability of social support.

Psychological underpinnings of SRDs among women

The systematic review included in this Research Topic showed that females with PTSD demonstrate greater emotional dysregulation than controls, as expressed both on the behavioral and neural level. Authors suggest that the findings reflect reduced neural activation when faced with positive stimuli and increased activation when faced with negative stimuli, related to the negative attention bias found in posttraumatic stress disorder. Authors

further present data to support the relationship between these biases and traits like neuroticism as well as coping mechanisms, such as rumination. Women may, perhaps due to heightened neuroticism, be biased toward negative information, ruminate on this information, experience emotional dysregulation due to reductions in top-down control, expressed at the neural level, thus displaying a distinct symptom profile (Eder-Moreau et al.).

In one study, authors explored the associations between attachment, mentalizing, and posttraumatic stress symptoms among pregnant women with a history of childhood maltreatment. The authors present findings supporting mentalizing as a resilience factor and a potential mechanism for reducing symptoms within this population by mitigating the association between childhood maltreatment and SRDs (Ensink et al.).

Another study (Azoulay and Gilboa-Schechtman) suggests exploring sex difference in SRD prevalence through the lens of two theoretical frameworks: social construction theory vs. evolutionary theory. Social construction theory suggests women's increased risk for such disorders may be tied to lower perceived and actual social status, while the evolutionary theory suggests it depends on the interruption of specific sociobiological goals, and that women are more susceptible to physical threats, while men are more sensitive to status losses. An experimental design produced results consistent with the evolutionary theory such that status losses were not associated with posttraumatic distress among women.

Articles in this section suggest that women may be susceptible to SRDs due to gender biases in psychological traits, such as neuroticism, use of coping mechanisms, such as rumination, and negativity biases. However, women may also be protected from these effects by utilizing more adaptive coping mechanisms such as mentalization and may not be susceptible to the contributing effects of specific types of stressful events, such as status loss, to SRD development.

SRDs and intergenerational (familial) effects

For women, SRDs are most prevalent during childbearing years (13). As a consequence, research on intergenerational effects of trauma has largely focused on mothers, as have several studies in this special section.

One study focused on mothers with breast cancer. These mothers experience compound stress, coping with the intensive treatments and their physical side effects as well as continued childcare demands. According to the family stress model, stressful conditions may cause emotional distress which may deplete the psychological resources of the parents, lending to harsh parenting practices. In this study, the authors found a positive association between maternal post-traumatic stress symptoms during breast cancer treatment and harsh parenting practices, and maternal posttraumatic stress symptoms fully mediated the association between paternal support and parenting practices (Zamir et al.).

However, motherhood can be conceptualized as beginning in the peripartum period. Stress experienced by mothers in the prenatal period affects their children's mental health and development. In the systematic review included here, findings suggest maternal prenatal stress associates with self-regulation problems, difficulties with executive functioning, and subsequent externalizing behavioral problems in children (Eder-Moreau et al.).

An intergenerational study examined this association between maternal stress and child outcomes within a diverse sample of mother-child dyads (Ahmad et al.). Their results emphasize the role of parenting as a protective factor and the importance of positive parent-child interactions and supportive parenting behaviors in mitigating intergenerational risks. Notably, intimate partner violence emerges as a prenatal stressor significantly associated with a child's subsequent executive functioning.

In the study discussed in the previous section (Ensink et al.), mentalizing regarding early attachment relationships moderated the association between childhood maltreatment and SRDs, specifically posttraumatic symptoms, among pregnant women. This finding, coupled with the study demonstrating the importance of maternal symptoms in determining parenting practices, suggests that the capacity to mentalize may serve as a potential mechanism for curbing intergenerational effects of trauma.

Conclusions

Reviewing results across these studies, the interdisciplinary articles in this Research Topic examine the impact of multiple types of stressful experiences on the mental and physical health of women and girls: sexual assault, interpersonal stress, childhood maltreatment, breast cancer, and the COVID-19 pandemic. The findings suggest that sex- and gender-specific risk factors may include factors such as hormonal contraceptive use or the type of stressor experienced and its subjective perception. They also delineate potential protective and resilience factors that may mitigate the negative impact of stress and trauma on mental health outcomes. External interpersonal resources (such as familial, social, and partner support, parenting practices) as well as personal resources (such as the capacity to mentalize regarding parental relationships) and financial resources are all identified as potential buffers against adverse mental health effects. Taken together, the articles in this collection suggest that behavioral, neural, and endocrine mechanisms may underlie these processes. Better understanding of these mechanisms and their interactions will lead to more effective, targeted assessment and intervention practices for women and girls across development. Such practices would consider sex as a biological variable in risk assessment and intervention timing, as well as in pharmacologic and device-oriented intervention, and bear in mind structural, social, and familial factors that impact women specifically alongside individual, psychological factors. We hope the current collection will contribute to the growing research base that recognizes sex as a biological variable and gender as a psychosocial variable in the explanation of risk, recovery, and resilience in the face of adversity. We encourage the translation of such knowledge into sex-and gender-specific mental health practices. The findings described here may inform both intervention and policy by identifying specific protective factors that may be enhanced and risk factors that may be reduced.

Author contributions

LH: Conceptualization, Project administration, Writing—original draft, Writing—review and editing. DL: Writing—review and editing. RZ: Writing—review and editing. CM: Writing—review and editing. MD: Writing—review and editing.

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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ORIGINAL RESEARCH
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A Year Through the COVID-19 Pandemic: Deleterious Impact of Hormonal Contraception on Psychological Distress in Women

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Background: Women are more at risk than men of suffering from psychological distress during disease outbreaks. Interestingly, no biological factors have been studied to explain this disparity in such contexts. Sex hormone variations induced by hormonal contraceptives (HC) have been associated with mental health vulnerabilities. However, most studies have examined current effects of HC without considering whether a chronic modulation of sex hormone levels could induce long-lasting effects that persist after HC cessation.

Objectives: To date, the role of HC on psychological health in women during a disease outbreak is still unknown. We aimed to investigate both current and long-term effects of HC on psychological distress throughout the COVID-19 pandemic.

Method: At four time points during the COVID-19 pandemic (June 2020, September 2020, December 2020, March 2021), we collected self-reported data on psychological distress, assessing symptoms of post-traumatic stress [*via* the Impact of Event Scale-Revised (IES-R)], symptoms of depression, anxiety, and stress [*via* the Depression Anxiety Stress Scales (DASS-21)]. Linear mixed models were first used to compare men ($n = 49$), naturally cycling women ($n = 73$), and women using HC ($n = 32$) across time. To examine long-lasting effects of HC, exploratory analyses were restricted to women, comparing current HC users ($n = 32$), past users ($n = 56$), and never users ($n = 17$).

Results: The first model revealed that women taking HC reported stable post-traumatic stress symptoms across time, compared to naturally cycling women and men who showed a significant decrease from T1 to T2. HC users also reported greater DASS-21 total scores over time. Moreover, HC users reported higher stress and anxiety symptoms than men. In the second model, results showed that past HC users had similar anxiety levels as current HC users. These two groups reported significantly more anxiety symptoms than never users.

Conclusion: HC users report increased distress during the pandemic relative to naturally cycling women and men. Our results also suggest a long-lasting effect of HC intake, highlighting the importance of considering both the current use of HC and its history. This could provide some insight into potential avenues for explaining why some women are prone to higher psychological distress than men.

Keywords: COVID-19, distress, sex differences, sex hormones, hormonal contraceptives

INTRODUCTION

Mental Health Consequences of the COVID-19 Pandemic

The mental health impacts of the COVID-19 pandemic are being increasingly documented around the world (1–3). Factors related to the virus itself, such as fear of being infected or infecting others and witnessing the increasing number of victims, were reported to be associated with poorer mental health outcomes (1, 4). In addition, factors related to the disruption of basic human needs including restrictive measures such as physical and social distancing, cessation of daily activities, and working from home were also shown to impact the wellbeing of the population (2, 5). With this, literature on disease outbreaks suggests that there are strong predictors of mental health outcomes during these stressful situations, such as psychological distress (6, 7). Psychological distress is a broad construct that encompasses a range of negative psychological symptoms [e.g., anxiety, depressive, post-traumatic stress symptoms (PTSS)]. Distress may play a role in the development of psychiatric disorders, as well as in its severity (8, 9). Indeed, there is evidence that acute anxiety, depressive, and PTSS were worsened in the general population during the pandemic (10). According to a longitudinal study, this increase in mental health burden was found in individuals without pre-existing mental health diagnoses (11). In general, among various sociodemographic factors, gender was an important variable to account for individual differences with regard to the COVID-related mental health crisis (12).

Gender Differences in Mental Health Outcomes

In response to the COVID-19 pandemic, men and women differed significantly in adapting to the new living/working conditions, which led to higher psychological stress in women compared to men (13). Moreover, women appear to have higher levels of anxiety, depressive, and post-traumatic stress symptoms than men when facing various stressors of the pandemic (14, 15). A recent longitudinal study showed that the highest levels of depression and anxiety occurred at the onset of confinement, and that being a woman was a risk factor for higher levels of these psychological distress symptoms (16). Twenty weeks later, depression and anxiety symptoms improved, perhaps because individuals adapted to the circumstances, but gender inequalities were still present as women seemed to improve faster than men (16). However, more studies are needed to understand the different trajectories of long-term psychological distress symptoms and their relationship with gender.

Reviews on expected roles in women proposed some hypotheses to explain why women are more likely to develop higher levels of psychological distress during COVID-19 (10, 17, 18). Carli (17) noted that more women lost their job, thus, putting more economic stress on them compared to men. As a matter of fact, unemployment rates were higher for women than men in several countries (e.g., United States, United Kingdom, Canada) during the pandemic (19). In addition, women are more often the ones who hold jobs categorized as essential (e.g., nursing) (20). Consequently, they were on the front lines during the pandemic, leading to more exposure to the virus, in addition to physical and psychological consequences (17). Moreover, traditionally, women are mainly the ones who take care of responsibilities at home such as cooking, cleaning, and childcare (21). The COVID-19 regulations led to the closure of many important services (e.g., educational facilities), which served to uphold this traditional view as it put high expectations on women's shoulders to take care of children and domestic tasks (17). Currently, differences between men and women regarding psychological distress outcomes during the pandemic are often attributed to gender inequalities pertaining to environmental or social factors. However, factors related to biological sex could also play a role in this disparity and have yet not been investigated (13).

Hormonal Contraceptives and Mental Health Outcomes

Among biological mechanisms accounting for sex disparity in mental health outcomes, sex hormones variations induced by hormonal contraceptives (HC) have been targeted as a potential vulnerability factor for women (22–24). HC contain synthetic progesterone (progestin) and, in many cases, synthetic estrogen (ethinyl estradiol), which are effective for both birth control and menstrual cycle regulation (25). HC are long-acting and reversible methods that can be taken orally, by injection, under or on the skin, or in the vagina or uterus. At the contraceptive level, hormonal effects of HC lead to the inhibition of ovulation, sperm penetration, and to desynchronization of the endometrial changes necessary for implantation (25). Moreover, this contraceptive method also has effects on the brain and is thought to impact mental health (26). It has previously been shown that the hormone-induced changes modulate the hypothalamic-pituitary-adrenal (HPA) stress axis and limbic brain regions (27). Also, through their impact on key brain regions involved in emotion and its regulation, HC have been associated with fear regulation deficits (28, 29), lowered brain

serotonin binding markers (30), as well as the onset of affective disorders (31, 32).

As long-acting methods, HC are frequently taken beginning in adolescence, which is a crucial period for brain development. Therefore, HC use could potentially lead to important hormonal changes that can have neural and psychological effects in the long-term (33). A study in rats showed that early use of ethinyl estradiol during development generated more anxious behaviors compared to a control group of mature male rats (34). In humans, a study showed that women who took HC during adolescence were at a greater risk of developing depression years after first HC exposure compared to women who had first used HC in adulthood (35). Among the few studies that have looked at the long-term effects of HC on the brains of women, it has been shown that there are cognitive effects that may persist for several years after cessation of hormonal use. Indeed, HC users had better performances in domains of visuospatial abilities, speed, and flexibility when compared to the group of never users, with a duration-dependent trend (36). In women who previously used HC, the duration of contraceptive use correlated positively with hippocampal and basal ganglia volumes, even though they had been off HC for 3 years on average (37). Although these studies are correlational and the effects and mechanisms have yet to be clarified, the current literature suggests that hormone alterations through HC use could have durable effects on the brains of women, and thus may potentially impact psychological health in a long-lasting manner.

To date, no COVID-19 studies have investigated the impact of HC on psychological distress outcomes. Moreover, the vast majority of existing HC studies have only considered the current effects of HC without considering whether a chronic modulation of sex hormones levels could induce long-lasting effects that would persist after HC cessation. These studies have generally compared HC users to naturally cycling (NC) women and men, without acknowledging previous intake of HC in NC women. Thus, NC grouping is solely based on current hormonal status, which implies that the potential influence of HC use in former users has not yet been explored. The present study aimed to investigate the effects of both current and previous use of HC on psychological distress throughout the COVID-19 pandemic. We hypothesized that women taking HC will exhibit greater psychological distress than NC women and men during the COVID-19 pandemic. Moreover, compared to women who never used HC, we hypothesized that women who previously used HC will show similar levels of distress than women currently using HC.

MATERIALS AND METHODS

Participants

This project fell within the framework of a broader longitudinal study assessing various psychological and physiological reactions to the COVID-19 pandemic. Men and women recruited for this study had all previously participated in other experiments in our laboratory between 2017 and 2019. Of the 246 individuals recontacted in May 2020, 156 (63.41%) agreed to take part in this longitudinal follow-up. Two of these individuals, both women having used HC in the past, were excluded from the analyses as they were pregnant as of May 2020 (given the important hormonal changes induced by pregnancy). All things considered, our final sample was composed of 154 participants aged between 19 and 55 years old ($M = 34.56$, $SD = 10.03$). Participants were distributed as follows: 32 HC users, 73 NC women (17 never users, 56 past users), and 49 men. A HC was considered to be any contraceptive method altering an individual's hormonal status. Thus, of the 32 participants in the HC user group, 20 used a combined oral contraceptive (COC), seven used a hormonal intra-uterine device (IUD), three used a progesterone-only oral contraceptive, one used the vaginal ring, and one used the patch. Of note, participants using a non-hormonal IUD (i.e., copper) were classified as NC women. Therefore, our HC sample was mainly composed of women using a COC (62.5%). As this project was longitudinal, three participants (two HC users, one past user) changed their hormonal profile during the study (e.g., stopped using HC). Therefore, their data were excluded from our analyses from the moment they declared this change. Given that all questionnaires were completed online and that we wanted to optimize the validity of our results, it was important to ensure that participants were attentive when reading the various questionnaire items. As such, three random questions were added to the battery of questionnaires administered at each time point to verify whether participants were paying attention (e.g., were prompted by the following "*select the choice 'Strongly agree'*"). One NC woman (past user) answered these three questions incorrectly (did not follow the prompt) at the second time point. Therefore, the participant's data for this time point were excluded. **Table 1** shows the final participant distribution across the four time points of the present study.

TABLE 1 | Distribution of participants at each time point.

	NC women		HC users	Men
	Past users	Never users		
T0	56	17	32	49
T1	55	17	32	47
T2	53	16	31/29*	46
T3	52	15	31	43
T4	45	12	28	37

**31 for the IES-R and 29 for the DASS-21.*

When initially recruited between 2017 and 2019, participants had to be French-speaking (as the questionnaires administered were all in French) and free of any physical or mental health conditions. Since then, some participants developed health conditions, depression being the most prevalent. However, these participants were statistically well distributed across our different groups (see **Table 2**) and results did not change when re-running the analyses without these individuals. Therefore, we decided not to control for this variable in our analyses.

Measures

Hormonal Profile

In May 2020 (T0), participants declared their entire contraception history via self-reports, which allowed for

TABLE 2 | Sample characteristics for men, women using HC, and NC women (past and never users).

Variable	Men	HC users	NC women			*P*-value	
				Past users	Never users	Model 1	Model 2
Age	38.51 (9.90)	30.47 (8.91)	33.71 (9.76)	35.29 (9.02)	28.53 (10.59)	**<0.001**	**0.010**
Ethnicity—Caucasian	37 (75.51%)	32 (100%)	53 (72.60%)	47 (83.93%)	6 (35.29%)	**0.084**	**<0.001**
Education level—Bachelor's	17 (34.69%)	18 (56.25%)	34 (46.58%)	24 (42.86%)	10 (58.82%)	0.729	0.336
Income—100,000$ +	19 (38.78%)	6 (18.75%)	17 (23.29%)	13 (23.21%)	6 (35.29%)	0.413	0.209
Mental health diagnosis	5 (10.20%)	7 (21.88%)	15 (20.55%)	13 (23.21%)	2 (11.76%)	0.260	0.590
Physical health diagnosis	7 (14.29%)	6 (18.75%)	19 (26.03%)	16 (28.57%)	3 (17.65%)	0.279	0.471
Medication use	20 (40.82%)	18 (56.25%)	37 (50.68%)	31 (55.36%)	6 (35.29%)	0.356	0.304
Having children	33 (67.35%)	12 (37.50%)	41 (56.16%)	36 (64.29%)	5 (29.41%)	**0.030**	**0.009**
Full time cohabitation with children	24 (72.73%)	11 (91.67%)	36 (90%)	31 (88.57%)	5 (100%)	0.211	0.709
Having a romantic partner	29 (59.18%)	12 (37.5%)	38 (52.78%)	32 (58.18%)	6 (35.29%)	0.156	**0.091**
Living in an urban area	45 (91.84%)	29 (90.63%)	67 (93.06%)	51 (92.73%)	16 (94.12%)	0.909	0.896
Number of rooms in the house	6.94 (2.70)	7.55 (3.49)	7.63 (2.86)	7.83 (2.76)	7.00 (3.16)	0.426	0.617
Religious beliefs	15.22 (7.95)	16.25 (7.57)	17.25 (9.11)	16.09 (8.51)	21.06 (10.24)	0.432	**0.099**
Neuroticism	31.55 (7.25)	33.59 (8.61)	36.81 (8.22)	37.65 (8.22)	34.06 (7.84)	**0.002**	**0.060**
Traumatic events	4.23 (2.59)	4.33 (2.32)	4.12 (2.32)	4.13 (2.13)	4.07 (3.01)	0.912	0.910
Stressful events before the onset of the study	17 (34.69%)	9 (28.13%)	37 (50.68%)	30 (53.57%)	7 (41.18%)	**0.054**	**0.067**
Stressful events during the study	0.17 (0.28)	0.27 (0.28)	0.19 (0.30)	0.20 (0.26)	0.09 (0.18)	0.334	0.118

Model 1 refers to comparisons between men, HC users, and NC women, while model 2 refers to HC users, past users, and never users. For age, number of rooms in the house, religious beliefs, neuroticism, traumatic events, and having lived stressful events during the study (mean of the four time points), data represent group means (SD) in men, naturally cycling (NC) women, and women using hormonal contraceptives (HC). For ethnicity, education level, income, mental health diagnosis, physical health diagnosis, medication use, cohabitation with children, relationship status, living in an urban area, and having lived stressful events before the onset of the study, data represent group N (group %). For categorical variables with many subcategories (ethnicity, education level, income, cohabitation with children), data are shown according to the most frequent subcategory. Bold characters indicate covariates set at $p < 0.100$ that are included in the statistical analyses.

their classification into one of four groups (HC users, never users, past users, men). For current and past HC users, the mean duration of their contraceptive use was 9.08 years ($SD = 6.63$; range of 0.5–28). Previous users had stopped using HC for a mean duration of 7.52 years ($SD = 6.33$; range of 0.5–23).

Psychological Distress

Psychological distress was measured using the Impact of Event Scale-Revised (38, 39) and the Depression Anxiety Stress Scales (40, 41).

Impact of Event Scale-Revised

The French version of the IES-R is a 22-item scale assessing perceived stress arising from a traumatic event (38). Items address PTSS felt in the last 7 days. The main question was adapted to assess COVID-related PTSS. The questionnaire is based on the English version developed by Weiss and Marmar (39). Items such as "Any reminder brought back feelings about it" (intrusion), "I stayed away from reminders of it" (avoidance), or "I felt irritable and angry" (hyperarousal) assess different PTSS that could arise in response to a traumatic event. Participants answered each item on a Likert scale ranging from 0 (not at all) to 4 (extremely). All answers were summed, yielding a total score between 0 and 88. Higher scores indicated more severe distress symptoms. This questionnaire has an excellent internal consistency, with a total score alpha value of 0.93 (38). The IES-R has been widely used to assess PTSS in the context of the COVID-19 pandemic [for a systematic review and meta-analysis, see (42)].

Depression Anxiety Stress Scales

The French version of the DASS-21 is a 21-item scale assessing the respondent's depression, anxiety, and stress symptoms in the last seven days (40). This version has been shortened and translated from the original 42-item English version developed by Lovibond and Lovibond (41, 43). Items include "I felt that I had nothing to look forward to", "I felt scared without any good reason", and "I experienced trembling (e.g., in the hands)". Respondents could rate them on a scale from 0 (did not apply to me at all) to 3 (applied to me most of the time). Each item's score is doubled to allow for interpretation based on the original 42-item version. The DASS-21 includes three subscales (depression, anxiety, stress) and a total score, ranging from 0 to 126. The latter is obtained via the summation of scores from each of the three subscales. Similar to the IES-R, a higher score indicates more severe distress symptoms. The DASS-21 has shown to be reliable in adult populations (41, 44). The translated French version of the questionnaire exhibits acceptable internal consistency, with alpha values varying from 0.72 to 0.79 (40).

Questionnaire Completion

Participants answered the aforementioned questionnaires (among others) on Qualtrics, a secure online platform. A member of the research team sent participants a unique URL via email at each time point, where participants had 2 weeks to

complete the questionnaires. During this period, participants could pause their questionnaire completion and continue later, with the condition that the questionnaires were completed within the 2-week time frame.

Procedure and Timeline

The first case of COVID-19 was reported in February 2020 in the province of Quebec, Canada. In March 2020, the Quebec government decreed several confinement measures and declared a public health emergency to limit the spread of COVID-19. We recontacted participants who had already taken part in one of our laboratory's studies. In May 2020 (T0), we obtained either verbal or written informed consent to pursue their implication in this added follow-up, in addition to the collection of socio-demographic data and potential confounding variables. Thereafter, participants were sent a series of questionnaire every 3 months in the following year: in June 2020 (T1), September 2020 (T2), December 2020 (T3), and March 2021 (T4; see **Figure 1** for an overview of the study's timeline). Therefore, the IES-R and DASS-21 were completed at four different times (T1, T2, T3, T4). Participants received financial compensation proportional to their implication in this longitudinal study.

Statistical Analyses

Data were examined where z-scores of $\geq \pm 3.29$ were considered as outliers (45, 46). Using this criterion, <1.5% of the IES-R and DASS-21 scores were considered extreme. Participants whose scores exceeded DASS-21 clinical thresholds were recontacted and offered psychological resources. All extreme scores were winsorized with respect to study groups, using the next highest value of each group (47).

Prior to conducting the statistical analyses, we assessed the skewness and kurtosis of our main variables. Our data were normally distributed according to indices for acceptable limits of $\pm$ 2 and $\pm$ 7, respectively (48). Therefore, we used the raw values in our final analyses. All analyses were performed using SPSS 27 (IBM).

Preliminary Analyses

Covariates were selected from the analyses performed on sociodemographic variables. We tested variables that have been linked to psychological distress and on which our groups may have differed. Groups were compared with ANOVAs and chi-square tests for continuous and categorical variables, respectively. Variables that reached a p-value of <0.10 were included as covariates in the analyses.

Main and Exploratory Analyses

To examine the impact of current HC use on psychological distress, our first subset of analyses compared HC users, NC women (never users, past users), and men, as these subgroups are generally compared when studying the role of hormonal contraception (49–56). We conducted linear mixed models to compare the evolution of PTSS (IES-R), general distress (DASS-21 total score), as well as depression, anxiety, and stress symptoms (DASS-21 scales) in HC users, NC women, and men. In the second subset of analyses, we explored long-term effects of HC use on women's psychological distress. To do so, we subdivided the NC women group using women's contraceptive history. As such, we obtained two subgroups: never and past users. This second set of linear mixed models was limited to women as we tracked the evolution of the same distress symptoms in HC users, past users, and never users. Restricted maximum likelihood (REML) was applied to allow for robust analysis with various and relatively small sample sizes (57). "Subjects" were considered as a random effect. Factors consisted of Time (four levels: T1, T2, T3, T4), Group (three levels in each subset—model 1: HC users, NC women, men; model 2: HC users, past users, never users), as well as the interaction term Time*Group. Between-subject and within-subject *post-hoc* comparisons were performed using Bonferroni's multiple comparisons test. Statistical significance was set at $p < 0.05$. An autoregressive covariance structure was first considered. Model residuals were inspected for normality and homoscedasticity by visual examination of residual plots. Deviations from homoscedasticity was observed for the main analyses. Therefore, a heterogenous version of the autoregressive covariance structure was selected. Visual inspection of residual plots for our exploratory analyses did not reveal any obvious deviations from homoscedasticity or normality.

RESULTS

Main Analyses

Preliminary Analyses

Descriptive statistics for the three participant groups (i.e., women taking HC, NC women, and men) are shown in **Table 2**. Groups did not differ with respect to income, education level, relationship status, living in an urban area, number of rooms in the house, cohabitation with children, use of medication, having a diagnosis related to either physical or mental health, religious beliefs, traumatic events, and stressful events that occurred during the study (mean score of T1 to T4). However, groups were statistically different with regards to age ($p < 0.001$), having children ($p = 0.030$), and neuroticism ($p = 0.002$). Men were significantly older than both groups of women and had more children than HC users. As for neuroticism, NC women reported higher levels than men. Ethnicity was also quite unbalanced across groups ($p = 0.084$), as HC users were solely of Caucasian origin compared to NC women and men. Having experienced stressful events that occurred before the onset of the study was also marginally significant ($p = 0.054$). Pairwise z-tests did not yield any significant comparisons, although a higher proportion of NC women reported having lived a stressful event prior to the study compared to HC users. Given the non-randomized group assignment of this study and the potential interference with our main analyses, these five variables (age, having children, neuroticism, ethnicity, and stressful events prior to the pandemic) were considered as covariates in all subsequent analyses.

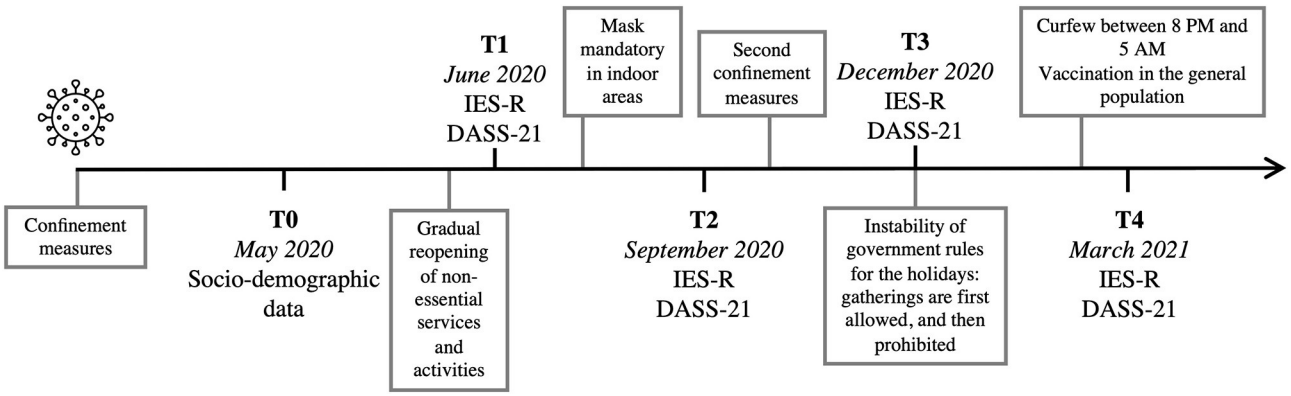

FIGURE 1 | Timeline overview.

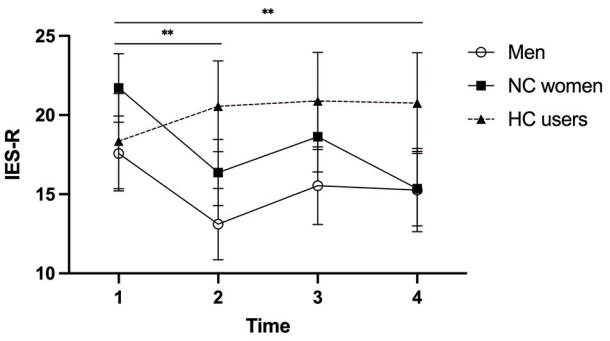

FIGURE 2 | Post-traumatic stress symptoms (measured by the IES-R) of men, naturally cycling (NC) women, and women using hormonal contraceptives (HC) during the COVID-19 pandemic. A significant decrease from T1 to T2 was observed for NC women and men, as well as from T1 to T4 for NC women. Men, NC women, and HC users are illustrated by circles, squares, and triangles, respectively. Error bars represent standard error. $^{**}p < 0.01$.

IES-R

Comparing women taking HC, NC women, and men, our model for PTSS revealed a main effect of Time ($p = 0.026$) and a trend toward a Group effect ($p = 0.079$). A significant Time*Group interaction was found [$F_{(6, 236.03)} = 2.212$, $p = 0.043$], with women using HC reporting stable levels of PTSS across the four time points [$F_{(3, 41.36)} = 0.486$, $p = 0.694$] relative to NC women and men who showed a significant decrease from T1 to T2 (both ps < 0.01). NC women also exhibited a significant decrease between T1 and T4 ($p = 0.009$) (**Figure 2**).

DASS-21

As for the DASS total score (**Figure 3A**), results showed main effects of Time ($p = 0.031$) and Group ($p = 0.013$). The Time*Group interaction was significant [$F_{(6, 194.07)} = 2.217$, $p = 0.043$], with HC users reporting increasing levels of general psychological distress from T1 to T3 [$F_{(3, 38.74)} = 3.428$, $p = 0.026$] compared to NC women ($p = 0.374$) and men ($p = 0.096$).

When examining the three DASS scales, a main effect of Group was found for stress symptoms [$F_{(2, 165.62)} = 6.816$, $p = 0.001$] (**Figure 3B**) and for anxiety symptoms [$F_{(2, 153.80)} = 5.483$, $p = 0.005$] (**Figure 3C**). Both effects were driven by the fact that women using HC reported higher symptoms than men ($p < 0.001$ and $p = 0.004$ for the stress and anxiety scales, respectively). HC users also exhibited marginally higher stress symptoms than NC women ($p = 0.076$). The analysis also revealed a main effect of Time for stress symptoms [$F_{(3, 216.81)} = 2.972$, $p = 0.033$], where stress levels increased from T1 to T3 ($p = 0.027$). As for the depression scale, a main effect of Time was found [$F_{(3, 199.94)} = 2.841$, $p = 0.039$], indicating an increase of depressive symptoms from T2 to T3 ($p = 0.052$). No other main effect or interaction reached significance for the three subscales (ps > 0.125; **Figure 3D** showing the non-significant group comparison for the depression scale).

Exploratory Analyses

Preliminary Analyses

As presented in **Table 2**, current HC users, past users, and never users were similar regarding income, education level, living in an urban area, number of rooms in the house, cohabitation with children, use of medication, having a diagnosis related to either physical or mental health, traumatic events, and stressful events during the study. Groups differed in terms of age ($p = 0.010$), with past users being older than never and current users. Groups also differed according to ethnicity ($p < 0.001$), with fewer never users being of Caucasian origin and more so of Asian, Arabic, and Hispanic origins than both past and current users. Having children was also a discriminant factor between the three groups of women ($p = 0.009$), with past users having more children than current and never users. Trends were found for neuroticism ($p = 0.060$) and having lived stressful events before the study ($p = 0.067$). Past users tended to report more neuroticism than current users. Although pairwise z-tests did not reach significance, more past users reported having

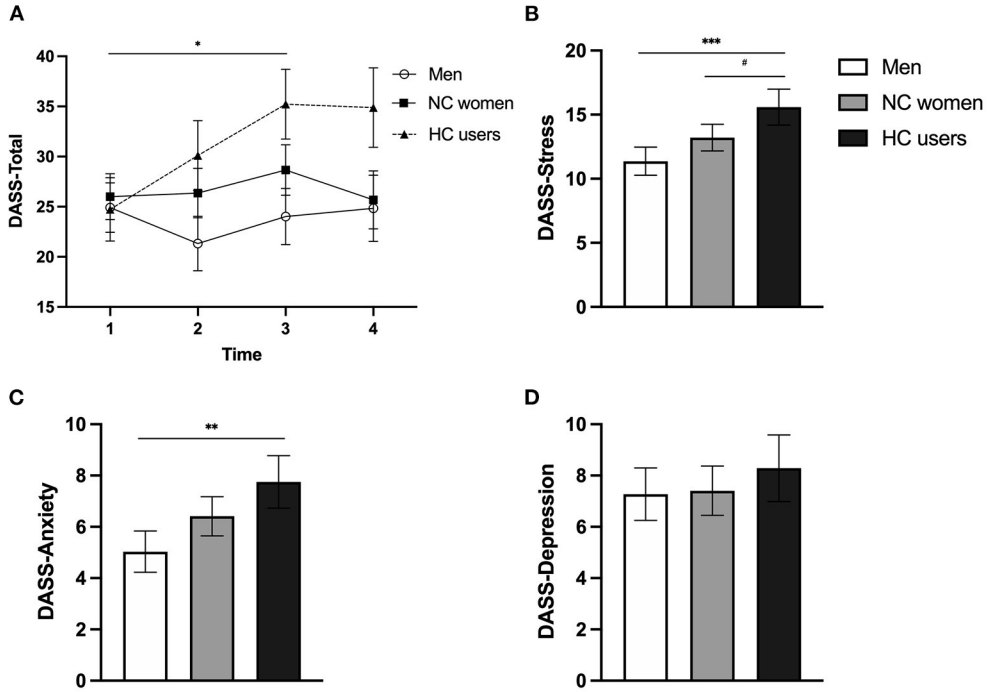

FIGURE 3 | Symptoms of depression, anxiety, and stress (measured by the DASS-21 scores) of men, naturally cycling (NC) women, and women using hormonal contraceptives (HC) during the COVID-19 pandemic. **(A)** General distress evolution during the pandemic. Men, NC women, and HC users are illustrated by circles, squares, and triangles, respectively. **(B)** Mean stress symptoms. **(C)** Mean anxiety symptoms. **(D)** Mean depressive symptoms. Men, NC women, and HC users are illustrated by white, gray, and black bars, respectively. Error bars represent standard error. #<0.08, $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

lived a stressful event before the study than current and never users. Even though relationship status did not reach statistical significance ($p = 0.091$), a greater proportion of past users tended to have a romantic partner compared to current and never users. Finally, strength of religious faith also tend to vary between our groups ($p = 0.099$), with never users reporting higher religious beliefs than past and current users. To better evaluate the impact of HC on psychological distress in women, age, ethnicity, having children, neuroticism, stressful events before the study onset, relationship status, and religious beliefs were entered as covariates in the statistical models.

IES-R

With regards to the second set of analyses, results showed a nearly significant effect of Time for PTSS [$F_{(3,\ 258.45)} = 2.612$, $p = 0.052$] but no significant *post-hoc* comparisons emerged ($ps > 0.400$). No effect of Group ($p = 0.623$) nor Time*Group ($p = 0.147$) were found for PTSS.

DASS-21

According to the DASS total score (**Figure 4A**), a main effect of Group was found [$F_{(2,\ 104.92)} = 3.045$, $p = 0.052$], with HC users experiencing more general distress than never users ($p = 0.047$). A trend toward an effect of Time was detected [$F_{(3,\ 261.02)} = 2.516$, $p = 0.059$] but no significant *post-hoc* comparisons emerged ($ps > 0.084$). No Time*Group interaction was found ($p = 0.277$).

A significant Group effect was revealed for the anxiety scale [$F_{(2,\ 107.96)} = 5.242$, $p = 0.007$] (**Figure 4B**). Irrespective of time, past and current HC users exhibited similar anxiety symptoms, which were significantly higher than those reported by women who never used HC ($p = 0.006$ and $p = 0.015$ when compared to HC and past users, respectively). The analysis for the stress scale also yielded a main effect of Group [$F_{(2,\ 104.22)} = 4.054$, $p = 0.020$], where HC users reported higher stress symptoms than never users ($p = 0.022$; **Figure 4C**). A marginal effect of Time was also found for the stress scale [$F_{(3,\ 259.18)} = 2.351$, $p = 0.073$] but no significant *post-hoc* comparisons emerged ($ps > 0.121$). No other main effect or interaction reached significance for the three subscales ($ps > 0.095$; **Figure 4D** showing the non-significant group comparison for the depression scale).

Parameters of HC Use

Past and current users were combined in order to explore the relationship between duration of HC use and psychological distress. Using hierarchical regressions, we entered covariates in the first step based on their correlates with each distress scale. Then, duration of use was entered in the second step. For each distress scale, no effect of duration of use was found ($ps > 0.478$). We also ran the same analyses according to the age of onset. For each distress scale, no effect of age of onset was found ($ps >$

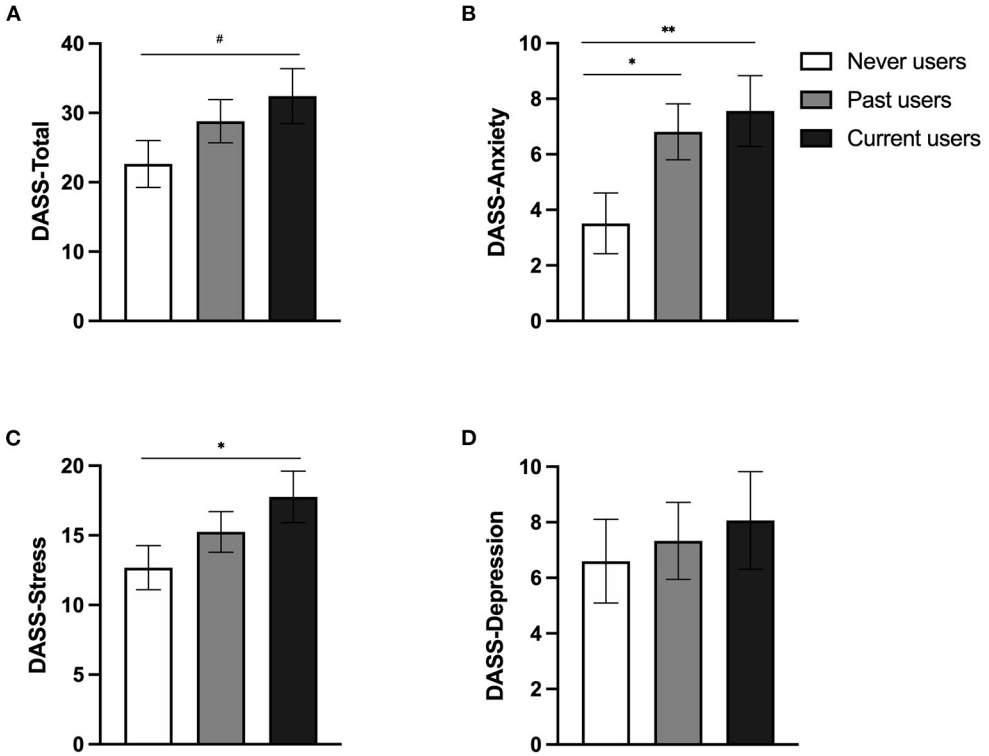

FIGURE 4 | Symptoms of depression, anxiety, and stress (measured by the DASS-21) of current hormonal contraceptive (HC) users, past users, and never users during the COVID-19 pandemic. **(A)** Mean general distress. **(B)** Mean anxiety symptoms. **(C)** Mean stress symptoms. **(D)** Mean depressive symptoms. Never users, past users, and current users are illustrated by white, gray, and black bars, respectively. Error bars represent standard error. #<0.08, *$p < 0.05$, **$p < 0.01$.

0.417). Note that non-significant results are also obtained when running these analyses separately for past and current users.

DISCUSSION

In this study, we investigated the impact of hormonal contraceptives on psychological distress during the COVID-19 pandemic. Over a year, we followed distress evolution in women using HC, naturally cycling women (either never or past HC users), and men. Our models showed that HC intake was associated with elevated distress during the pandemic and that past HC users resembled current HC users in terms of anxiety symptoms. These findings suggest current and long-lasting effects of HC on psychological health.

In our first model, we compared men, NC women, and HC users based on the existing literature on hormonal contraception (49–56). First, we observed a lack of decreasing levels of PTSS in women using HC compared to NC women and men. As it has been reported that PTSS and COVID-related fear tends to decrease over time (7, 58), our result suggests that HC use is associated with a maladaptive response to a long-term stressor. This symptom maintenance could be explained by deficits in fear extinction, as HC use (i.e., oral contraception) was previously linked to poorer extinction recall, as assessed via laboratory experiments (28) and exposure-based treatment (29, 59). We also found an increase in general distress over time in women using HC compared to NC women and men. Finally, HC users were more stressed and anxious than men overall. The finding that HC users stood out by showing higher distress patterns supports our hypothesis that psychological impairment is associated with current HC intake. Distress differences between men and women relative to the COVID-19 pandemic were reported extensively in previous studies (5, 14, 15, 60–63). Interestingly, our data explains this gap by extending beyond psychosocial factors related to feminine gender (e.g., job loss, virus exposure, domestic responsibilities) (17). Indeed, it emphasizes the importance of also considering biological sex-related factors in order to understand what may render women more vulnerable to psychological distress and mental health disorders. In addition, contrary to what is generally assumed by most studies, our findings suggest that women might not represent a homogenous group. When hormonal status is considered, the lack of differences between NC women and men is noteworthy. As no other COVID-19 study to our knowledge has considered the role of sex hormones, this raises the possibility that previous results regarding psychological distress in women during the COVID-19 pandemic might be driven or accentuated by samples containing women using HC.

Accordingly, current HC use could exert its negative effects on mental health via different neurobiological mechanisms. First, fear and other emotions potentially evoked by the virus outbreak, are regulated through limbic circuitry linking the amygdala and

prefrontal cortex, among other structures. Dysregulation of this circuitry has often been associated with mood, anxiety, and fear-related disorders (64). Animal studies have shown that the amygdala and prefrontal cortex have a particularly high density of sex hormones receptors. In humans, HC studies focused mostly on oral contraceptives and showed that its use could be linked to emotional regulation (65, 66). Graham and Milad (2013) found that HC use was negatively associated with fear regulation in women and female rats. In ovariectomized rodents, estrogen drops were associated with a decrease of dendritic density in the prefrontal cortex (28). Another study found a reduction in the volume of the left amygdala and gray matter following a 3-month use of oral contraceptives. Connectivity between the amygdala and prefrontal cortex was also shown to be altered (67). Volume of many other brain structures playing a role in emotion regulation seems to be altered following HC intake (e.g., insula, anterior cingulate cortex, orbitofrontal cortex) (66). Also, although exact mechanisms remain unclear, endogenous female sex hormones seem to play a role in anxiety reactions. Among other things, allopregnanolone (a progesterone metabolite) acts on GABA receptors, leading to either anxiogenic or anxiolytic effects, depending on metabolite and receptor concentrations (65, 68). As synthetic doses of progesterone lead to chronically low concentrations of endogenous progesterone, HC use may result in alterations of anxiety regulation (65). Finally, it is worth noting that sex hormones interact with the HPA axis and may modulate stress regulation (65, 69). Indeed, oral contraceptive users and non-users exhibited different neural responses following cortisol (stress hormone released by the HPA axis) administration (52). Interestingly, fMRI data suggested that, in the occurrence of a stressful situation (in this case, provoked by cortisol administration), oral contraceptive users had enhanced hippocampal activity during fear learning compared to their naturally cycling counterparts and men (52). Another study indicated that oral contraceptive users show blunted salivary cortisol reactivity in response to a psychosocial stress relative to NC women in the luteal phase and men (70). Thus, the stress response of HC users and non-users seem to differ according to biomarkers such as cortisol (70). These interactions between sex hormones and the HPA axis could be linked to differential distress symptomatology among HC users and non-users during the COVID-19 pandemic. In sum, the results of this study align with the existing work on mechanisms underlying the association between HC use and mental health. Due to the longitudinal design of this study, our results also support the idea that chronic use of HC (rather than its synthetic compounds) may have the most influence on psychological distress.

Regarding other results from our main analyses, no sex differences were found in terms of depressive symptoms in our sample. Women (HC users or NC women) did not show more depressive symptoms than men during the COVID-19 pandemic. This is an intriguing result as women generally report higher levels of depression than men (10, 60). However, another study conducted during the COVID-19 pandemic also found equivalent depressive symptoms between men and women (71). Pre-pandemic analyses were carried out on this study's sample to assess differences between men and women on depressive symptoms. In controlling for the time elapsed between the completion of the initial questionnaire and T1 of this COVID-19 study, Arcand et al. (in preparation) showed that women scored higher than men on depressive symptoms before the pandemic. Among the numerous ways to explain this finding, it is possible that women in our sample tended to mitigate their depressive symptom levels (e.g., less fatigue, more time to do meaningful activities) compared to men. Another possibility is that men may have had a larger increase in depressive symptom levels in response to the pandemic (e.g., difficulty reaching out to others, social isolation) compared to women.

When examining the main effects of time in our first subset of analyses, the context around T3 (December 2020) seemed to have particularly deleterious effects on mental health. Indeed, stress symptoms increased from T1 to T3, depressive symptoms increased from T2 to T3, and HC users showed greater general psychological distress levels at T3 compared to T1. Apart from these statistically significant comparisons, all psychological distress measures were heightened at T3. As illustrated in **Figure 1**, the Quebec government first announced that small gatherings would be allowed during the holidays but retracted this decision soon thereafter. Measurements from T3 coincided with these contradictory announcements. Thus, the changing governmental measures, declaration of a prolonged confinement period (immediately following an increase in hope that we would have an "almost normal" holiday period), and the beginning of winter (72) may have contributed to the decrease in psychological wellbeing.

Despite the relevance of studying the impact of current HC use, investigating its long-lasting effects is of great interest to better understand how sex hormone modulation can affect the brain and behavior of women. As a small body of evidence supports this standpoint (33, 35–37, 73), it appeared essential to explore if previous use of HC could induce a durable influence on psychological health. Thus, according to our secondary objective, our results showed that current and past users exhibited higher anxiety than never users, a pattern that was also found for stress symptoms with current users reporting more stress than never users, and past users not differing from any of the two groups. These findings partially support our hypothesis. In fact, our results suggest that a durable trace of HC could be suspected, particularly for anxiety manifestations, in response to a chronic stressor such as the COVID-19 pandemic. Two potential pathways have been highlighted according to previous studies on HC. First, prolonged intake of HC, therefore abolishing high levels of sex hormones for a considerable amount of time, could underlie a potential mechanism on how HC impacts brain anatomy and function. Indeed, Pletzer et al. (37) have linked the duration of previous oral contraceptive use to gray matter volumes of subcortical structures. Although women were no longer using any HC, longer durations of oral contraceptive use were associated with larger hippocampi and basal ganglia (37). Second, timing of HC intake could also be responsible for long-lasting changes in the brain. Recent investigations support this idea, where pubertal onset of oral contraceptives was associated with differences in stress reactivity, brain structures, and functional connectivity compared to an adult onset of use (73, 74). In knowing that adolescence represents a crucial time frame for brain development and reorganization (75, 76),

it is plausible to consider a disruption of these processes by HC intake (e.g., synaptic pruning, myelination, dendritic elaboration). However, duration of use and age of onset were not associated with psychological distress in our study. This contradicting finding could reflect the complexity of obtaining reliable data on these retrospective data. Indeed, women often switch from one HC to another, pause their HC for various amount of time, and might also have difficulty recalling with precision their history of use (37). Of note, data about history of use were all collected online, which could have prevented to obtain the level of details needed to accurately reflect the total duration of HC use. For example, some women with a complex history of HC use might not electronically report their duration of use as accurately as if they spoke on the phone with a research assistant trained to guide them into taking time to think, summarize what has been said, and revalidate the information.

Yet, if there is truly no impact of these two HC parameters, it is plausible that other factors such as interrupted use of HC could hamper the relationship between duration or age of onset and psychological outcomes.

For most of our scales, no clear distinction was observed between women who previously used HC and those who never did. Reversibility of the effects of HC is undoubtedly a natural phenomenon that occurs as a consequence of brain plasticity and homeostasis (37, 77–79). As such, it is essential to remain careful when making assumptions about the long-term potential of HC. As mentioned, women frequently pause their HC. It would be interesting to develop a more comprehensive approach by taking into account the total duration of use with respect to the time spent without using an HC. It would also be of great relevance for future investigations conducted in former HC users to consider the amount of time elapsed since HC discontinuation. This would help to get a better grasp of the dynamic interplay between onset and duration of HC use and its cessation duration. Longitudinal studies carried out over extended periods of time would also allow for an improved comprehension of the balance between both the durable and reversible effects of HC.

The present study has limitations. First, we used data from a larger study where individuals were recruited based on their past participation in a study at our laboratory. Consequently, our final sample was rather small and group formation was made *a posteriori*, as it was constrained by the context of the pandemic. Nonetheless, linear mixed models can manage unbalanced designs in longitudinal datasets, therefore allowing for a more robust examination of unequal sample sizes and prevention of a decrease in power due to attrition (80, 81). Second, given that our sample was not selected for the purposes of the current study and that group assignment was non-randomized, it cannot be assumed that there was equivalence across our comparison groups. Despite controlling for several covariates, other non-controlled factors could bring unwanted variability to the results such as heterogenous hormonal events. For example, experiencing one or many pregnancies, taking hormone-related medication, or having used or currently using different HC methods could decrease internal validity and statistical power. Even if combined oral contraceptives were the most frequently used method in our sample, it is still unknown if all HC methods provide the same effects. As our study did not allow for this level of precision, this highlights the importance of refining future methodologies in order to unveil specific mechanisms. Studying HC onset use and mental health prospectively would also provide stronger evidence of the deleterious impact of HC. Additionally, distress scores observed in this study were below the clinical threshold of the scales. Thus, the negative impact of HC may not impair the normal functioning of women, suggesting that clinical significance is weak. Nevertheless, it remains quite informative to see that HC could affect women in the general population to some extent and that the effects of HC seem to persist after cessation of use.

In terms of its strengths and contributions, our study highlights the value of adding biological factors to further understand gender differences in mental health. It also covered a considerable time frame, which allowed for a more complete assessment of distress evolution during a chronic stressor such as the COVID-19 pandemic. We have taken into account numerous aspects at the bio-psycho-social levels with the intention of isolating the impact of HC on psychological distress. Moreover, this is one of the few studies that has explored the long-lasting effects of HC by investigated both never and past HC users. Our results converge with the limited literature on the topic and promote avenues for further research in the field. Considering not only current use of HC but also its history could provide insight for understanding why certain subgroups of women are prone to higher psychological distress than men.

CONCLUSION

The COVID-19 pandemic challenged everyone's mental health, yet some people have adapted to this situation better than others. Thus, we sought to examine whether certain subgroups of the population, depending on their HC use, were more vulnerable than others in a context of chronic stress. Our results support our hypotheses as HC use seems to have worsened distress symptoms among our participants. Moreover, it is worth noting that HC use may have a prolonged impact on mental health, even years after women ceased their intake. These results highlight the importance of conducting further research that considers not only psychosocial, but also biological factors like sex hormones as potential determinants of mental health outcomes.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Centre intégré universitaire de santé et de services sociaux de l'Est-de-l'Île-de-Montréal. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

AB and MFM contributed to the conception and design of the study. AB performed the statistical analyses. AB, LMD, and JF wrote sections of the manuscript. All authors contributed to manuscript revision.

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Isolation, Economic Precarity, and Previous Mental Health Issues as Predictors of PTSD Status in Females Living in Fort McMurray During COVID-19

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Objectives: The COVID-19 pandemic represents an instance of collective trauma across the globe; as such, it is unique to our lifetimes. COVID-19 has made clear systemic disparities in terms of access to healthcare and economic precarity. Our objective was to examine the mental health repercussions of COVID-19 on adult females living in Fort McMurray, Canada in light of their unique circumstances and challenges.

Method: To investigate this issue, we analyzed responses gathered from an anonymous cross-section of online survey questionnaire responses gathered from females living in the Fort McMurray area (n = 159) during the COVID-19 pandemic (April 24–June 2, 2021). This included relevant demographic, mental health history, and post-traumatic stress disorder (PTSD), as well as COVID-19 data. Chi-squared analysis was used to determine outcome relevance, and binary logistic regression was employed to generate a model of susceptibility to PTSD.

Results: 159 females completed the survey. The prevalence of putative PTSD in our sample was 40.8%. A regression analysis revealed 4 variables with significant, unique contributions to PTSD. These were: a *diagnosis of depression*; a *diagnosis of anxiety*; *job loss due to COVID-19*; and *lack of support from family and friends*. Specifically, women with a previous diagnosis of either depression or anxiety were ∼4–5 times more likely to present with PTSD symptomatology in the wake of COVID-19 (OR = 3.846; 95% CI: 1.13–13.13 for depression; OR = 5.190; 95% CI: 1.42–19.00 for anxiety). Women who reported having lost their jobs as a result of the pandemic were ∼5 times more likely to show evidence of probable PTSD (OR = 5.182; 95% CI: 1.08–24.85). Receiving inadequate support from family and friends made the individual approximately four times as likely to develop probable PTSD (OR = 4.258; 95% CI: 1.24–14.65), while controlling for the other variables in the regression model.

Conclusions: Overall, these results support our hypothesis that volatility in factors such as social support, economic stability, and mental health work together to increase the probability of women developing PTSD in response to a collective trauma such as COVID-19.

Keywords: trauma, collective trauma, precarity, isolation, COVID-19, PTSD, resilience, retraumatization

INTRODUCTION

In March 2020, regions across the globe were impacted by the spread of the SARS CoV-2 virus (COVID-19). COVID-19 has had a large and devastating impact on mental health, in part due to increased social isolation (lockdowns, social distancing, and potential negative effects on relationships), economic ramifications (industries which could not withstand lockdown, job losses in some high contact sectors), and effects of the illness itself. According to one meta-analysis, the overall prevalence of stress in the general population due to COVID-19 approaches 30% (1). Negative mental health effects have been observed in groups as disparate as university students (2) and seniors (3, 4).

It is possible that some of these effects unevenly impact women. RBC economics reports[1] that females were disproportionately affected by job loss, with women making up the majority of labor force exits, particularly in the service sector (5). Moreover, while men categorized themselves as "unemployed" (i.e., actively looking for work), many females changed their status to "out of the labor force". These decisions appear to have been driven by the presumed need for females to stay home and take care of family members. Yet, the pandemic also resulted in increases in household conflict and gender-based violence (6), with women being unsure of how to access support services due to COVID-19, and related concerns about overburdening the system. Accordingly, higher rates of anxiety were observed in women during the pandemic (4).

We were interested in the impact of COVID-19 on rates of likely post-traumatic stress disorder (PTSD) among female residents of Fort McMurray, Alberta, a remote northern town. Fort McMurray has a large (almost 20% of residents) "shadow population" (7), most living in temporary accommodations and labor camps (8). Until the recent price collapse, the economic driver for the townsite has historically been the nearby oil sands. Accordingly, the town population is skewed toward being young (over 47% aged 20 to 44) (9) and male,[2] (roughly 54.0% of the population, compared to 49.1% nationally) (10). A 2013 crime statistics report (11) notes that the region experiences relatively high rates of cocaine distribution and impaired driving. Fort McMurray also collects a very large proportion of video lottery terminal revenue in the province, second only to neighboring High Level (12). Overall, the town has a reputation of being somewhat patriarchal, catering mainly toward young males working in the resource industry (13). One magazine article went so far as to argue that Fort McMurray "has become synonymous with crime, an explosion in prostitution and the tough, young, bored single men with too much money and little to do" (14). Perhaps not surprisingly, the impact of COVID-19 in the surrounding region higher than average, with rates several times the provincial average (2045.2 vs. 574.4 per 100,000).[3]

The situation for females in Fort McMurray is decidedly different. It has been argued that, "[b]eliefs and visions of women's identities in resource communities and industries are especially prone to extreme polarization" (13), limiting their opportunities. In situations where women's options are already marginalized, it is reasonable to suggest that pandemic restrictions might have narrowed them still further (15). This may make females a vulnerable population in terms of dealing with COVID-19. For instance, women primarily dependent on spousal income may have simply left their jobs due to the pandemic while single women could not. Lockdowns may have also affected women disproportionately from involvement in social and community activities. Thus, power asymmetries, borne of pre-existing social structures, generate "unequal exposure to risk, making some groups of people… more prone to hazards" (16), including mental health risks associated with collective trauma. We speculate that females living in Fort McMurray may be at greater risk for post-traumatic consequences of COVID-19.

It has also been suggested that social support prior to a disaster appears to affect one's mental health adjustment to a collective trauma (17). Effects have been demonstrated in terms of both depressive symptomatology (18) and psychological distress (19)—although the latter showed no increase in post-traumatic stress. Nonetheless, a meta-analysis found "lack of support" to be one of the top three predictors of PTSD risk (20). We theorized that individuals who were in a relationship at the time of COVID-19 would fare better in terms of PTSD symptomatology than those living alone. Since previous research in Fort McMurray found that female residents had higher PTSD rates in response to the wildfire than men (21), and because reviews have suggested that, generally, women are more likely than men to experience PTSD in the wake of disasters (20, 22, 23), we focused our analysis exclusively on females. Both the living situations and the stressors experienced by women in Fort McMurray are likely different from those of local men.

Thus, this paper has two related objectives. The first is to look at the impact of relationship status of females on variables that

[1]https://thoughtleadership.rbc.com/canadian-women-continue-to-exit-the-labour-force/

[2]https://www12.statcan.gc.ca/census-recensement/2016/dp-pd/prof/details/page.cfm?Lang=E&Geo1=POPC&Code1=0292&Geo2=PR&Code2=01&SearchText=Canada&SearchType=Begins&SearchPR=01&B1=All&TABID=1&type=0

[3]https://www.alberta.ca/maps/covid-19-status-map.htm

appear to be important for dealing with adversity. The second is to examine potential predictors of PTSD in response to the COVID-19 pandemic.

METHODS

Survey Details

Questionnaire responses were gathered via an online survey from a cross-section of Fort McMurray residents during the COVID-19 pandemic (April–June 2021). Data represent all responses received from respondents who identified as female, during this time period. Responses were self-reported, and participation was anonymous, via the secure, browser-based REDCap program (24). The questionnaire was comprised of demographic questions, self-reported history of common mental health disorders including PTSD [the PCL-C (25)], and questions pertaining to COVID-19. Consent was implied via survey completion. The study received approval from the University of Alberta Research Ethics Board (Pro00066054).

Statistical Analysis

Data were analyzed using SPSS v25 (26). Descriptive statistics were analyzed for demographic, clinical, and COVID-19 related variables, based on relationship status. Chi-squared/Fisher exact analysis then examined the variables in relation to putative PTSD status. Binary logistic regression analysis identified potentially important predictors of PTSD, excluding strongly intercorrelated predictor variables (Spearman's correlation coefficients $\geq$0.7). The model included all significant ($p \leq 0.05$) or nearly significant ($p < 0.10$) variables identified in the univariate analysis. Odds ratios and confidence intervals were calculated, to determine the association between each of the predictor variables and self-reported levels of PTSD. Missing data were not imputed; data represent all responses obtained.

Sample Size Estimation

With a population of 111,687 as of the 2018 municipal census[4] a 95% confidence interval, and a $\pm$ 3% margin of error, the sample size needed for prevalence rate estimates for PTSD would be 1058.

RESULTS

Of the 249 residents who accessed the online survey, 186 ultimately completed it, yielding a response rate of 74.7%. Of those 186, 85% (159) were females. Our analysis is limited to this subgroup of respondents.

Demographics and Mental Health Status

As we were interested in how relationship status might affect life circumstances in light of the pandemic (i.e., the added stress of having to rely solely on one's own income; lack of emotional support), demographic variables were examined separately as a function of relationship status. Chi-squared tests were used to assess whether there were group differences between the different relationship status groups.

In the overall group, 115 (72.3%) were in a relationship, while 44 (27.7%) were not. Females who were not in a relationship were approximately the same age (54.5% over age 40 vs. 48.7% $\leq$ 40, ns; all results presented as "not in a relationship" vs. "married/co-habiting", respectively) and equally likely to be employed (95.5% vs. 94.8%, *ns*). Interestingly, although the numbers were too small to draw any conclusions, nearly twice as many single females were employed in the oilsands (3.7%) as their married/co-habiting comparison group (7.1%). Jobs in this sector are far more likely to be contract positions, compared to some of the other sectors in the survey (e.g., government; school boards; healthcare), potentially suggesting higher precarity. Unmarried females were statistically twice as likely (36.4%) to be renting their accommodations as married women (13.9%; $\chi^2 = 9.98$, $p < 0.01$), again possibly linked to decreased security in terms of living circumstances.

Women not in a relationship showed a tendency toward a higher probability of some previous mental health diagnosis (63.6% vs. 48.7%; $\chi^2 = 2.85$, $p < 0.10$), and were almost twice as likely to report having had a previous mental health diagnosis of depression (45.5% vs. 27.8%; $\chi^2 = 4.49$, $p < 0.05$). In terms of current use of psychotropic medications, single women were more likely to have a prescription than were married/co-habiting women (50.0% vs. 30.4%; $\chi^2 = 5.30$, $p < 0.05$). Specifically, women not in a relationship were almost twice as likely to be on antidepressants as were those in a relationship (50.0% vs. 26.1%; $\chi^2 = 8.27$, $p < 0.01$). There was also a trend toward higher use of mood stabilizers (11.4% vs. 3.5%; $\chi^2 = 3.71$, $p < 0.10$), although numbers were low and should be viewed with caution. Similarly, women who were single were slightly more likely to have received mental health counselling in the past year (45.5% vs. 37.4%, *ns*) and to report wanting counselling (61.4% vs. 53.9%, *ns*), although neither of these differences was significant. Taken together, these data suggest that women not in a relationship were at higher risk for negative mental health effects as a result of COVID-19.

While one's relationship status might have some impact on dealing with difficult circumstances, it is also plausible that it might make some difference in terms of one's level of exposure to COVID-19 and its sequelae. In fact, we found no significant difference between the two groups with regard to these variables. Thus, the rest of this section reports on this group as a whole.

The vast majority (95.3%) of respondents reported being fearful about contracting the virus, and approximately the same proportion (97.3%) reported feeling fearful about friends or family contracting it. Just over two-thirds of respondents reported that their close friends or family had actually gotten sick with COVID-19 (69.8%). Similarly, almost two-thirds (61.7%) of individuals in the two groups reported having to self-isolate or quarantine due to symptoms or suspected contact with an affected individual. However, the vast majority did not lose their job due to COVID-19 (87.3%).

In terms of exposure to pandemic-related media imagery, 43.3% said they saw images depicting sick or dying people daily, and approximately the same number (42.7%) said they saw it

[4]https://www.rmwb.ca/en/permits-and-development/resources/Documents/Latest-Census-Report-2018.pdf

TABLE 1 | Demographic profile, clinical characteristics, and responses to COVID-19 of female respondents in Fort McMurray, as a function of relationship status.

Variable	In a relationship *n* (%)	Not in a relationship *n* (%)	Total *n* (%)	Chi square/Fisher Exact	*p*-value	Effect size (Cramer's V)
DEMOGRAPHIC CHARACTERISTICS						
Age						
≤40y	59 (51.3)	20 (45.5)	79 (49.7)	0.436	0.509	0.052
>40y	56 (48.7)	24 (54.5)	80 (50.3)			
Employment status						
Employed	109 (94.8)	42 (95.5)	151 (95.0)	0.30	0.862	0.014
Unemployed	6 (5.2)	2 (4.5)	8 (5.0)			
Housing status						
Own home	99 (86.1)	28 (63.6)	127 (79.9)	9.978	**0.002**	0.251
Renting	16 (13.9)	16 (36.4)	32 (20.1)			
CLINICAL CHARACTERISTICS						
Past mental health diagnosis (any)						
No	59 (51.3)	16 (36.4)	75 (47.2)	2.851	0.091	0.134
Yes	56 (48.7)	28 (63.6)	84 (52.8)			
Past mental health diagnosis (specific)						
Depression	32 (27.8)	20 (45.5)	52 (32.7)	4.494	**0.034**	0.168
Bipolar Disorder	3 (2.6)	2 (4.5)	5 (3.1)	**	**0.617**	0.050
Anxiety	47 (40.9)	22 (50.0)	69 (43.4)	1.080	0.372	0.082
Schizophrenia	0 (0.0)	0 (0.0)	0 (0.0)	–	−0.075	−0.182
Personality Disorder	0 (0.0)	2 (4.5)	2 (1.3)	**0.046	0.830	0.017
Other	9 (7.8)	3 (6.8)	12 (7.5)			
Presently taking psychotropic medication (any)						
No	80 (69.6)	22 (50.0)	102 (64.2)	5.297	**0.021**	0.183
Yes	35 (30.4)	22 (50.0)	57 (35.8)			
Presently taking psychotropic medication (specific)						
Antidepressants	30 (26.1)	22 (50.0)	52 (32.7)	8.269	**0.004**	0.228
Antipsychotics	1 (0.9)	0 (0.0)	1 (0.6)	**	1.00	0.049
Benzodiazepines	3 (2.6)	1 (2.3)	4 (2.5)	**	1.00	0.010
Mood stabilizers	4 (3.5)	5 (11.4)	9 (5.7)	3.706	0.054	0.153
Sedative hypnotics	10 (8.7)	7 (15.9)	17 (10.7)	1.734	0.188	0.104
Other	2 (1.7)	0 (0.0)	2 (1.3)	**	1.00	0.070
Has received MH counselling in past year	43 (37.4)	20 (45.5)	63 (39.6)	0.865	0.352	0.074
Would like to receive MH counselling	62 (53.9)	27 (61.4)	89 (56.0)	0.717	0.397	0.067
COVID-19 VARIABLES						
Reports having been fearful about contracting the coronavirus	104 (94.5)	39 (97.5)	143 (95.3)	0.576	0.448	0.062
Reports having been fearful about close friends/family members contracting the coronavirus	107 (97.3)	39 (97.5)	146 (97.3)	**	0.99	0.006
Reports having close friends or family members who have been sick from the coronavirus disease	80 (73.4)	24 (60.0)	104 (69.8)	2.490	0.115	0.129
Had to self-isolate or self-quarantine due to symptoms, recent travel, or contact with someone who may have COVID-19?	69 (63.3)	23 (57.5)	92 (61.7)	0.417	0.518	0.053
Lost job due to the COVID-19 pandemic						
No	97 (88.2)	34 (85.0)	131 (87.3)	0.268	0.604	0.042
Yes	13 (11.8)	6 (15.0)	19 (12.7)			
Frequency of viewing television images of sick and dead people caused by coronavirus						
Daily	49 (44.5)	16 (40.0)	65 (43.3)	1.633	0.442	0.104
Less than daily	48 (43.6)	16 (40.0)	64 (42.7)			
Never	13 (11.8)	8 (20.0)	21 (14.0)			
Frequency of reading newspaper and internet articles related to the pandemic						
Daily	62 (56.4)	25 (62.5)	87 (58.0)	1.337	0.505	0.095
Less than daily	45 (40.9)	15 (37.5)	60 (40.0)			
Never	3 (2.7)	0 (0.0)	3 (2.0)			

(Continued)

TABLE 1 | Continued

Variable	In a relationship *n* (%)	Not in a relationship *n* (%)	Total *n* (%)	Chi square/Fisher Exact	*p*-value	Effect size (Cramer's V)
Received sufficient support from family and friends for COVID-19 pandemic						
Some-to-high level support	82 (75.2)	29 (72.5)	111 (74.5)	0.115	0.735	0.028
Limited or no support	27 (24.8)	11 (27.5)	38 (25.5)			
Received sufficient support from Government of Canada for COVID-19 pandemic						
Some-to-high level support	33 (30.8)	10 (25.6)	43 (29.5)	0.372	0.542	0.050
Limited or no support	74 (69.2)	29 (74.4)	103 (70.5)			
Received sufficient support from Government of Alberta for COVID-19 pandemic						
Some-to-high level support	27 (28.7)	8 (21.1)	35 (26.5)	0.817	0.366	0.079
Limited or no support	67 (71.3)	30 (78.9)	97 (73.5)			
Received sufficient support from the employer for COVID-19 pandemic						
Some-to-high level support	81 (75.0)	27 (67.5)	108 (73.0)	0.833	0.362	0.075
Limited or no support	27 (25.0)	13 (32.5)	40 (27.0)			

***Indicates use of Fisher exact statistic. Bold values indicate signif./near-signif. effects.*

occasionally, while only 14.0% reported never seeing this type of imagery.

The support individuals reported receiving was substantial, with approximately three-quarters (74.5%) of respondents saying they received moderate to high levels of family support. That said, reported levels of support by the federal government were quite a bit lower, with only 29.5% of respondents having received financial support from the Government of Canada. Provincial financial relief was about the same level, reported by 26.5% of respondents. Interestingly, these results stand in stark contrast to support provided by the individuals' employer, with almost three-quarters (73%) reporting moderate to high support from these local sources. These results are presented in **Table 1**.

Overall, 40.8% of the respondents to the survey showed evidence of a likely PTSD diagnosis. A univariate analysis examined the relationship between respondents' demographic profile, mental health status, and COVID-19 experience, with probable PTSD. Overall, 16 variables were significant or near-significant predictors of PTSD, including: *employment status*, *relationship status*, *previous mental health diagnosis* (any, depression, anxiety), *current medication status* (any, antidepressants, benzodiazepines, sedative-hypnotics), *mental health counselling in the past year, desire to receive mental health counselling*, and a number of COVID-19 variables, including being *fearful about contracting Covid, pandemic-related job loss*, *family support*, *government support*, and *employer support*. These results are presented in **Table 2**.

All variables that demonstrated asymptotic significance were then tested as potential predictors in the logistic regression model. Two of these variables were ultimately removed, as high correlations with other variables would have meant they were duplicating other data in the model. These were: *history of any mental health diagnosis* (which showed high correlations with both a depression or anxiety diagnosis, as well as with medication use), and *antidepressant use* (which correlated highly with mental health status and medication use more generally). Two other variables—*current employment status* and *benzodiazepine use*—were also dropped from the model due to low overall *n*'s in some cells. Thus, the model ultimately retained 12/16 potential chi-squared predictors.

The overall model was statistically significant; χ^2 (df = 12; n = 137) = 66.12, $p < 0.001$, suggesting it could distinguish between respondents who did or did not go on to develop probable PTSD during the pandemic. Variables in the model accounted for between 38.3% (Cox and Snell R^2) and 51.5% (Nagelkerke R^2) of the overall variance. The model correctly classified 81.0% of all cases (82.3% of individuals without PTSD, and 79.3% of those with likely PTSD). Results of the multivariate logistic regression model used to predict likely PTSD are presented in **Table 3**.

Four variables showed significant predictive power in terms of identifying probable PTSD in the model, after controlling for other potential causes. These were: *diagnosis of depression*, *diagnosis of anxiety*, *job loss due to COVID-19*, and *lack of family support*. Respondents who had a diagnosis of depression were almost four times as likely to develop PTSD symptoms as those without (OR = 3.846; 95% CI: 1.13–13.13). Similarly, respondents with a prior diagnosis of anxiety were five times as likely (OR = 5.190; 95% CI: 1.42–19.00). Losing one's job as a result of COVID-19 made them approximately five times more likely to develop this diagnosis (OR = 5.182; 95% CI: 1.08–24.85). Finally, receiving little or no family support made one approximately four times as likely to develop probable PTSD (OR = 4.258; 95% CI: 1.24–14.65). It is worth noting that relationship status did not make a significant, unique contribution to the model, counter to our prediction.

TABLE 2 | Chi square test of association between demographic variables, mental health status, COVID-19 characteristics, and probable PTSD.

Variable	Not likely PTSD	Likely PTSD	Chi square/ Fisher Exact	*p*- value	Effect size (Cramer's V)
DEMOGRAPHIC CHARACTERISTICS					
Age categories					
≤40y	40 (58.8)	28 (41.2)	0.006	0.939	0.006
>40y	44 (59.5)	30 (40.5)			
Employment status					
Employed	84 (61.8)	52 (38.2)	**	**0.004**	0.253
Unemployed	0 (0.0)	6 (100.0)			
Relationship status					
In a relationship	66 (63.5)	38 (36.5)	2.98	**0.084**	0.145
Not in a relationship	18 (47.4)	20 (52.6)			
Housing status					
Own home	67 (58.8	47 (41.2)	0.035	0.851	0.016
Renting	17 (60.7)	11 (39.3)			
CLINICAL CHARACTERISTICS					
Past mental health diagnosis: Any					
No	52 (77.6)	15 (22.4)	17.885	**0.000**	0.335
Yes	32 (42.7)	43 (57.3)			
Past mental health diagnosis: Depression					
No	69 (72.6)	26 (27.4)	21.575	**0.000**	0.390
Yes	15 (31.9)	32 (68.1)			
Past mental health diagnosis: Bipolar Disorder					
No	82 (59.4)	56 (40.6)	**	1.00	0.032
Yes	2 (50.0)	2 (50.0)			
Past mental health diagnosis: Anxiety					
No	61 (75.3)	20 (24.7)	20.36	**0.000**	0.379
Yes	23 (37.7)	38 (62.3)			
Past mental health diagnosis: Personality Disorder					
No	83 (58.9)	58 (41.1)	**	1.00	0.070
Yes	1 (100.0)	0 (0.0)			
Current medications: Any					
No	61 (67.0)	30 (33.0)	6.508	**0.011**	0.214
Yes	23 (45.1)	28 (54.9)			
Current medications: Antidepressants					
No	64 (66.7)	32 (33.3)	6.921	**0.011**	0.221
Yes	20 (43.5)	26 (56.5)			
Current medications: Benzodiazepines					
No	84 (60.9)	54 (39.1)	**	**0.026**	0.205
Yes	0 (0.0)	4 (100.0)			
Current medications: Mood stabilizers					
No	81 (60.0)	54 (40.0	**	0.444	0.075
Yes	3 (42.9)	4 (57.1)			
Current medications: Sedative-hypnotics					
No	81 (63.8)	46 (36.2)	10.642	**0.002**	0.274
Yes	3 (20.0)	12 (80.0)			
Current medications: Other psychotropic					
No	82 (58.6)	58 (41.4)	**	0.513	0.099
Yes	2 (100.0)	0 (0.0)			
Received mental health counselling in the past year					
No	63 (71.6)	25 (28.4)	14.81	**0.000**	0.323
Yes	21 (38.9)	33 (61.1)			
Reports wanting to receive mental health counselling					
No	51 (81.0)	12 (19.0)	22.268	**0.000**	0.396
Yes	33 (41.8)	46 (58.2)			

(Continued)

TABLE 2 | Continued

Variable	Not likely PTSD	Likely PTSD	Chi square/ Fisher Exact	*p*- value	Effect size (Cramer's V)
COVID-19 VARIABLES					
Reports having been fearful about contracting the coronavirus					
No	5 (71.4)	2 (28.6)	**	**0.070**	0.057
Yes	79 (58.5)	56 (41.5)			
Reports having been fearful about close friends/family members contracting the coronavirus					
No	4 (100.)	0 (0.0)	**	0.145	0.141
Yes	80 (58.0)	58 (42.0)			
Reports having close friends or family members who have been sick from the coronavirus disease					
No	24 (54.5)	20 (45.5)	0.561	0.454	0.063
Yes	60 (61.2)	38 (38.3)			
Had to self-isolate or self-quarantine due to symptoms, recent travel, or contact with someone who may have COVID-19?					
No	31 (58.5)	31 (58.5)	0.015	0.901	0.010
Yes	53 (59.6)	53 (59.6)			
Lost job due to the COVID-19 pandemic					
No	79 (64.2)	44 (35.8)	9.790	**0.002**	0.263
Yes	5 (26.3)	14 (73.7)			
Frequency of viewing television images of sick and dead people caused by coronavirus					
Daily	34 (56.7)	26 (43.3)	1.416	0.493	0.100
Less than daily	41 (64.1)	23 (35.9)			
Never	9 (50.0)	9 (50.0)			
Frequency of reading newspaper and internet articles related to the pandemic					
Daily	46 (56.1)	36 (43.9)	0.765	0.682	0.073
Less than daily	36 (63.2)	21 (36.8)			
Never	2 (66.7)	1 (33.3)			
Received sufficient support from family and friends for COVID-19 pandemic					
Some-to-high level support	71 (66.4)	36 (33.6)	10.28	0.0**01**	0.270
Limited or no support	12 (35.3)	22 (64.7)			
Received sufficient support from Government of Canada for COVID-19 pandemic					
Some-to-high level support	28 (70.0)	12 (30.0)	3.176	0.0**75**	0.151
Limited or no support	53 (53.5)	46 (46.5)			
Received sufficient support from Government of Alberta for COVID-19 pandemic					
Some-to-high level support	24 (75.0)	8 (25.0)	2.646	0.104	0.144
Limited or no support	56 (58.9)	39 (41.1)			
Received sufficient support from the employer for COVID-19 pandemic					
Some-to-high level support	70 (66.0)	36 (34.0)	9.073	**0.003**	0.254
Limited or no support	13 (37.1)	22 (62.9)			

***Indicates use of Fisher exact statistic. Bold values indicate signif./near-signif. effects.*

DISCUSSION

Our study focused on the prevalence and the predictors of PTSD arising from COVID-19 among females in Fort McMurray. Over 40% of respondents showed evidence of likely PTSD. This number is quite high compared to rates reported in a systematic review of other natural disasters (27). It is, however, comparable to our previous research, where Fort McMurray adolescents showed rates exceeding 37%, even 4.5 years after the wildfire (28). It is worth considering whether these rates are elevated due to the large amount of previous trauma faced by this town: Inhabitants confronted the devastating wildfire in 2016, were hit by the oil price crash, and faced flooding in 2020, along with the onset of COVID-19. This means that their population faced many consecutive traumas. As one resident put it in a news report[5] following the flood, "That odd feeling I felt 4 years ago when we had to evacuate because of the wildfire is that

[5]https://edmontonjournal.com/news/local-news/boil-water-advisory-issued-north-of-athabasca-river-evacuation-orders-issued-for-parts-of-downtown/

TABLE 3 | Logistic regression model for respondents' likelihood to present with probable PTSD.

Characteristics	Coefficient	S.E.	Wald statistic	*p*-value	Odds Ratio	95% C.I. for Odds Ratio	
						Lower	Upper
Relationship status	0.468	0.514	0.829	0.362	1.597	0.583	4.376
Depression diagnosis	1.347	0.626	4.624	**0.032**	3.846	1.127	13.129
Anxiety diagnosis	1.647	0.662	6.186	**0.013**	5.190	1.418	18.999
Not on any medication for mental health concerns	−1.449	0.783	3.423	0.064	0.235	0.051	1.090
Medication (sedative-hypnotics)	1.659	0.902	3.383	0.066	5.256	0.897	30.799
Counselling past year	0.900	0.624	2.081	0.149	2.459	0.724	8.351
Would like to receive counselling	0.605	0.578	1.096	0.295	1.832	0.590	5.689
Fearful about the COVID-19 pandemic	0.072	1.198	0.004	0.952	1.074	0.103	11.238
Job loss due to COVID-19 pandemic	1.645	0.800	4.230	**0.040**	5.182	1.081	24.849
Limited or no support from family and friends for COVID-19 pandemic	1.449	0.630	5.284	**0.022**	4.258	1.238	14.649
Limited or no support from Government of Canada for COVID-19 pandemic	0.275	0.587	0.220	0.639	1.317	0.417	4.159
Limited or no support from employer for COVID-19 pandemic	0.793	0.558	2.023	0.155	2.210	0.741	6.591
Constant	−3.075	1.356	5.140	0.023	0.046		

Bold values indicate signif./near-signif. effects.

same old feeling again… [Except t]his time, there's that extra worry because we have the pandemic" (29). It is plausible that the PTSD seen in our sample following the pandemic really reflects the cumulative effects of multiple traumas. This is in line with previous research suggesting that additional life stressors—particularly those severe enough to result in PTSD (17) and those that could be classified as continuous life stress (30)—put people at increased risk for developing PTSD following a disaster. A number of factors were shown to be predictive of negative mental health in response to the pandemic for women in Fort McMurray. Our finding that a prior diagnosis of either depression or anxiety significantly predicted developing PTSD symptoms supports the idea that existing mental health difficulties put one at greater risk in the event of a collective trauma. To the extent that depression and anxiety may reflect responses to prior trauma (e.g., adverse childhood events), it would seem that these results support the idea that prior trauma increases reactivity to and potential harm of new trauma.

Interestingly, media exposure was not found to make a difference in terms of whether one was likely to develop symptoms of PTSD. In fact, individuals who were in the Not Likely PTSD group reported more daily exposure to COVID-19 news and imagery than those in the Likely group. This is somewhat surprising, given predictions of negative effects associated with our 24-hour news cycle (31). Moreover, being fearful about the pandemic was also not a good predictor of who went on to develop PTSD. Both of these findings point to the conclusion that, as Neria and Sullivan (30) suggest, "longer-term PTSD to [media] exposure may have more to do with the preexisting vulnerability than with the indirect exposure severity *per se*" (p. 3). In other words, neither exposure to negative information, nor anxiety about the stressor itself, appear to be good predictors of who goes on to develop PTSD.

The finding that job loss was associated with developing probable PTSD fits with our hypothesis that economic precarity puts one at risk for mental health issues. In some sense this is unsurprising, as unemployment has been shown to negatively affect mental health (32, 33). However, this finding may be more specific to COVID-19, as the pandemic directly affected employment for some individuals but not others. McKee-Ryan and co-workers (32) identified four factors as mediating the relationship between unemployment and mental health—work-role centrality, coping resources, cognitive appraisals, and coping strategies—all of which could potentially have been impacted by COVID-19. That said, it is noteworthy that neither government nor employer support had a measurable effect on who showed probable PTSD. It might be that, while Canada provided comparatively generous financial support (the Canadian Emergency Response Benefit, or CERB) to those negatively impacted economically by COVID-19, it may still have been insufficient to meet the needs of individuals living in Fort McMurray, which has unusually high rates of inflation and housing costs. Similarly, job sharing agreements, which were instituted in many work environments with the advent of COVID-19 (34), may not have had general applicability to positions in work camps, many of which were contract positions. In other words, these forms of government support may have had limited applicability to this specific population, or been insufficient to meet their needs. Finally, there may have been difference in terms of how job loss was experienced in different sectors. It would appear that the effects of economic instability are not necessarily symmetrical, with consequences of job loss having worse mental health effects than positive impacts of employment support.

The finding that lack of social support was predictive of probable PTSD in women fits with the idea that social isolation is associated with greater potential harm in the context of collective trauma. A recent literature review suggested that high rates of support prior to natural disasters appear to mitigate psychological trauma in the aftermath of a crisis (35). This is

interesting in terms of the lack of effects of governmental and employer support discussed above; it would appear that supports might need to be more personal and less bureaucratic in order to have a positive impact. Having supportive loved ones = people to discuss potential fears, problem-solve solutions when problems arise, and express empathy when bad things happen—is undoubtedly advantageous. That said, contrary to our hypothesis [and the findings of other authors (36)], relationship status was *not* found to be predictive of developing post traumatic stress. It is possible that being in a relationship lacking emotional encouragement (e.g., downplaying the partner's fears about possible dangers due to skepticism, or not supporting the partner's coping strategies) may in fact be even more traumatizing than being alone. These types of negative "cognitive reappraisals" have been speculated as being key mechanisms in the link between social support and PTSD (37). In other words, being in a relationship cannot necessarily be equated to having social support.

Finally, we should note that relatively little work has been done to look at factors that increase vulnerability to PTSD in women as a result of COVID-19, specifically. While many papers note that being female is in itself a risk factor, they generally report on a wide variety of other risk factors [e.g., being a strong internet user (38), the specific classification of population to which the individual belongs (39), one's perception of racial discrimination (40) and one's perception of the pandemic as a crisis (36)]. Yet, women have been shown to have a different pattern in terms of the PTSD symptoms and sleep quality experienced during COVID-19 (41), suggesting potentially distinct physiological mechanisms at work. Supporting this idea, other authors suggest that the genders may even respond differently to peritraumatic stress (experienced during and immediately after the event) compared to posttraumatic stress (42). As we have argued here, there can be a number of factors that affect female vulnerability to stressors differentially than males—economic, social, and emotional. Females' different sociocultural milieu warrants consideration. We suggest that future studies should focus specifically on females and the issues they encountered with COVID-19 (and other mass traumas) specifically.

LIMITATIONS

Our study has several limitations. The sample size is fairly small, and the individuals responding to this study constitute a self-selected group, and so do not represent a random sampling of all individuals, or even all females, in the region. In particular, the high rates of PTSD seen in this analysis likely reflect that people with intrusive and problematic symptoms will be more likely to seek resources online. Moreover, our overall low sample size resulted in fairly broad Confidence Intervals, which decrease the resultant certainty of the estimates we have put forth. Besides, as the sample size of this study was much less than the sample size estimates that we projected, the margin error of our prevalence estimates was ±7% rather than the ±3% which we projected initially.

In addition, due to the small overall population of Fort McMurray (<100,000), and the personal nature of the mental health data requested, precautions were taken to ensure that no combination of question responses could lead to identifiable data. This included limiting questionnaire items mainly to those concerned with mental health or COVID-19. Thus, we chose to exclude information regarding ethnicity and educational attainment, as well as some health items such as physical disease history, pregnancy status, and vaccination status. This means some potentially important effects were not examined. For example, one meta-analysis has reported that pregnancy history is associated with PTSD, with high-risk pregnancies resulting as in rates as high as 18%, either pre- or post-partum (43). This calls into the question some of our findings, as we cannot exclude the possibility that some of the respondents in our sample, who we know had gone through multiple traumas, might be pregnant. As another significant example, educational attainment has been linked to one's misperception of falsehoods regarding COVID-19 (44), leading to riskier behaviour and worse outcomes (45). Similarly, the decision to exclude benzodiazepine use as a predictor of PTSD due to low *n*'s is unfortunate, as some research attempting to use prophylactic benzodiazepines to prevent PTSD actually found a paradoxical increase in PTSD (46, 47) diagnosis. Future research on COVID-19 and other mass trauma incidents should seek to examine some of these factors and their impacts on PTSD more directly.

It should also be noted that PTSD categorizations were based upon questionnaire measures of mental health. These cannot replace clinical assessment. An individual may struggle with depression or anxiety, never discuss it formally with a doctor, and it may resolve itself. Thus, presumed rates of probable PTSD must be viewed as suggestive. More generally, self-report questionnaires can show validity problems, demand effects, and be prone to issues associated with recollection of facts and events.

This study is also subject to problems observed with cross-sectional analyses more generally. We do not have information on the ultimate effects of any predictor, simply the correlations simultaneously observed in the data, so cause-and-effect conclusions cannot be drawn. This study would benefit from follow-up research to determine whether the associations predicted by this analysis are confirmed longitudinally.

Finally, this study was limited to females, and results cannot be generalized beyond this subset of the population. For instance, it has been theorized that the pandemic exacerbated the precarious positions of women by reinforcing existing patriarchal structures while eroding female friendships given necessary measures such as lockdowns and social distancing (15). It is likely that variables such as social support and economic precarity due to collective trauma play a different role in terms of modeling potential mental health effects in men.

CONCLUSION

This study focused on the prevalence of PTSD in female residents of Fort McMurray, Canada, in response to the COVID-19 pandemic. This community has experienced a series of negative events, economic as well as environmental, since the

2016 wildfire that made it the subject of national attention. This includes evacuation, relocation, rebuilding after the fire, the economic collapse of oil prices, flooding, and COVID-19. This string of events has led to a situation where life for residents never truly "got back to normal". With climate crises becoming all the more common, our understanding of multiplicative effects of retraumatization will gain importance. This points to the necessity of broad governmental income security measures, such as a Basic Income, to help support communities in situations where multiple traumas occur. Our findings support the thesis that factors influencing this constant instability had negative mental health effects on the women of Fort McMurray. Instability, in terms of poor family support, economic precarity, and a history of mental health issues were all found to predict probable PTSD symptoms. Taken together, these results suggest that promoting interventions that contribute to a sense of stability is key to mental health recovery following collective trauma.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by University of Alberta Ethics Research Board (Pro00066054). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

The study was conceived and designed by VA. HP drafted the initial manuscript. RS conducted data analysis. All authors contributed to study design, review, and revision of the initial draft manuscript. The final draft was read and approved by all authors prior to submission.

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Intergenerational Transmission of Effects of Women's Stressors During Pregnancy: Child Psychopathology and the Protective Role of Parenting

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Objective: Experiences of stress and adversity, such as intimate partner violence, confer risk for psychiatric problems across the life span. The effects of these risks are disproportionately borne by women and their offspring—particularly those from communities of color. The prenatal period is an especially vulnerable period of fetal development, during which time women's experiences of stress can have long-lasting implications for offspring mental health. Importantly, there is a lack of focus on women's capacity for resilience and potential postnatal protective factors that might mitigate these intergenerational risks and inform intervention efforts. The present study examined intergenerational associations between women's prenatal stressors and child executive functioning and externalizing problems, testing maternal parenting quality and child sex as moderators, using a large, prospective, sociodemographically diverse cohort.

Methods: We used data from 1,034 mother-child dyads (64% Black, 30% White) from the Conditions Affecting Neurocognitive Development and Learning in Early Childhood (CANDLE) pregnancy cohort within the ECHO PATHWAYS consortium. Women's prenatal stressors included stressful life events (pSLE) and intimate partner violence (pIPV). Measures of child psychopathology at age 4–6 included executive functioning and externalizing problems. Parenting behaviors were assessed by trained observers, averaged across two sessions of mother-child interactions. Linear regression models were used to estimate associations between women's prenatal stressors and child psychopathology, adjusting for confounders and assessing moderation effects by maternal parenting quality and child sex.

Results: Women's exposures to pSLE and pIPV were independently associated with child executive functioning problems and externalizing problems in fully-adjusted models. Maternal parenting quality moderated associations between pSLE and both outcomes,

such that higher parenting quality was protective for the associations between women's pSLE and child executive functioning and externalizing problems. No moderation by child sex was found.

Discussion: Findings from this large, sociodemographically diverse cohort suggest women's exposures to interpersonal violence and major stressful events—common for women during pregnancy—may prenatally program her child's executive functioning and externalizing problems. Women's capacity to provide high quality parenting can buffer this intergenerational risk. Implications for universal and targeted prevention and early intervention efforts to support women's and children's wellbeing are discussed.

Keywords: prenatal stress, executive functioning, externalizing behavior, parenting, child psychopathology

INTERGENERATIONAL TRANSMISSION OF EFFECTS OF WOMEN'S STRESSORS DURING PREGNANCY: CHILD PSYCHOPATHOLOGY AND THE PROTECTIVE ROLE OF PARENTING

Exposure to various forms of stressors, including economic precarity, housing insecurity, loss of a loved one, and interpersonal violence, are well-established predictors of psychiatric problems across the life span (1–5). The impact of these experiences is disproportionately borne by women—especially women in underserved communities of color (6–9) and with lower incomes (10)—which also places their offspring at increased risk for later psychiatric problems. Indeed, the World Health Organization considers intimate partner violence against women a "major public health problem and a violation of women's human rights," estimating that roughly one in three women are subjected to intimate partner violence during their lifetime, with up to 13% of women experiencing intimate partner violence during pregnancy (pIPV) (11). Further, the most common form of violence committed against women is intimate partner violence, and women who experience partner violence are at increased risk for a range of mental health problems, such as depression, posttraumatic stress, anxiety, and suicidality (11). In addition, according to the Centers for Disease Control and Prevention's Pregnancy Risk Assessment Monitoring System, in 2010 about 70% of pregnant women experienced at least one stressful life event (pSLE) in the year before their infant's birth (12). These include: emotional stressors (e.g., a family member being hospitalized or dying), financial stressors (e.g., moving, losing a job, being unable to pay rent/bills), partner-related stressors (e.g., separation/divorce), and traumatic stressors (e.g., becoming homeless) (12). Despite these alarming rates of exposure to stressors during pregnancy—a time when women's social and biological wellbeing is in flux and particularly vulnerable to stress (13, 14)— there has been limited focus on the intergenerational transmission of the effects of stressors, such as pSLE and pIPV, on offspring psychopathology and related developmental processes. The perinatal period is a critical time for offspring development, wherein such intergenerational risks pose a threat to offspring mental health across the lifespan. Crucially, there is also a lack of focus on women's capacity for resilience and associated research on potential postnatal resilience-promoting factors that might mitigate these intergenerational risks for child mental health problems and shed light on opportunities to support maternal and child wellbeing after exposure to prenatal adversity in affected communities.

A large body of research has documented the association of both pSLE and pIPV with deleterious outcomes for women, including maternal mortality, labor and delivery complications, poor perinatal mental health (such as depression, post-traumatic stress disorder, and substance use disorder), and enduring alterations to women's immune function (13, 15, 16). The intergenerational impact of pIPV and pSLE is seen in neonatal outcomes of higher rates of preterm birth and low birth weight, but also in longer-term neurodevelopmental problems that extend into childhood and beyond (17–20). Investigations of maternal IPV exposure are especially crucial considering the established continuity of IPV within families and across generations. For example, women who witness IPV as children have greater odds of experiencing IPV as adults, and their own children are more likely to witness IPV (21, 22). Children exposed to IPV also have increased risk for both externalizing and internalizing problems, as well as higher levels of symptoms of trauma, compared to non-exposed children (15, 23). Women's exposure to stressors in pregnancy might affect offspring development through both pre- and post-natal pathways, with potentially cumulative effects, making it important to expand empirical understanding of these risks.

Prenatal programming of offspring neurodevelopment and psychopathology in the context of maternal prenatal stress is a complex biopsychosocial phenomenon that requires attention to the social dynamics and biology that is unique to women. Women's experiences of stress during pregnancy result in altered fetal exposure to maternal glucocorticoids, immune tolerance, and nutrient supply that can shift trajectories of offspring growth and stress reactivity in the postnatal environment (24–27). Despite the fact that prenatal stressors such as pIPV and pSLE for women can co-occur, their dual contributions to child

Abbreviations: EF, executive functioning; pIPV, prenatal intimate partner violence; pSLE, prental stressful life events.

psychopathology are rarely studied—especially in communities of color (17, 28, 29). This is a particularly important population within which to examine such stressors given that women of color have higher prevalence rates of intimate partner violence compared to non-Hispanic White women (6–9).

Studies examining the intergenerational associations between maternal prenatal stress and risk for offspring psychopathology during infancy and early childhood have found that maternal prenatal stress is generally linked to her child's subsequent inability to self-regulate, manifesting as more difficult temperaments and increased stress reactivity (17, 30). These problems with self-regulation during early school-ages (i.e., preschool and kindergarten) can manifest as executive functioning (EF) deficits, which are also closely related to externalizing psychopathology, such as ADHD (31, 32). Given the high prevalence rates of EF problems and externalizing behavior in young children (33, 34) and how they set the stage for later, more severe psychopathology and health risk (35, 36), examining their etiology and development in early childhood is critical. Although some studies have found associations between prenatal maternal stress and offspring externalizing psychopathology, including risk for ADHD (28), fewer studies have examined this potential link between prenatal stress and child EF problems (37, 38), and to our knowledge, none have examined both executive functioning and externalizing problems within the same conceptual model. Importantly, very few studies have prospectively examined these associations in large, sociodemographically diverse samples, which is particularly salient given that lower SES places both women and their offspring at increased risk for psychopathology, in part due to greater exposure to stressors across generations (17, 18, 39).

There is evidence regarding differential sex effects of maternal stress on offspring psychopathology; however, to date these findings have been quite mixed—necessitating additional inquiry (17, 33, 40–43). This is particularly important to examine in outcomes with well-established sex differences, such as externalizing behavior problems during childhood. Sex-dependent differences in offspring responses to prenatal stress are complex biopsychosocial phenomena, wherein socially patterned norms for gendered child behavior interact with developmental psychobiology. Female and male fetuses exhibit sexually dimorphic responses to the maternal stress-related hormonal and cytokine milieu, investing differentially in placental and somatic growth in ways that may confer sex-dependent trajectories of buffering and risk in the wake of prenatal adversity (41, 44). While female fetal buffering from maternal inflammation or nutritional stress may confer increased resilience in terms of viability relative to males, trade-offs in increased sensitivity to HPA axis programming and risk for psychopathology may also occur (45, 46). For example, Graham and colleagues (47) found that elevated cortisol levels during pregnancy predicted increased amygdala and default mode network connectivity and mediated increased internalizing symptoms in 24-month-old girls but not boys. There is some evidence that boys might be more likely to develop externalizing problems during childhood within the context of maternal prenatal stress (40, 48, 49). Yet, findings here are still mixed, and fewer studies have examined these potential sex differences in early childhood, when externalizing problems are less sex differentiated (43, 47, 50).

Although research on integrational transmission of stress effects has burgeoned recently, there remains a dearth of research identifying opportunities for intervention or prevention regarding prenatal stress and risk for offspring psychopathology (17, 51–53). Identifying malleable, postnatal environmental factors that capitalize on women's strengths is also critical to reducing potential intergenerational risk (19). Parenting is certainly a key factor, with a wealth of research indicating that it can serve as both a risk and a protective factor for child mental health. For example, negative aspects of parenting, such as harsh discipline, neglect, and punishment, are associated with increased risk for offspring psychopathology—especially externalizing behavior problems (54, 55). In addition, multiple studies have found that prior exposure to IPV has a negative impact on parenting behaviors (56), and that such parenting behaviors are also associated with child behavior problems (57–59). However, the increased focus on the negative aspects of parenting has perhaps overshadowed the benefits that the positive aspects of parenting (such as warmth, responsiveness, and scaffolding) can have on offspring mental health. Indeed, positive parent-child interactions have been shown to confer beneficial effects on executive functioning and externalizing psychopathology in both observational and intervention studies (39, 60–62), and positive parenting has been identified as an important resilience-promoting factor for children at increased risk for psychopathology (63). Sensitive caregiving in the context of ongoing stressors is contingent on a caregiver's ability to harness emotional, cognitive, and material resources, especially when caregiving demands are high, such as when children are young (64). Notably, research findings emphasize the ability of caregivers to buffer children from adversity and support healthy child development through supportive parenting, even when facing socioeconomic barriers and other high-adversity contexts (65). For example, Narayan and colleagues found that women with high levels of childhood trauma and positive memories of nurturing care were able to buffer their children from future intergenerational trauma exposure (66). In another example, effective parenting and parental use of positive coregulation skills were associated with higher child executive functioning skills and had positive benefits at school among families who were experiencing homelessness (67). Most studies examining the associations between women's parenting behaviors and child psychopathology, however, rely on parent self-report of their own parenting behaviors, which can produce biased results (68, 69). Fewer studies use more objective, observer ratings of mother-child interactions and parenting behaviors which are less influenced by such biases.

The present study examined the intergenerational association between maternal prenatal stress and risk for executive functioning and externalizing behavior problems during early childhood (ages 4–6) in a large, prospective, pregnancy cohort study of mother-child dyads. We had three main aims to address gaps in extant literature. First, we tested whether women's stressors during pregnancy, including exposure to multiple types of pSLE and pIPV, were predictive of two key aspects

of self-regulation and psychopathology in their children: EF and externalizing behavior problems. Importantly, we utilized a large, racially diverse (64% Black, 30% White) sample with a broad representation of lower-income families, characteristic of an urban Southern metropolitan area in the United States—a population that is largely understudied in extant literature and, due to structural inequalities, are likely to be exposed to higher levels of stressors during pregnancy (10, 70, 71). Second, we tested whether observer-rated parenting behaviors might serve as a postnatal environmental factor that moderates the association between prenatal stressors and risk for child psychopathology. Finally, given the potential for differential effects of prenatal stress on male vs. female offspring, we examined whether child sex moderated the effects of women's pregnancy stressors on both child outcomes.

MATERIALS AND METHODS

Participants and Procedure

The present study utilized data from the Conditions Affecting Neurocognitive Development and Learning in Early Childhood (CANDLE) study, which is part of the ECHO PATHWAYS consortium (72, 73). CANDLE is a longitudinal pregnancy cohort study that enrolled 1,503 women from Memphis/Shelby County, Tennessee, between 2006 and 2011 during their second trimester of pregnancy. Women were between ages 16–40, did not have pre-existing chronic conditions that required medication, and had low-risk pregnancies. Overall, the sample was racially diverse (64% Black, 30% White) and, although the sample had a broad range of socioeconomic status, it was predominantly low-income (59% having federal or state-supplemented health insurance)—representative of the urban area from which it was drawn. All women provided informed consent and the study was approved by the University of Tennessee Health Science Center Institutional Review Board.

Baseline data were collected at study enrollment during the women's second trimester of pregnancy. Subsequent perinatal data were collected during a third trimester visit and at childbirth. Families were then prospectively followed, with data collected at a home visit 4-weeks postpartum, a 6-month phone follow-up, and subsequently at multiple clinic visits occurring at approximately child ages 1-, 2-, 3-, 4–6-, and 8-years. The final analytic sample comprised 1,034 women for whom child data were available on at least one outcome measure. Compared to the total enrolled sample of 1,503, women in the analytic sample tended to be older at study enrollment ($t = 3.94$, $p < 0.001$), but did not otherwise significantly differ on study variables.

Measures

Prenatal Predictors

Stressful Life Events

Women reported retrospectively on whether they experienced 14 different types of major pSLE during pregnancy, using a measure adapted from the widely used Centers for Disease Control and Prevention Pregnancy Risk Assessment Monitoring System survey (74), within the age eight visit maternal questionnaire. This scale included the following 14 items: a family member was hospitalized; death of a close friend/family member; moving to a new address; loss of job/employment; partner lost their job; participant/partner had a reduction in work hours or pay; problems paying the rent/mortgage or other bills; separation/divorce from partner; was apart from partner due to military deployment or extended work-related travel; argued with partner more than usual; partner did not want participant to be pregnant; close friend/family member had a problem with drinking/drugs; participant/partner was incarcerated; participant was homeless. Women responded yes or no to each item; all responses were summed into a total count of different types of pSLE experienced (range 0–14). Given the magnitude and significance of these stressful life events, such measures are thought to have limited recall bias and be accurate over a span of years (75, 76).

Intimate Partner Violence

Women reported on their experiences of pIPV via the short-form version of the revised Conflict Tactics Scale (77), which assesses multiple forms of partner violence. Information was collected during the third trimester of pregnancy, wherein women indicated if they experienced any of four different forms of partner violence (including physical, sexual, or emotional abuse, and/or injury) during the past year. Each item (answered yes or no) was summed to create a total pIPV score (range 0–4).

Moderators

Parenting Quality

Parenting behaviors were assessed at both the age 2 and age 3 clinic visits using the Nursing Child Assessment Satellite Training (NCAST) Parent-Child Interaction Teaching Scale (78, 79). The NCAST comprises 73 items, each endorsed yes or no. This form was completed by study staff members who received rigorous training in the NCAST coding system, and was filled out by a staff member immediately after observing interactions between the mother and child as the mother teaches her child a developmentally challenging task (80). This measure has been utilized with diverse populations and has shown good internal consistency and test-retest reliability. Cronbach's alphas for the present sample were also good ($\alpha = 0.83$ for Total Caregiver score and $\alpha = 0.81$ for Total Caregiver-Child score) (81). We use the term "parenting quality" to describe the overall measure of parenting behavior captured by the Total Caregiver score. This comprises a range of parenting behaviors, including social, nurturant, and didactic caregiving (81). The Total Caregiver score consists of four subscales, including: parental sensitivity to cues, response to distress, social-emotional growth-fostering, and cognitive growth-fostering. Higher scores indicate more sensitivity, supportiveness, and scaffolding by mothers during observed interactions with their child. We created a composite parenting quality score across both the age 2 and age 3 clinic visits by averaging the Total Caregiver score across both visits. Data from one visit was used if both visit data were not available.

Child Sex

We tested the potential moderating effects of child biological sex, ascertained from birth records, on both outcome variables, given

the mixed evidence regarding potential differences from previous research (17, 40).

Child Outcomes

Child psychopathology was assessed using two measures at the age 4–6 clinic visit.

Executive Functioning Problems

Women reported on their children's EF using the Behavior Rating Inventory of Executive Functioning–Preschool version (BRIEF-P) (82) at the age 4–6 clinic visit. The BRIEF is a widely used measure that assesses a broad range of executive functioning problems in everyday life and is used in clinical and research settings. The BRIEF-P comprises 3 indexes—inhibitory self-control, flexibility, and emergent metacognition, which make up the overall global executive composite. Cronbach's alpha for the present sample was excellent ($\alpha = 0.96$). The present study utilized *t*-scores of the overall composite to assess problems with executive functioning.

Externalizing Problems

Women reported on their children's externalizing problems via the well-validated and widely-used Child Behavior Checklist for ages 1.5–5 (CBCL) (83) at the age 4–6 clinic visit. Consistent with prior research, we used *t*-scores from the broadband Externalizing Problems scale, which has been widely used to assess overall problems of externalizing psychopathology, including hyperactivity/impulsivity, self-regulation, oppositionality, conduct, and aggression in children. Internal consistency for the Externalizing Problems scale was excellent (Cronbach's $\alpha = 0.91$).

Covariates

Several pre- and postnatal covariates were included to address potential confounding. We included several socioeconomic factors, given they have demonstrated associations with child psychopathology. The following were obtained from women during study enrollment: age, annual household income (adjusted for number of dependents), education, marital status, and self-reported race [the authors acknowledge that race is not a biological variable and is a political and social construct that often serves as a proxy for the impact of racist practices and structural inequality (84); thus, it is examined in the current paper with this premise in mind]. We also included women's full-scale IQ from the Wechsler Abbreviated Scale of Intelligence, Second Edition (85) assessed at the postnatal 1-year clinic visit, or thereafter if that visit was missed. Given that parent psychopathology, in particular depression, is also associated with later child psychopathology, we included both postpartum and concurrent maternal depression as covariates. Women's postpartum depression across the 1st year of the child's life was measured with the 10-item, self-reported Edinburgh Postnatal Depression Scale (86), which was assessed at 4-, 6-, and 12-months post-birth; the total depression score across all three time points was averaged into a single composite. Concurrent maternal depression was measured at the age 4–6 clinic visit with the Center for Epidemiologic Studies Depression Scale, a 20-item self-report (87). Finally, child biological sex and age at the outcome timepoint were included as covariates in all models.

Statistical Analyses

All linear regression models were conducted using R (RStudio version 1.2.5033) and fitted using the *lm* function. Data were first examined for normality and for the presence of outliers in study variables. The missForest package (88) was used to impute missing data using the random forest multiple imputation method. In comparison with other multiple imputation methods (e.g., MICE), this machine learning technique can accommodate non-linearities and interactions and does not need a specific regression model to be specified, which makes this approach more useful for imputing larger data sets where some participants have missing data (89). All variables had missing data of 5% or less except for maternal pSLE, which was missing for 22%. Linear regressions were conducted to test hypotheses using the imputed data set. All predictor variables and covariates were standardized before being entered into the models. The following analyses were conducted in two separate models, one for each outcome variable (EF and externalizing problems).

In Step 1, we estimated main effects by performing multiple linear regressions to examine the relation between both prenatal predictors (pSLE, pIPV) and each outcome variable without including covariates in the model. In Step 2, we added all covariates to the models in Step 1 to obtain our fully-adjusted models. In Step 3, we examined potential interactions with parenting quality by additionally incorporating the two interaction terms between each prenatal predictor and the parenting quality moderator (pSLE x parenting quality; pIPV x parenting quality) into both of the fully-adjusted models for our two outcome variables. Significant interaction terms were then probed to test for simple slopes at three different values of the moderator (+1 SD, mean, −1 SD) (90). Finally, we repeated the same procedures to examine potential interaction effects of child sex by prenatal predictors on both outcome variables by including interaction terms between each prenatal predictor and child biological sex.

RESULTS

Descriptive statistics of the primary study variables are presented in **Table 1**. Median education level was completion of high school; mean household-adjusted income was $18.4 k. Regarding pSLE, 28% of women reported experiencing no pSLE; 50% reported experiencing at least 1 type of pSLE; 32% reported experiencing at least 2; and 21% reported experiencing 3 or more. For pIPV, 28% of women reported experiencing no forms of pIPV; 66% reported experiencing at least 1 form; 18% reported experiencing at least 2; and 7% reported experiencing 3 or more forms of pIPV. Thirty four percent of women reported experiencing both pIPV and pSLE. Children's EF problems were strongly correlated with externalizing problems ($r = 0.7$, $p < 0.001$). Bivariate correlations are provided in **Table 2**. Of note, maternal pSLE and pIPV were weakly correlated ($r = 0.19$, $p < 0.001$), suggesting they captured largely unique domains of stress

TABLE 1 | Demographic information and model variables (N = 1,034).

Variable	Characteristics (range)	Mean (SD) or *n* (%)
Maternal variables		
Age (years)	Age at study enrollment	26.4 (5.6)
Education	Some elementary/high school	113 (10.9)
	Graduated high school/GED	493 (47.6)
	Graduated technical school	98 (9.5)
	Bachelor's degree	209 (20.2)
	Graduate/professional degree	121 (11.7)
Partner status	Married/living with partner	579 (56.0)
	Single/divorced/not married	454 (43.9)
Adjusted household income	Adjusted for household size	$18.4 k ($17.0 k)
Race	Black	661 (63.9)
	White	308 (29.8)
	Other	65 (6.3)
Postnatal depression	Edinburgh Postnatal Depression Score (0–22)	4.4 (3.6)
Concurrent depression	Center for Epidemiologic Studies Depression (0–49)	8.5 (7.1)
Intimate partner violence	Conflict Tactics Scale (0–4)	0.9 (0.88)
Stressful life events	PRAMS SLE (0–14)	1.7 (1.9)
Parenting quality	NCAST Total Caregiver scale (19–50)	39.7 (5.3)
Child variables		
Age (years)	Age at 4–6 year clinic visit	4.3 (0.4)
Sex	Female	519 (50.2)
	Male	515 (49.8)
Externalizing problems	CBCL T-score (28–88)	44.8[a] (10.3)
Executive functioning problems	BRIEF-P T-score (33–104)	47.9[b] (11.3)

[a] *8% of children had T-scores that fell within or above the borderline range on the CBCL.*
[b] *9% of children had T-scores that fell in the clinically significant range on the BRIEF-P.*

exposure. Also of note, observed parenting quality was neither correlated with pSLE ($r = -0.03$, $p = 0.49$) nor pIPV ($r = -0.05$, $p = 0.16$), suggesting the consideration of parenting as a potential moderator, rather than a mediator, was appropriate.

Tables 3, **4** present results from the regression analyses, examining both main and moderated effects, for child EF problems and externalizing problems, respectively. Results for the fully-adjusted model for child EF problems (**Table 3**) showed maternal pSLE (b = 1.13, $p = 0.004$) and pIPV (b = 1.02, $p = 0.004$) independently predicted child EF problems, such that higher levels of pSLE and pIPV were uniquely, positively associated with levels of child EF problems. There was a marginally significant main effect of observed parenting quality on child EF problems, wherein higher levels of parenting quality were associated with lower levels of EF problems in childhood (b = −0.81, $p = 0.044$). Regression results for the fully-adjusted model for child externalizing problems (**Table 4**) similarly showed women's pSLE (b = 1.30, $p < 0.001$) and pIPV (b = 0.94, $p = 0.003$) independently predicted child externalizing problems, such that higher levels of pSLE and pIPV were uniquely, positively associated with levels of child externalizing problems. In addition, higher levels of parenting quality were significantly associated with fewer child externalizing problems (b = −1.11, $p = 0.003$). Of note, women's postpartum depression and concurrent depression independently predicted both child outcomes.

Next, we examined whether parenting quality moderated the aforementioned associations. Two significant interactions emerged, qualifying the main effects found. Regarding child EF problems (**Table 3**, Step 3), there was a significant pSLE x parenting interaction (b = −0.98, $p = 0.010$). **Figure 1** provides illustration of the continuous interaction term plotted, with tests of the simple slopes, at the mean and +/− 1 SD, showing a significant positive association between women's pSLE and children's EF problems at average (b = 1.00, SE = 0.40, $p = 0.012$) and at low levels (−1 SD; b = 1.99, SE = 0.53, $p < 0.001$) of observed parenting quality. However, at higher levels of observed parenting quality (+1 SD), there was a buffering effect such that pSLE was not significantly associated with child EF problems (b = 0.01, SE = 0.57, $p = 0.985$). Parenting quality did not significantly interact with pIPV to predict child EF problems (b = 0.51, $p = 0.146$).

A similar pattern was found for child externalizing problems (**Table 4**, Step 3), revealing a significant pSLE × parenting interaction (b = −0.75, $p = 0.034$). **Figure 2** provides illustration of the continuous interaction term plotted, with tests of the simple slopes, showing a significant positive association between women's pSLE and children's externalizing problems at average (b = 1.22, SE = 0.36, $p < 0.001$) and low levels (−1 SD; b = 1.96, SE = 0.49, $p < 0.001$) of parenting quality. At higher levels of observed parenting quality, there was again a buffering effect, such that pSLE was not significantly associated with child externalizing problems (b = 0.46, SE = 0.52, $p = 0.373$). There was no significant interaction between pIPV and parenting quality for child externalizing problems (b = 0.53, $p = 0.100$). Finally, we examined associations between child sex and both measures of women's pregnancy stress exposure, predicting both outcomes. Although girls displayed lower problems in adjusted models for both outcomes, there was no evidence for moderation by child sex for either stress exposure (results not shown).

DISCUSSION

Understanding the complex biopsychosocial phenomenon of relations between women's exposure to stressors in pregnancy and child psychopathology is important for the prevention of mental illness and the promotion of women and children's wellbeing. The aim of the present study was to examine the intergenerational associations between women's stress exposures during pregnancy and young childhood executive functioning and externalizing problems in a large, sociodemographically diverse sample. Crucially, we also examined women's observed parenting quality as a potential postnatal protective factor that might buffer children from the risks of later psychopathology. To our knowledge, this is one of the largest U.S. pregnancy cohorts examining intergenerational associations of maternal

TABLE 2 | Correlations between study variables.

	1	2	3	4	5	6	7	8	9	10	11
1. Maternal age	1										
2. Child age	−0.14***	1									
3. Adjusted annual income	0.49***	−0.09*	1								
4. Maternal full-scale IQ	0.42***	−0.08*	0.60***	1							
5. Postnatal depression	−0.01	0.04	−0.08*	−0.03	1						
6. Concurrent depression	−0.10**	0.02	−0.21***	−0.16***	0.39***	1					
7. Prenatal SLE	−0.15***	−0.03	−0.23***	−0.04	0.19***	0.22***	1				
8. Prenatal IPV	−0.08*	0.05	−0.14***	−0.07	0.17***	0.10**	0.19***	1			
9. Parenting quality	0.35***	−0.11**	0.43***	0.52***	0.04	−0.11**	−0.03	−0.05	1		
10. EF problems	0.01	0.04	−0.04	−0.01	0.26***	0.30***	0.13**	0.14***	−0.07	1	
11. Externalizing problems	0.00	−0.05	−0.04	−0.01	0.26***	0.29***	0.19***	0.14***	−0.08*	0.70***	1
Sample size per variable[a]	1,034	1,034	1,030	1,022	1,004	1,024	799	974	977	1,024	1,030

EF, Executive Functioning; IPV, Intimate partner violence; SLE, Stressful life events.
[a]*Analytic dataset N = 1,034.*
*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

TABLE 3 | Regression models of maternal prenatal stress and child executive functioning.

Model	Predictors	*B*	95% CI	SE	*P*
Step 1:	Prenatal predictors				
Predictors only[a]	Prenatal SLE	1.78	[1.01, 2.56]	0.40	< 0.001***
	Prenatal IPV	1.43	[0.72, 2.14]	0.35	< 0.001***
Step 2:	Covariates				
Full model[b]	Maternal age	0.71	[−0.12, 1.53]	0.42	0.093
	Adjusted household income	0.26	[−0.78, 1.31]	0.53	0.626
	Maternal race (Black)	4.96	[2.94, 6.97]	1.02	< 0.001***
	Maternal full-scale IQ	−0.45	[−1.50, 0.60]	0.54	0.404
	Postpartum depression	1.38	[0.66, 2.11]	0.37	< 0.001***
	Concurrent depression	2.69	[1.97, 3.40]	0.36	< 0.001***
	Parenting quality	−0.83	[−1.52, 0.06]	0.40	0.044*
	Child age	0.54	[−0.11, 1.19]	0.33	0.106
	Child sex (female)	2.45	[1.17, 3.73]	0.65	< 0.001***
	Prenatal predictors				
	Prenatal SLE	1.13	[0.35, 1.91]	0.40	0.004**
	Prenatal IPV	1.02	[0.33, 1.70]	0.35	0.004**
Step 3:	Moderators				
Interaction effects	SLE × Parenting quality	−0.98	[−1.74, −0.23]	0.38	0.010*
	IPV × Parenting quality	0.51	[−0.18, 1.19]	0.35	0.146

[a]*Predictors-only model accounted for 4% of variance in child EF problems.*
[b]*Fully-adjusted model accounted for 18% of variance in child EF problems.*
*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

prenatal stress exposures and child psychopathology that includes a large percentage of Black women as well as a broad representation of families with lower household income—a sample with particular generalizability to Southern metropolitan U.S. populations. We found that women's exposure to intimate partner violence and stressful life events during pregnancy independently predicted higher levels of EF and externalizing problems in their 4–6-year-old children, even after controlling for a variety of pre- and post-natal factors. Notably, these two prenatal stress exposures were very weakly correlated, suggesting that different domains of women's risk exposure during pregnancy have unique relevance to child development and psychopathology. In addition, we found that higher levels of sensitivity, supportiveness, and scaffolding provided by women to their children during observed parent-child interaction tasks served as a postnatal protective factor, buffering their children

TABLE 4 | Regression models of maternal prenatal stress and child externalizing problems.

Model	Predictors	*B*	CI 95	SE	*p*
Step 1:	Prenatal predictors				
Predictors only[a]	Prenatal SLE	1.94	[1.24, 2.64]	0.36	< 0.001***
	Prenatal IPV	1.19	[0.54, 1.83]	0.33	< 0.001***
Step 2:	Covariates				
Full model[b]	Maternal age	0.37	[−0.39, 1.13]	0.39	0.338
	Adjusted household income	0.30	[−0.66, 1.26]	0.49	0.536
	Maternal race (Black)	3.16	[1.31, 5.01]	0.94	< 0.001***
	Maternal full-scale IQ	0.32	[−0.65, 1.28]	0.49	0.524
	Postpartum depression	1.12	[0.46, 1.79]	0.34	< 0.001***
	Concurrent depression	2.26	[1.60, 2.92]	0.34	< 0.001***
	Parenting quality	−1.11	[−1.84, −0.38]	0.37	0.003**
	Child age	−0.72	[−1.32, −0.12]	0.31	0.019*
	Child sex (female)	1.19	[0.02, 2.37]	0.60	0.047*
	Prenatal predictors				
	Prenatal SLE	1.30	[0.58, 2.02]	0.36	< 0.001***
	Prenatal IPV	0.94	[0.31, 1.57]	0.32	0.003**
Step 3:	Moderators				
Interaction effects	SLE × Parenting quality	−0.75	[−1.45, −0.06]	0.35	0.034*
	IPV × Parenting quality	0.53	[−0.10, 1.16]	0.32	0.100

[a]*Predictors-only model accounted for 5% of variance in child externalizing problems.*
[b]*Fully-adjusted model accounted for 16% of variance in child externalizing problems.*
*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

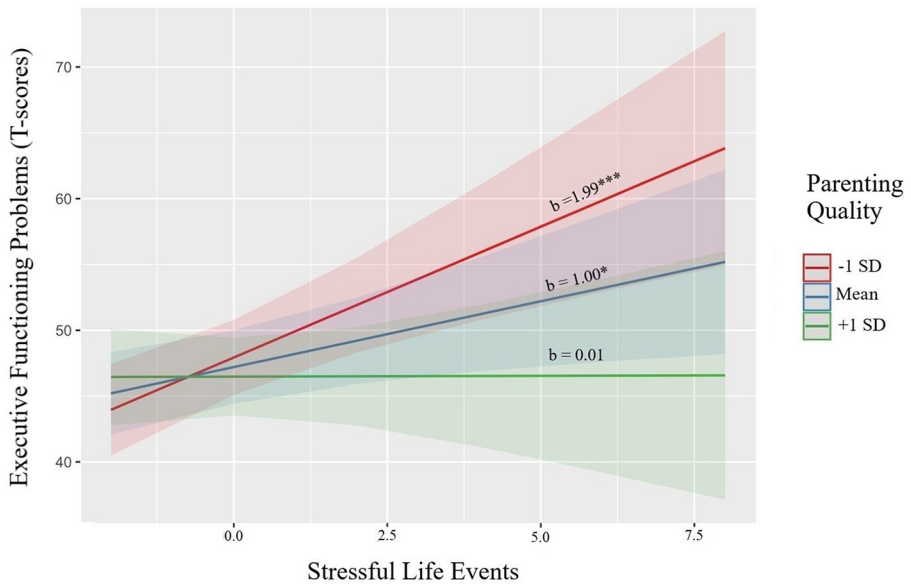

FIGURE 1 | Parenting quality moderates the association between maternal prenatal stressful life events and child executive functioning problems.

from the association between pSLE and both child outcomes—providing insights into heterogeneity of main effects and potential targets for intervention.

Our findings for the associations between women's prenatal stressors and child externalizing problems are largely consistent with extant literature (17, 28), yet they expand the evidence base to EF outcomes within a large, sociodemographically diverse sample. Although the operationalization of child EF across the few existing studies has varied (37, 38), our findings—which utilized a behaviorally-based measure of EF—are generally consistent with the few prenatal programming studies that have used lab-based measures of EF, indicating

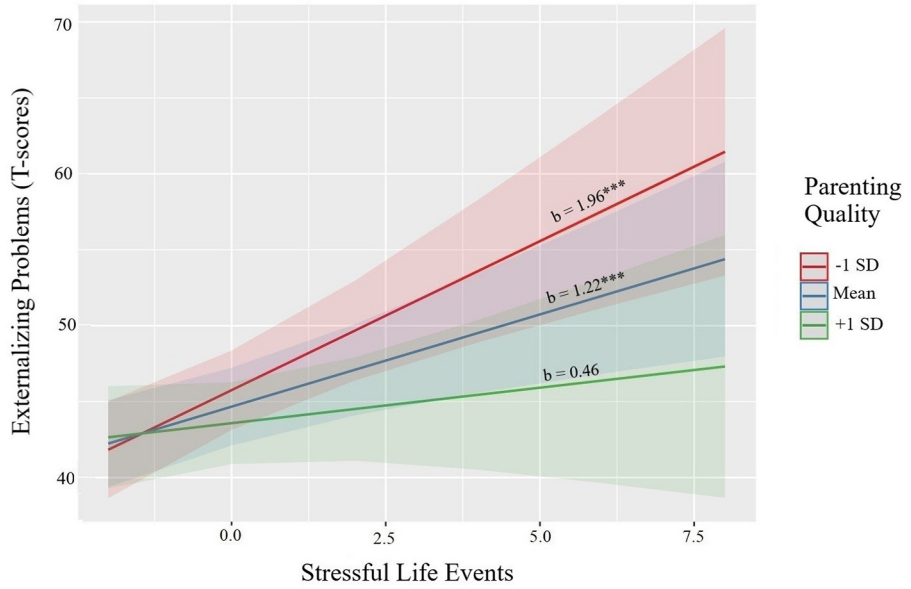

FIGURE 2 | Parenting quality moderates the association between maternal prenatal stressful life events and child externalizing problems.

that women who experienced more forms of stress during pregnancy reported that their children demonstrated poorer overall inhibition, flexibility, planning and/or working memory in everyday settings. Given the strong association between child EF and externalizing problems, the fact that we see a similar pattern in prediction by both prenatal stressors is not necessarily surprising and further suggests shared etiology or developmental mechanisms (91). In addition, our finding regarding the negative associations between maternal parenting quality and child EF and externalizing problems is also consistent with a large body of extant research on parenting and child behaviors. Women who have the social/emotional/economic resources, structural supports, and ability to provide more scaffolding, warmth, and nurturing to their children are more likely to help mitigate and reduce potential externalizing behavior problems. Interventions that support a caregiver's ability to harness resources for supportive parenting may thus play a crucial role in mitigating the impact of early adversity in children most at risk. Importantly, although parenting behaviors can certainly be shaped by prior experiences of stress and adversity, we found that neither stress exposure was associated with observer-rated postnatal parenting behaviors in the present study, suggesting that these parenting behaviors were not influenced by women's experiences of stressful life events or intimate partner violence during pregnancy.

A robust literature documents the effects of the postnatal environment on child mental health, including stressors within the home, parental psychopathology, and parenting behaviors (70, 92–96). Accordingly, the present study accounted for many of these in our models—including several socioeconomic, psychosocial, and environmental factors—though this was not an exhaustive list. Although a growing body of work also documents the intergenerational associations between the prenatal environment and offspring psychopathology, such prenatal stressors likely operate through multiple pre- and postnatal pathways (both psychobiological and psychosocial). Findings presented herein should be interpreted within this context. Indeed, our findings suggest that these main effects of prenatal stressors should be considered within the context of the postnatal caregiving environment. Our study makes a particularly novel contribution in demonstrating that multi-year assessments of observer-rated maternal parenting behaviors moderated the association between women's pSLE and both child EF and externalizing problems. Specifically, for women who were able to provide higher levels of scaffolding, support, and encouragement to their children across several parent-child interaction tasks spanning two assessment time points, there was no increased risk of later child psychopathology associated with higher levels pSLE. This is contrasted with women who might not have had the necessary resources, structural supports, and ability to provide the same levels of scaffolding and encouragement to their children, wherein there was an increased risk of both later child EF and externalizing problems associated with higher levels of pSLE. These findings also suggest that many individuals are capable of providing high quality parenting despite prior exposure to adversity and violence (14, 66, 97). Interestingly, this moderating pattern was not found for prenatal intimate partner violence and either measure of child functioning. Methodology may be a possible explanation, given the difference in the range of possible values for each measure of maternal prenatal stress. Whereas, the pSLE measure had a range of 0–14, the measure for pIPV only had a range of 0–4, which might have reduced the ability to

detect variations in scores between study participants based on differences in parenting quality. It is also possible that women's violence exposure, specifically, has less heterogeneous effects on offspring.

The present study highlights the importance of supporting and fostering women's capacity to optimize the caregiver-child relationship—often ignored in the prenatal programming literature—which served as a potential resilience-promoting factor in the prediction of child mental health problems. Women's capacity to provide sensitive, supportive parenting is not simply the product of—or responsibility of—a single caregiver, but rather a reflection of the larger community and societal context within which that parenting occurs (98). Many social determinants that affect maternal or child health and wellbeing also affect children's rearing environments, and therefore the resources that parents and caregivers have available to them within a given environment. Viewed in that framework, it is not surprising that community-based parenting programs that promote caregiver self-care, connection to resources, and knowledge of child attachment have proven efficacious in communities affected by violence (99, 100). Beyond community-based interventions that focus on providing more supports to parents and caregivers in higher-risk settings, national policies that increase resources for pregnant women and other caregivers—such as expansion of perinatal Medicaid coverage, increased parental leave, and perinatal cash transfer programs—can uplift our capacity to break intergenerational cycles of risk for child psychopathology and poor health (101–103). A growing body of literature highlights the importance and benefits of offering universal access to evidence-based parenting support and training programs—especially early in child development (104). In addition to improving child functioning, such intervention programs have also been shown to improve women's mental health (105). Indeed, multiple studies have shown that interventions focused on either parents or the parent-child relationship among families exposed to IPV, for example, have positive effects for both mothers and children (106, 107). Further, providing such universal access at a population level would not only allow all families to benefit from such programs but would also help in destigmatizing them.

Finally, regarding our test of moderation by child sex, we did not find that child sex significantly moderated the association between women's prenatal stressors and child psychopathology—although our sample was likely sufficiently powered to do so. This is not necessarily surprising, given the mixed findings regarding sex differences in previous examinations (17, 40). Indeed, although there was a main effect of child sex, wherein, on average, girls displayed marginally lower levels of EF problems, and significantly lower levels of externalizing problems, compared to boys—consistent with prior literature—these associations were not moderated by maternal stressful life events or intimate partner violence during pregnancy.

Also of note, fully one half of our sample experienced at least one type of pSLE (with almost one-third experiencing at least two), two-thirds reported experiencing at least one form of pIPV, and fully one third experienced at least one form of both pSLE and pIPV. These rates are in the higher range of estimates for pIPV prevalence, and may reflect unmet need for violence prevention and perinatal adversity support for women in this population (6, 8). Social inequity in the greater Memphis/Shelby County, Tennessee area—from which the present study cohort was recruited—has been associated with poor child health and educational outcomes, yet our findings also indicate the need for attention to upstream perinatal prevention and intervention efforts for families in this and similar populations (108–110). Further, we found that the associations between both pIPV and pSLE and child outcomes were independent of each other and, considered cumulatively, may have a greater impact on child mental health. Indeed, the stress exposures amounted to roughly 20–30% of the overall variance in psychopathology risk accounted for by each model.

The present study has a number of strengths: the use of a large, sociodemographically diverse sample including understudied Black urban Southern women, broad socioeconomic distribution across the sample, multiple indicators of prenatal stress exposure, and observer-rated parenting quality. However, there are several limitations. First, child outcome measures were reported by mothers. Recent work suggests limited bias from maternal report of child psychopathology (111), though we included important maternal covariates in our models to minimize potential reporter biases. Future studies would benefit from utilizing other informants and objective measures of child behavior. Second, although the inclusion of multiple domains of stressors, using two fairly distinct measures of exposures, is a strength—and adverse exposure counts are increasingly found to be strong predictors of health (112)—our measures did not consider the frequency or severity of the events, or the perceived experiences of distress from these stress exposures—all of which can contribute to the intergenerational effects of toxic stress on child functioning. Third, women retrospectively reported on pSLE when their children were ∼8 years old. Although this approach is commonly used and recent evidence further supports validity of its use (especially for more significant and memorable life events) (75, 76, 113), there is still a potential for event recall bias. In addition, women's pIPV was assessed in the third trimester of pregnancy, wherein women reported their experiences over the past year, leaving the possibility that some pIPV was experienced in the few months prior to pregnancy. Finally, other sources of stress and adversity—both during pregnancy and postnatally—are relevant to offspring psychopathology (such as maternal experiences of daily stressors, racism, discrimination, as well as offspring exposure to traumatic events during childhood) but were not assessed with the present sample. Future intergenerational research would benefit from their inclusion.

Our findings add support to a growing body of research indicating the importance of *preventing* women's experiences of traumatic and stressful events during pregnancy—not just to protect women, but also for the potential intergenerational benefits with respect to offspring mental health. Moreover, our novel findings show that prenatal risks for child psychopathology are not uniform across families and may be buffered by strengthening and supporting the caregiving environment in

the home. Interventions that provide additional support to families—both during the prenatal and postnatal period—and that include strategies and resources to strengthen caregiver-child relationships can play a key role in promoting caregiver and child resilience—even in the context of adversity (114). Indeed, caregiver wellbeing and behavior is key to promoting the development of child self-regulation skills, and could help prevent the development of later psychopathology (32, 54, 63). Further, given the transactional and cascading nature of the parent-child relationship—especially with regard to child externalizing psychopathology—ameliorating or preventing child mental health problems can also have downstream benefits of improving or preventing mental health problems for women who are mothers (115–117). Future research and intervention work, as well as health policy efforts, should focus on providing standard screening and universal preventative care to women during pregnancy (118) as a means of preemptively eliminating or reducing stressors for pregnant women and expecting families. Finally, additional research is certainly needed to identify more modifiable, postnatal resilience-promoting factors (19, 119, 120) in order to promote wellbeing across two generations and ameliorate risks for child psychopathology.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary materials, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

This study was reviewed and approved by the University of Tennessee Health Science Center Institutional Review Board. Written informed consent to participate in this study was provided by the participants and/or their legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

NB, KL, CK, SS, and FT played a role in funding acquisition for the project supporting this manuscript. FT, JG, NB, and KL contributed to conception and design of the cohort study from which the data were drawn. FT was primarily responsible for project administration and supervision of data acquisition and curation, with support for data curation from NB and KL. SA and NB devised the manuscript study question. SA and ES designed the analytic approach for the study, with oversight by NB and wrote the first draft of the manuscript. ES performed the statistical analyses. LR and NB wrote sections of the manuscript. NB supervised the writing. All authors contributed to the interpretation of results, manuscript revision, and read and approved the submitted version.

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BRIEF RESEARCH REPORT
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Social Construction and Evolutionary Perspectives on Gender Differences in Post-traumatic Distress: The Case of Status Loss Events

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Women report greater post-traumatic distress (PTD) than men following physically threatening events. However, gender differences in PTD following social stressors such as status losses are understudied. Whereas the social construction account points to a general sensitivity in women following any type of stressor, the evolutionary account suggests enhanced sensitivity to status losses in men, especially following inter-males aggressions. These propositions were examined in two studies (Study 1, $N = 211$; Study 2, $N = 436$). Participants were asked to recall a status loss and to fill out measures assessing PTD and depression severity. In line with the evolutionary account, men, as compared to women, displayed enhanced PTD following status loss. Status losses conducted by men against men were associated with greater PTD than were instances involving other target-aggressor pairings. Finally, age was negatively associated with PTD in men but not in women. The examination of evolutionary challenges modifies the standard view linking the female gender to enhanced sensitivity to trauma. Thus, the pattern of enhanced sensitivity to stressful events appears to be affected by gender- and development-specific adaptive challenges.

Keywords: trauma, gender, social-rank, evolutionary psychology, humiliation, status, sex, PTSD

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INTRODUCTION

Studies have shown small to moderate effect sizes of gender on the prevalence of post-traumatic distress (PTD) following exposure to trauma [For review: (1)]. Women are diagnosed with post-traumatic stress disorder approximately twice as often as men (2), and report higher levels of both re-experiencing, avoidance, and arousal symptoms (3). Furthermore, consistent meta-analysis results documented enhanced PTD in women compared to men following a wide variety of events including assaults, accidents, disasters, combat of war and injury or death witnessing, whereases enhanced PTD in men compared to women was not found following any type of stressor (4).

However, the scope of these gender differences is debated. On the one hand, the social construction account points to a *general* sensitivity in women due to lower (perceived and actual) social status and a propensity for more internalized coping styles (5). The evolutionary account, in contrast, suggests that the traumatic impact of an event is associated with its *interruption* of sociobiological goals, and thus, is likely to differ between the genders (6, 7). Specifically, evolutionary theorists argue that whereas women tend to be more susceptible to physical threats,

men are more sensitive to status losses (8–10). Notably, most studies examining gender differences and PTD focused on physically threatening events [falling inside Criterion A definition in the DSM-V, (11, 12)]. Clearly, such data do not differentiate between the predictions of the social construction and the evolutionary accounts. Examining gender differences in response to status loss events (SLEs; e.g., humiliation, demotion) which are known to provoke PTD (13), is central to differentiating between the two theories. This is the main goal of the present study.

Social Construction Theory

According to social construction theorists, women's propensity to develop PTD is explained by their perceived lower status, feelings of powerlessness, and reinforced shame responses following traumatic events (5). According to this reasoning, PTD is expected to be more severe in women following *any type* of traumatic event (including SLE). Indeed, low-status individuals report higher distress following SLEs (14), and feelings of powerlessness or increased activation of shame responses contribute to reported distress following such events (15–17). Notably, if women's enhanced PTD originates from status deficiency as suggested by social constructionists, that tendency is expected to be present, and even emphasized, in events that compromise social status.

Furthermore, the social construction account suggests that, due to status gender inequality, women tend to encounter more SLEs instigated by men (18, 19). Importantly, according to this account, because traditional male gender roles emphasize dominance and power, men are more prone to challenge the status of women, often as an inter-gender aggressive means to maintain low status in women and enhance men's own social standing (5, 18, 19). Notably, women experience more shame and display more submissive behaviors following SLEs that are committed by men (20, 21). Thus, according to the social construction theory, SLEs conducted by men against women are suggested to be more traumatic than other types of victim-aggressor gender combinations.

Finally, according to the social construction theory, gender-roles are predicted to become more salient with age due to continuous endorsements of social constructs (22). Because gender-roles predict response to trauma more than biological gender does, PTD severity in women is expected to *increase* with age (23). Moreover, the status differential between genders increases throughout adulthood (24, 25), again consistent with women's predicted vulnerability to SLEs. In summary, social construction theory is consistent with a *generalized* scope of women's vulnerability and predicts that such vulnerability echoes the women's endorsement of their traditional cultural gender-roles.

Evolutionary Theory

According to the evolutionary perspective, SLEs reduce access to resources and mating options for both genders (26, 27, 94, 96). However, status is more strongly linked to reproductive prospects and wellbeing among men, than among women (28–30). Importantly, status change in men is often determined by *single* events (such as SLE) whereas in women this change tends to be associated with continuous accumulation of events (31, 32). Moreover, SLEs were found to affect objective markers of social dominance (e.g., testosterone) to a greater extent in men than in women (33, 34). Taken together, evolutionary theories suggest that, as compared to men, men are likely to be more susceptible to severe PTD following SLEs.

Evolutionary models further suggest that status is attained differently among men and women (35), and is more preferentially determined *via* intrasexual conflicts among men [(36); *p. 429*; (37, 98)]. Indeed, replicated findings indicate that social status in males, but not females, is strongly associated with the (perceived and actual) ability to physically win intrasexual conflicts [for reviews, see (37, 38)]. Notably, the exercise of status-related physical inter-males competition was partially replaced by knowledge- and skills-based competition among humans (39). Moreover, in primates, losing in intrasexual conflicts is the most common precursor to social demotion only among males (32, 40, 41). Accordingly, evolutionary accounts indicate that sensitivity for SLEs may be enhanced when both the aggressor and the victim of SLEs are men.

Finally, evolutionary theorists expect status concerns to mirror men's fertility (42). Consequently, status concerns are predicted to be weakened by age due to age-related reductions in reproductive goals (43, 44). Indeed, testosterone levels decline with age especially among men (45). Moreover, results based on large samples document that discrepancy in status motivations between men and women, which emerges in adolescence and persists throughout early adulthood, is diminished in late adulthood (46). Hence, the enhanced sensitivity in men in response to SLEs is suggested to be age dependent.

Taken together, evolutionary models highlight the differences between women and men's reproduction strategies which map onto discrepancies in psychological features such as anxiety, intra-gender aggression and status seeking (47, 48, 99). Those discrepancies are postulated to be amplified in early adulthood, when reproduction goals are most salient (49). Accordingly, the predictions of the evolutionary theory are consistent with a limited and specific scope of vulnerability in women which mirrors the activation of survival and reproductive goals.

CURRENT RESEARCH

The aim of the current research is to contrast the social construction and the evolutionary theories regarding gender differences in PTD following SLEs. Specifically, according to the social construction account, SLE would induce more severe PTD in women as compared to men, especially when the aggressor is a man. Furthermore, because the status differential between genders increases with age (24), women's sensitivity to SLE is expected to increase with age. In contrast, the evolutionary theory hypothesizes that SLEs would induce more severe PTD in men compared to women, especially following SLEs that were carried out by other men. Finally, the evolutionary account further suggests that the enhanced PTD among men following SLE would decrease with age.

Accordingly, we contrasted three pairs of hypotheses. First, we hypothesized that women would differ in their PTD levels compared to men following SLEs (the *men sensitivity vs. women sensitivity hypotheses*); Second, we hypothesized that the gender of the aggressor would affect PTD levels. Specifically, we predicted based on evolutionary theories that SLEs conducted by men against men would be most traumatic (the *inter-males aggression hypothesis)* or that in accordance with social construction theories, SLEs conducted by men against women would be the most distressing (the *males against females aggression hypothesis)*. Finally, we expected that gender and age would interact to predict PTD. In line with the evolutionary account, we predicted that SLEs would correlate with age especially among men (the *age-men link hypothesis)*, whereases based on the social construction theory we predicted that age would correlate especially with PTD among women (the *age-women link hypothesis)*.

Two studies were conducted to address these hypotheses. In both studies, we asked participants to recall an SLE and report on event related, as well as general, measures of distress. In the first study we invited participants who encountered a *significant* SLE (N = 212), whereas in the second study we included all individuals who were able to identify *any* specific SLE experience (N = 436). Notably, because detecting interaction in regression requires a sample size four times larger than that requires to detect the main regression effect (50), we examined the age-related PTD hypotheses by combining our two samples. Furthermore, depression was included as a covariate due to its robust association with distress following SLEs (51).

METHOD

Study 1

Participants

Based on the reported moderate effects in studies that investigated the relation between gender and PTD (4), a sample size of 210 was chosen as providing sufficient power for identifying the anticipated effects [G*Power 3.1; (52)]. A greater number of participants (N = 374) was recruited based on the exclusion rate in prior similar studies (53). Participants were recruited *via* the Amazon Mechanical Turk (MTurk) platform and received 5$ for their participation. All participants were from the United States with English as their native language. Exclusion criteria were: (a) filling out the survey from an I.P used by another participant/s [(53); n = 37]; (b) completing the autobiographical task in a non-conscientious manner (i.e., writing irrelevant text in the description of the memory as assessed by the two authors; n = 126). The final sample consisted of 211 participants (80 women). Participants' ages were between 22 and 69 (Mean = 36.7; SD = 10.2). The average number of education years was 15.1 (SD = 4.1).

Procedure

Participants were invited to take part in a 30-min survey geared to understand responses to severely stressful social events. After filling a consent form, participants were requested to recall an SLE. Following the recall, the participants were asked to indicate the age at which the recalled event occurred and the gender of their aggressor(s) (a man, a woman, or both). Next, they filled out PTD and depression severity questionnaires. Finally, they completed a series of demographic questions (e.g., age, education, gender) and were thanked and debriefed. All measures were administered in English.

Measures

Recollection of status loss was induced by asking participants to recall an event in which they "*felt belittled or that their dignity was compromised by others."* Next, they were asked to write a detailed description (at least 50 words) of the event. The instructions were based on the recall task used by Tangney et al. (54), which is designed to examine the characteristics of unpleasant social memories. Importantly, to modify the task for recollection of SLEs, we used Klein (55) definition for humiliation (an event in which one is being belittled or treated with indignity). In order to examine whether participants recalled SLEs, the two authors read all narrative independently. Narratives that were not social or did not include a threat to status were excluded (Inter-rater reliability = 0.96). Furthermore, to evaluate whether the recall task induced memories which are perceived as loss of status, we asked participants to rate their emotions during the event on five emotions scales (Humiliation, Shame, Sadness, Guilt, Anxiety). As expected, emotions which are associated with status loss such as humiliation and shame were significantly higher compared to the other negative emotions [$F(209,1) = 186.60$, $\eta_p^2 = 0.33$].

Post-traumatic distress (PTD) was assessed using the Post-traumatic Diagnostic Scale for DSM-V [PDS-5; (56)]. In PDS-5, the symptom items are rated on a scale of frequency and severity. Specifically, the scale includes items assessing intrusion (e.g., *Unwanted upsetting memories about the event*), avoidance (e.g., *Trying to avoid thoughts or feelings related to the even*t), negative cognitions and mood (e.g., *Having intense negative feelings like fear, horror, anger, guilt or shame*), and arousal (e.g., *Being jumpy or more easily startled*). Because the sample included participants who did not perceive the event as a trauma, the word "trauma" in the questionnaire was replaced with the word "event." The use of post-traumatic measures to assess PTD following socially stressful events was found to be reliable (13) and was constantly applied to assess PTD following SLEs (13, 57–59). The internal reliability of the scale was 0.85.

Depression severity was assessed using the Beck Depression Inventory [BDI–II; (60)], consisting of 20 items (the suicidality item was excluded due to the online nature of the study). The internal reliability of the questionnaire in our sample was 0.91.

Results

Descriptive statistics are presented in **Table 1**. As can be seen in the Table, there were no significant differences between men and women in age, trauma recency, or depression. To examine the *gender-sensitivity hypotheses,* we first conducted an ANCOVA with PTD as a dependent variable, gender as an independent variable, and depression and age as covariates. Consistent with the evolutionary account, we found a main effect for gender [$F(1,207) = 5.68$, $p = 0.01$, $\eta_p^2 = 0.03$], such as that the

TABLE 1 | Age, depression, and event related factors among men and women.

	Study 1		Study 2	
	Women (*N* = 80)	**Men (*N* = 131)**	**Women (*N* = 250)**	**Men (*N* = 187)**
Age	39.3 (11.4)	35.1 (9.1)	42 (13.1)	38.9 (12.5)
Trauma Recency	13.2 (12)	10.6 (9.4)	12.1 (14.3)	11.0 (10.9)
Depression Severity	17.4 (14.8)	19 (14.8)	10.6 (11.9)	11.4 (10.9)
Post-traumatic distress	24.4 (23.8)^{A}	32.6 (24.7)^{B}	12.7 (17)^{A}	18 (11.1)^{B}
% PTSD	***40*^{A}**	***57*^{B}**	***7*^{A}**	***18*^{B}**
% Men as aggressors	***47***	***77***	***42***	***58***

Mean; (Standard deviation); Means at the same row and study that do not share the same superscript differ at $p < 0.05$.

PTD-severity was greater for men than for women (**Table 1**). Next, we examined the percentage of participants whose PDS scores were above the cutoff for PTSD [PDS Score above 28; (56)]. Again, we found a significant main effect of gender [$X^2(1) = 5.91$, $p = 0.01$]. Notably, men were more likely than women to meet the PTSD-cutoff.

Next, we examined the *aggression* hypotheses comparing events in which both the aggressor and the victims were men ($N = 101$) and events in which the aggressor was a man and the victim was a woman ($N = 35$). In line with the evolutionary account, SLEs that were conducted by men against men were associated with a more severe PTD compared to SLEs in which the aggressors were men and the victim woman [$t(187) = 2.02$, $p = 0.008$, Cohen's $d = 0.58$; **Figure 1**]. We further conducted a contrast between events in which both the aggressor and the victim were men and the three other aggressor-victim configurations (i.e., woman-man, man-woman, and woman-woman). In line with the evolutionary account, the contrast was significant [$t(187) = 4.64$, $p < 0.001$, Cohen's $d = 0.67$].

To sum, both hypotheses of the evolutionary account were supported. However, because we invited participants that define their recalled event as impactful, it is possible that gender differences are explained by higher prevalence or accessibility of impactful SLEs among men, as compared to women. To address this possibility, in Study 2 we invited participants who could recall a specific SLE regardless of the level of its impact.

Study 2

Participants

Based on the small effect size found in Study 1, and because we anticipated an even smaller effect due to the inclusion of less intense social events, a sample size of 400 was chosen to provide sufficient power for identifying the anticipated effects [G*Power 3.1; (52)]. Based on the exclusion rate in similar prior studies, 455 participants were recruited *via* TurkPrime, which enables to recruit more conscientious Mturk workers (61). All participants were from the United States with English as their native language. Exclusion criteria were: (a) filling out the survey from an I.P used by another participant/s ($n = 9$); (b) completing the recall task in a non-conscientious manner (i.e., writing irrelevant text in the description of the memory as assessed by the two authors; $n = 10$). The final sample consisted of 436 participants (250 women). Participants' ages were between 18 and 79 (Mean = 40.6; SD = 13.0). The average number of education years was 15.5 (SD = 2.3).

Procedure

The procedure was identical to Study 1 with one exception; Participants were invited to take part in a 30-min survey that sought to enhance our understanding of *unpleasant* social memories. All reliabilities of the scales were satisfactory as in Study 1 (PDS-5 = 0.87; BDI = 0.92).

Results

As can be seen from **Table 1**, there were no significant differences between the genders in age, trauma recency, or depression. To test the first two hypotheses, we repeated the analyses from Study 1. As in Study 1, we found a main effect for gender in ANCOVA [$F(1,433) = 15.96$, $p < 0.001$,$\eta_p^2 = 0.04$] and in Chi-square test [$X^2(1) = 14.2$, $p < 0.001$] such as that the PTD score and estimated PTSD-diagnoses percentages were higher for men than for women (**Table 1**). We also found that inter-males SLEs were associated with more severe PTD compared to PTD following SLEs conducted by men against women [$t(332) = 2.38$, $p = 0.02$, Cohen's $D = 0.12$; **Figure 1**]. As in Study 1, we contrasted events in which both the aggressor and the victims were men and the three other configurations: we found that inter-males SLEs were higher than the three other victim-aggressor type events [$t(332) = 3.28$, $p < 0.001$, Cohen's $D = 0.12$].

Finally, combining the data from both samples, we examined *the gender-age link hypotheses.* A GLM was conducted with PTD as a dependent variable, and depression, age, gender (man = 1; woman = 2), and Gender × Age as predictors. A significant Gender × Age [$\beta = 0.45$, $b = 0.31$, $SE = 0.1$, $t(646) = 2.95$, $p < 0.01$; 95% CI(0.10,0.51)] interaction was found. Further analysis revealed that the age was associated with PTD severity in men but not in women ($\beta = -0.11$, $b = -0.22$, $SE = 0.07$, $p = 0.01$;$\beta = -0.02$, $b = 0.64$, $SE = 0.07$, $p > 0.5$, for men and women respectively; **Figure 2**).

DISCUSSION

The present study examined gender differences in PTD following status loss using two competing theoretical perspectives: social construction and evolution. Accordingly, three pairs of hypotheses were tested. First, we hypothesized that women would differ in their distress levels compared to men; Second, we hypothesized that the gender of the aggressor would affect distress levels. Finally, we expected that *gender and age would interact to predict* distress following status loss. Overall, our results are consistent with the evolutionary account. Specifically, women reported less severe PTD following status losses as compared to men, thus exhibiting greater resilience to these events. In addition, men reported severe PTD following events in which another man was a perpetrator. Finally, the PTD severity was unrelated to age in women, whereas in men this association was negative.

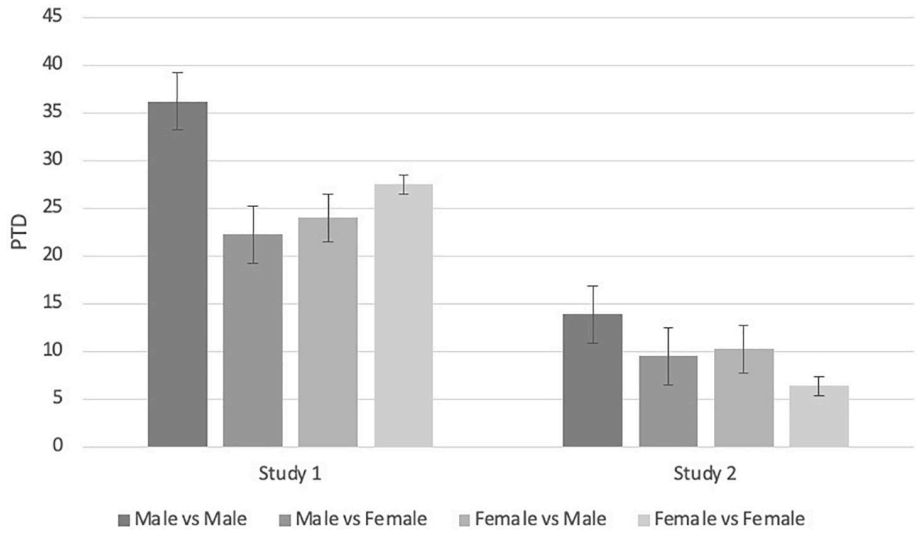

FIGURE 1 | Post-traumatic distress severity by gender of victim and aggressor. PTD, post-traumatic distress as measured by PDS-V.

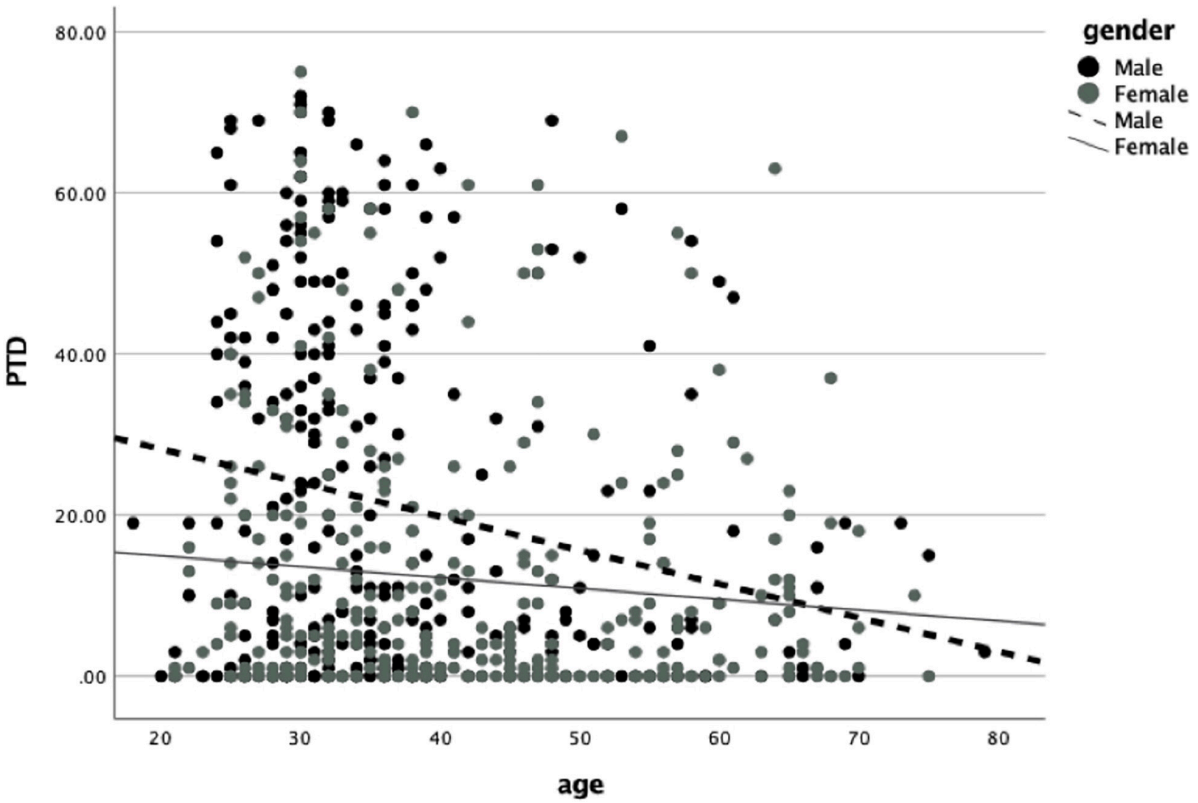

FIGURE 2 | Linear regression for PTD predicted by age in Women (gray solid line) and Men (black dashed line). PTD, post-traumatic distress as measured by PDS-V.

Our results joint those of van den Berg et al. (12) who reported gender differences in PTD following physical- but not social- stressors. Taking an evolutionary perspective, social and physical threats affect women's and men's reproductive success asymmetrically. Status is associated with low fertility and high offspring mortality among men but not women (62, 63), whereases women's, but not men's, fertility and attractiveness are highly linked with health (42). Differences in reproductive meanings of various stressors may partially account for gender discrepancy in PTD (6). For example, the cost of bodily harm

may be relatively greater for women because of their central role in ensuring infant survival (64–66). Furthermore, among women, offspring survival is linked with a strong dyadic support network (67, 95), indicating that inclusionary events may be more influential for women, as compared to men.

We also found that the gender of the aggressor was associated with PTD severity. The genderial context in which a stressful event took place may affect the levels of elicited distress by threatening specific salient goals. For example, due to females' high selectiveness, mating options for males are reduced and intra-sexual competition is enhanced (68) – leading to increased male sensitivity for intrasexual aggression (69). However, intra-sexual competition among females may take a different manifestation, such as covert verbal aggression (66, 70) or exclusion (71). Furthermore, the focus of the intrasexual competition may differ across genders. Whereas males tend more to compete on status, power, strength, and resources (47, 72), females' competition resolve more around attractiveness and promiscuity (73–76). Future studies could examine what types of intrasexual aggression are most distressing in women.

Finally, for men, but not for women, age was found to be associated with ameliorated distress following status losses. Those results are in-line with evolutionary accounts emphasizing the enhanced prevalence of intrasexual aggressions among young males ["The young male syndrome"; (77)]. Furthermore, our age-gender interaction mirrors other gender discrepancies which declined with age and are status related such as risk-taking (78). Notably, the decline in status loss distress among men may reflects a decline in competitiveness due to the decrease of women's reproductive value with age (79, 80). Importantly, the age-effect echoes gender-related differences in the prevalence of PTSD following physically threatening events which are reduced throughout adulthood (3, 81). It is possible that such changes in prevalence and severity mirror fluctuations in the levels of gonadal hormones associated with status motivations (34, 82). Specifically, reductions in testosterone levels in men and estradiol levels in women may contribute to the reduced gender discrepancy in the severity of distress following status losses (45).

THEORETICAL IMPLICATIONS

The current findings add to the growing body of research demonstrating pervasive and deleterious post-traumatic effects of status losses(91, 92, 93). These findings support the claim that reproduction threats may engender full-blown PTSD, given that reproductive goals are comparable to, and sometimes even outweigh, survival goals (83, 97). From an evolutionary perspective, any life event that interferes with the achievement of short-term biological goals such as status can qualify as a trauma due to its relevance to biological adaptation in the ancestral environment (6). A focus on physical threats as sole potential PTSD-provokers narrows essential goals pursuit to the physical arena and dismiss the evolutionary importance of our social environment. Importantly, our results challenge the *general* women sensitivity hypothesis. Following a variety of events, women report higher distress compared to men (84). Ignoring the evolutionary context may over-emphasize, and even over-pathologize, women's adaptive responses. As suggested by Troisi (6), social distress is induced following experiences which jeopardize sociobiological goals, as an adaptive response that facilitates the maintenance of the threaten goals. Thus, the distress is likely to be associated with the importance of sociobiological goals which is moderated by factors such as age and gender. Evolutionary theorists claim that to a certain level, gender differences in distress symptoms would remain, and that the gender gap in PTD could be narrowed by adopting a gender-sensitive nosology. Our results are in line with the latter position, indicating that gender by itself does not predict PTD and that its interaction with type of stressor need to be considered in PTSD classification.

LIMITATIONS

In closing, several limitations of the present research need to be noted. First, our study relies on self-report measures which may lead to biased report of PTD and depression severity (85). Second, gender differences in PTD may reflect some yet untapped distinctions in nature of the recalled events. Future studies may rely on response to pre-scripted status losses scenarios and examine gender differences in anticipated distress. Third, evolutionary approaches suggest that status can be reduced *via* loss of dominance (experiencing physical or psychological intimidation) as well as prestige [incompetence to display valued skills and abilities; (86)]. The current study did not distinguish between losses of status *via* prestige from those losses *via* dominance. Whereases loss of prestige is predicted to affect both genders, loss of dominance is predicted to affect mostly men (87). Forth, we decided to use the gender terminology (and not the sex terminology) due to the self-report nature of our study. Specifically, participants were asked to indicate their gender and not their assigned sex at birth, thus only their gender identity was examined. Future studies could investigate whether the reported discrepancies are present when biological markers of sex are examined. Finally, our data does not distinguish whether men's reactions to SLEs are less intense because it mirrors their fertility or because men tend to become more established in older age (and thus are less susceptible to status loss). Although prior studies indicate that both men and women tend to be more established with age, it is possible that the age-status enhancement affects more men than women (88).

CONCLUSION

The last decades are witnessing an evolutionary turn in clinical psychology (89, 90). Psychopathologies are examined through adaptiveness framework and therapy is formulated as a mean to acquire flexible ways to navigate, toward and between, evolutionary goals. Women and men differ in their evolutionary challenges, and consequently in the type of events most relevant to those challenges. To date, studies documenting greater vulnerability of women to traumatic events did not consider variability in evolutionary-relevant goals and challenges. The

evolutionary revolution is not complete without taking gender, age, and other survival and reproduction relevant variables into consideration. Consideration of these variables may help us appreciate the way the nature and timing of events individuals encounter on their unique journeys impact their development, identity, and wellbeing.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Bar-Ilan University, Psychology Department. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

RA: conceptualization, methodology, software, formal analysis, investigation, data curation, and writing – original draft. EG-S: conceptualization, supervision, writing – review and editing, and funding acquisition. Both authors contributed to the article and approved the submitted version.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2022.858304/full#supplementary-material

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Shorter Telomeres Related to Posttraumatic Stress Disorder Re-experiencing Symptoms in Sexually Assaulted Civilian Women

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Telomeres are short tandem repeats of "TTAGGG" that protect the chromosome ends from deterioration or fusion of chromosomes. Their repeat length shortens with cell division acting as a biomarker of cellular aging. Traumatic stress events during adulthood or childhood have been associated with posttraumatic stress disorder (PTSD) and short leukocyte telomere length (LTL). This study investigated whether LTL was associated with PTSD in a Brazilian sample of sexually assaulted civilian women at two time points: baseline and 1-year follow-up. At baseline, we assessed 64 women with PTSD following sexual assault (cases) and 60 women with no previous history of sexual trauma or mental disorders (healthy controls – HC). At follow-up visit, 13 persistent PTSD cases, 11 HCs, and 11 PTSD remitters patients were evaluated. PTSD diagnosis and severity were assessed using Mini International Neuropsychiatric Interview (Diagnostic and Statistical Manual of Mental Disorders III/IV criteria) and Clinician-Administered PTSD Scale for DSM-5 (CAPS-5), respectively. LTL was measured using multiplex real-time polymerase chain reaction (PCR). In the baseline analysis, we observed that LTL was associated with re-experiencing symptoms (B = −0.16; confidence interval (CI) 95% = −0.027—−0.005; Bonferroni-adjusted p-value = 0.02), but no association was observed between other PTSD symptoms and LTL. In the longitudinal analysis, telomere shortening was no longer observed in patients with PTSD and PTSD remitters. In conclusion, our findings indicate that shorter baseline LTL is associated with early stage of PTSD re-experiencing symptoms in recently sexually assaulted women.

Keywords: cellular aging, telomere–genetics, PTSD symptom clusters, sexual assault against woman, PTSD–posttraumatic stress disorder

INTRODUCTION

Telomeres are short tandem repetitions of the non-coding sequence TTAGGG (1) in the final portion of chromosomes and act as protective structures of the chromosome to maintain genomic stability (1, 2). Their repeat length shortens with cell division (3), possibly because of incomplete replication of the telomeric extremities, recombination, epigenetic regulation, cumulative exposure to oxidative stress, and stress hormones (2, 4). Telomere shortening over time establishes telomere length (TL) as a valuable marker of cellular aging (1). Trauma-induced stress has been associated with telomere shortening (4, 5) among individuals with posttraumatic stress disorder (PTSD) (6).

Posttraumatic stress disorder may occur after experiencing or witnessing a traumatic event and is characterized by four symptom clusters: re-experiencing, avoidance, hyperarousal, and negative alterations in cognitions and mood (7). The core symptoms of PTSD may lead to an overreaction of biological systems, including functions related to telomere length maintenance such as antioxidant defense and well-being (8). Moreover, this complex clinical condition is often associated with the onset of age-related diseases, e.g., cardiovascular, neurodegenerative, and inflammatory diseases, and early mortality (8, 9), suggesting that health decline in PTSD may be related to shorter TL. Previous findings suggest that repeated and prolonged activation of the stress response systems after trauma exposure may be one of the factors that contribute to cellular senescence in patients with PTSD (6, 10–17). Furthermore, trauma response and elevated psychological stress in PTSD may be implicated in telomere shortening through high inflammatory activity, increased sympathetic nervous system activation, and dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis (5, 18, 19).

Despite the increasing number of evidence of the association between telomere shortening and PTSD diagnosis (6, 10–14), there is still less research on the relationship between PTSD and TL in traumatized civilian women. Also, most studies on PTSD-related TL enrolled samples of chronic patients. Thus, we hypothesized that women who developed PTSD following exposure to a recent sexual assault (1 to 6 months before PTSD and TL assessment) would have shorter TL than healthy controls with no history of sexual trauma, through pathways and stress reactions related to trauma experience possibly related to cellular damage. We further hypothesized that severe PTSD symptoms related to brain hyperactivity, such as increased re-experiencing of recollections related to the traumatic event (i.e., flashbacks, nightmares, thoughts, and intrusive memories) and hyperarousal (i.e., hypervigilance, physiological reactivity, and sleep disturbances), expose the individual to psychological stress that may have a weathering effect on LTL.

Thereby, we aimed to investigate whether there are signs of accelerated telomere shortening in a Brazilian cohort of women who developed PTSD diagnosis after a recent sexual assault, using a cross-sectional and longitudinal design. We also explored the link between TL and PTSD symptom clusters. Further, increased comorbid alcohol use is commonly observed in patients with PTSD (20, 21), and research findings suggest that alcohol abuse is associated with shorter TL, possibly due to alterations in oxidative stress and inflammation (22–24); thus, we investigated the effects of alcohol use on TL in this cohort. We also examined the confounding effect of social deprivation and lower educational attainment, as the psychosocial stressful situations encountered by individuals with a low socioeconomic status have been reported in the literature to influence telomere decline (25–27). Then, to better understand the association between PTSD and TL, we considered the confounder effect related to alcohol use and social deprivation, and lower educational attainment.

MATERIALS AND METHODS

Study Population

In this longitudinal study, clinical assessments and blood samples were obtained at two time points: baseline and 1-year follow-up. At baseline, we recruited 63 women with a positive PTSD diagnosis who were the victims of sexual assault from 1 to 6 months before study inclusion (case group), and 60 women with no history of sexual trauma or mental disorders (healthy control – HC group). The longitudinal sample was comprised of 24 patients with PTSD and 11 HC participants who returned for follow-up assessments. Of the 24 patients with PTSD who completed the 1-year follow-up, 13 were classified as having persistent PTSD and 11 as being PTSD remitters based on the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5).

This study is the part of a larger study on neuroprogression in the early stages of PTSD that has been described in detail elsewhere (28). The Research Ethics Committee of Universidade Federal de São Paulo (UNIFESP) approved the study protocol, and all participants provided written informed consent.

Selection and Recruitment of Participants

Eligible women for the case and HC group were those aged 18–45 years. Women in the case group and HC that were undergoing psychiatric or psychological treatment were excluded. Other exclusion factors were having a sexually transmissible disease, unstable medical conditions, neurological disorders, schizophrenia, bipolar disorder, current use of corticosteroid medication, pregnancy, and menopausal symptoms. Participants included in the case group were recruited at Hospital Pérola Byington, a women's specialized health center that provides gynecological care for the victims of sexual assault in São Paulo, Brazil. Participants classified as HC were recruited in the community through social media and advertisement. Participation in the study was voluntary and no financial compensation was offered.

Clinical Assessments

Psychiatric disorder diagnoses were obtained using the Mini International Neuropsychiatric Interview (Diagnostic and Statistical Manual of Mental Disorders III/IV criteria) in all participants (29) in both visits: baseline and follow-up. PTSD diagnosis was assessed in patients in both visits by the CAPS-5.

CAPS-5 is the gold standard scale for assessing PTSD diagnostic status and symptom severity. It comprises 30 items that investigate the frequency and intensity of PTSD symptoms based on four symptom clusters related to PTSD diagnosis: avoidance, re-experiencing, negative alterations in cognitions and mood, and hyperarousal (30, 31). In addition, alcohol consumption over the past year was investigated at baseline for all participants using the Alcohol Use Disorders Identification Test (AUDIT) to identify early signs of hazardous drinking and dependence (32).

Sociodemographic Evaluation

We developed a sociodemographic inventory to collect baseline relevant sociodemographic characteristics of all participants, such as age, education, and income. Self-reported information regarding the participants' per-person income in Brazilian real (BRL) (1.00 BRL approximately 0.25 USD) was collected using the standard questionnaire, only at baseline assessments. Educational attainment was referred to in our study as the highest level of education the participant has completed at the time of the first assessment of this study. Based on the participants' years of study, educational attainment was categorized into three categories: less than 4 years of study (primary school incomplete - $N_{case} = 0$; $N_{HC} = 1$), 4 to 12 years of study (primary school and high school - $N_{case} = 34$; $N_{HC} = 4$), and over 12 years of study (Bachelor's degree or more - $N_{case} = 29$; $N_{HC} = 54$).

Telomere Measurement

Approximately 10 ml of blood in EDTA tubes (Becton Dickinson, United States) of each participant was collected for DNA extraction and telomere measurement in both visits: baseline and follow-up. According to the manufacturer's protocol, DNA was extracted using the Gentra Puregene Kit (Qiagen, United States). Leukocyte TL (LTL) was measured in triplicate wells following the protocol developed by Cawthon et al. (33) using multiplex real-time polymerase chain reaction (qPCR) to estimate the relative T/S ratio between the telomeric region copy number (T) and a single-copy gene (S, the albumin gene). T/S ratio is proportional to the mean LTL in the peripheral blood. Further, a positive control sample was used in all plates, as a quality control inter-assay, being that the inter-assay coefficient of variation for this study was 7.5%.

Statistical Analyses

Clinical and sociodemographic characteristics assessed in the first visit (baseline), i.e., age, per-person income, and alcohol consumption (AUDIT score), were compared between case-HC groups using independent sample *t*-tests, and Pearson's chi-square ($\chi 2$) was applied to assess the educational attainment category difference between groups. In addition, Spearman's correlations were used to assess the baseline correlations between per-person income and PTSD symptoms, and between per-person income and harmful alcohol use. These analyses identified the baseline association between clinical and sociodemographic measures that could potentially confound the relationship between PTSD and LTL.

The normality of LTL data was evaluated by Shapiro–Wilk (SW) tests using cross-sectional and longitudinal data. Primary analyses using linear regression models were conducted to investigate the effect of age on LTL measured at baseline and follow-up time. We used the unstandardized residual values of this regression as the predictor variable of relative LTL (called relative LTL adjusted by age) for all secondary analyses and Pearson's correlations to avoid bias related to age in the relative TL.

First, Pearson's correlations were applied to investigate the baseline effects of per-person income on relative LTL adjusted by age in the case and HC groups. Also, Pearson's correlations tested the baseline correlation between harmful alcohol use and relative LTL adjusted by age in all participants. Secondary analyses consist of a series of regressions models (logistic or linear regressions) to evaluate the effect of PTSD assessed at all time points, including PTSD diagnosis and PTSD symptoms on relative LTL adjusted by age, controlling these associations for potentially confounding baseline measures.

In the baseline analysis, logistic regression evaluated the association of relative LTL with trauma exposure (i.e., sexual assault) and evaluated whether shorter telomeres were associated with PTSD status compared to HC group, adjusting this model for alcohol dependence (AUDIT score), educational attainment, and per-person income. Linear regression adjusted by per-person income verified whether PTSD symptoms based on four clusters of CAPS-5 could predict the relative LTL using the baseline data. The partial regression plot was used for visualization of these linear model's results and reflects the scatter of partial correlation: the plot shows the residuals of relative LTL adjusted by age (i.e., unstandardized residuals of LTL) and per-person income vs. residuals of the predictor variable (i.e., PTSD status) on the dependent variable.

In the follow-up analysis, logistic and linear regressions were conducted to investigate, respectively, whether relative LTL was associated with PTSD status (persistent PTSD case, PTSD remitter, and HC) or whether PTSD symptoms could predict shorter relative LTL.

Finally, we performed *post hoc* power analysis using the function *pwr.f2.test* of R package *"pwr" - basic functions for power analysis* to calculate the power for regression models which are statistically significant.

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 21 and RStudio version 1.4.1103. Bonferroni correction was applied to adjust the significance threshold accounting for the number of regressions performed, and the level of significance was set at 0.05.

RESULTS

Participants' Characteristics

Table 1 summarizes the mean difference in baseline sociodemographic characteristics and alcohol use in 63 cases and 60 HCs. The groups significantly differed in age, education, and alcohol consumption. The case group was younger ($p = 0.003$), had lower per-person income ($p = 0.002$), and was more likely to have harmful alcohol consumption based on AUDIT scores ($p = 0.039$) than the HC group. Also, the case group had fewer years of education ($\chi 2 = 33.16$, df = 3, $p < 0.001$) showing that 54.68% of case participants had less than 12 years of

TABLE 1 | Descriptive participants' characteristics.

Variables	HC group	Case group	*t*-test	*p*-value
Age (mean, standard deviation–SD)	28.13 (7.365)	24.3 (6.616)	3.065	0.003
Per-person income (mean, SD)	2,259.56 (2,658.83)	1,001.62 (1,064.36)	3.223	0.002
AUDIT score (mean, SD)	2.62 (2.34)	3.89 (4.22)	−2.092	0.039

Age in years. Per-person income in BRL. AUDIT: Alcohol Use Disorders Identification Test.

study compared to 8.19% in the HC group. Sociodemographic characteristics were not evaluated in the follow-up visit.

Correlation tests using baseline measures showed that per-person income was significantly inversely correlated with CAPS-5 total score ($p = 0.003$) (**Figure 1A** and **Table 2**) and negative alterations in cognitions and mood ($p = 0.007$) (**Figure 1B** and **Table 2**), whereas avoidance, re-experiencing, and hyperarousal symptoms did not correlate with per-person income ($p > 0.05$; **Table 2**). Furthermore, we observed that per-person income was positively correlated with relative LTL adjusted by age ($p = 0.014$) (**Figure 1C** and **Table 2**). Likewise, alcohol consumption was positively correlated with relative LTL ($p = 0.045$) (**Figure 1D** and **Table 2**). We did not find a significant correlation between per-person income and alcohol consumption measured by AUDIT score (**Table 2**).

Leukocyte Telomere Length Findings

Baseline Leukocyte Telomere Length Measurements

The mean of baseline relative LTL measured in 63 patients with PTSD was 1.07 (standard deviation (SD) = 0.13), whereas the mean of LTL in 60 HC subjects was 1.09 (SD = 0.13). Furthermore, we did not find an association of shorter LTL with increasing age ($p = 0.331$). The Shapiro–Wilk test showed that LTL data were normally distributed ($SW_{baseline}$ $p = 0.70$).

We verified that baseline relative LTL adjusted by age was not associated with trauma exposure (i.e., sexual assault) ($p = 0.81$). Further, we observed that the discrimination between case and HC groups based on relative LTL adjusted by age was not significant ($p = 0.71$), even adjusting the model for confounder effects: alcohol dependence, educational attainment, and per-person income.

We observed that PTSD participants with higher PTSD re-experiencing symptoms scores at baseline had shorter relative LTL adjusted by age ($B = -0.016$, 95% confidence interval: −0.027 to −0.005; Bonferroni-adjusted $p = 0.02$, power = 0.79), suggesting that for each unit increase in PTSD re-experiencing scores, a 0.016 decrease in relative LTL is expected (**Figure 2**). Nonetheless, after Bonferroni correction for multiple comparisons, no significant difference in relative LTL was identified for the other PTSD symptom clusters and for CAPS_5 total score (CAPS-5 total → adjusted $p = 0.66$, avoidance → adjusted $p = 1.045$, negative alterations in cognitions and mood → adjusted $p = 1.2$, hyperarousal → adjusted $p = 3.24$).

Follow-Up Leukocyte Telomere Length Measurements

At 1-year follow-up, for the three groups evaluated (PTSD persistent ($n = 13$), PTSD remitter ($n = 11$), and HC ($n = 11$)), there was a trend for shorter relative LTL in the PTSD remitter group compared to other groups; however, this mean difference did not significantly different among the groups ($p > 0.05$; PTSD remitter: average = 1.09 (SD = 0.03), PTSD persistent: average = 1.13 (SD = 0.03), HC: average = 1.32 (SD = 0.03)). Also, we did not observe any association of shorter LTL with increasing age ($p = 0.531$).

In addition, the Shapiro–Wilk test showed that the distribution of follow-up LTL data was normally distributed ($SW_{follow-up} = 0.35$) among groups.

In the longitudinal study, telomere shortening was no longer observed in PTSD participants. Linear regression did not reveal any significant associations between PTSD cluster symptoms (CAPS-5 total, avoidance, re-experiencing, negative alterations in cognitions and mood, and hyperarousal) and relative LTL adjusted by age ($p > 0.05$).

DISCUSSION

This study used cross-sectional and longitudinal datasets to investigate whether PTSD psychopathology (diagnosis and symptoms) was associated with shorter LTL in a Brazilian population of sexually assaulted young women compared to the HC group, after accounting for the effects of socioeconomic deprivation and harmful alcohol use. These analyses revealed a small association between shorter baseline relative LTL and higher re-experiencing symptoms measured at baseline, which partially supports our hypothesis that PTSD symptoms may decrease LTL. However, the longitudinal association between re-experiencing symptoms measured at follow-up (persistent PTSD and PTSD remitter) could not explain the variation in LTL among the groups investigated at baseline. Further, no significant associations between trauma exposure (i.e., sexual assault), PTSD diagnosis, and three clusters of PTSD symptoms (avoidance, hyperarousal, and negative alterations in cognitions and mood) and LTL were detected both at baseline and at follow-up.

We found significantly lower per-person income and educational attainment in the case group compared to HC group, as described in the literature. Previous studies have shown that individuals with low income are more exposed to stressful and more violent environments, possibly increasing exposure to trauma and subsequent risk of developing PTSD (34–36). Also, low educational attainment has been considered a risk factor for PTSD (37, 38), suggesting that individuals with higher educational levels exposed to trauma have more coping mechanisms to deal with posttraumatic consequences, perhaps due to more access to information and treatment options (38, 39).

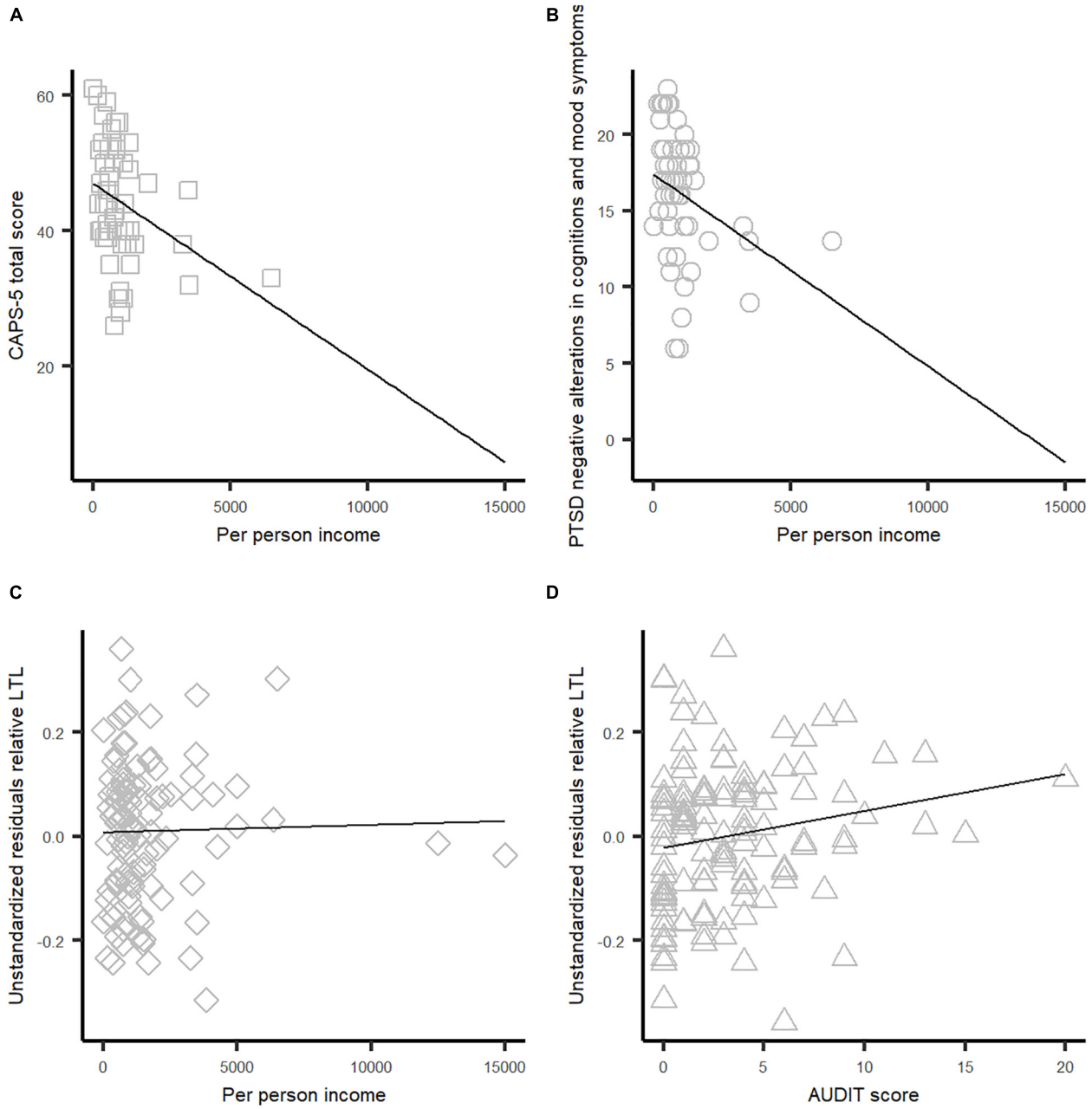

FIGURE 1 | Scatter plots of correlations tests among per-person income, PTSD symptoms, and relative LTL adjusted by age. **(A)** Correlation between CAPS-5 total score and per-person income. **(B)** Correlation between negative alterations in cognitions and mood score and per-person income. **(C)** Correlation between relative LTL and per-person income. **(D)** Correlation between relative LTL and AUDIT score.

We observed that participants with PTSD were more likely to present harmful alcohol use. Research findings report that alcohol use may function as a maladaptive coping behavior to mitigate PTSD symptoms (40, 41). Conversely, it may hamper PTSD recovery and indicate unfavorable psychopathological outcomes (42, 43). Further, the effects of increased alcohol drinking were previously associated with shorter TL (20–23) in patients with PTSD, corroborating our results. Our findings suggest that the combination of posttraumatic stress, socioeconomic deprivation, and harmful alcohol use may potentially lead to telomere erosion *via* alterations in the HPA axis responsiveness.

Telomere length is a complex phenotype related to genetic and environmental factors that may act as an important marker of stress and PTSD (19, 44). Telomere shortening observed in male war veterans (6, 10, 15) and women exposed to severely stressful events (16), including rape (17), has been associated with PTSD diagnosis. However, the results from published studies are

TABLE 2 | Correlation results of PTSD symptom clusters with per-person income, relative LTL adjusted by age and per-person income or alcohol consumption, and per-person income or alcohol consumption.

Correlations tests	Correlation coefficient	*p*-value
Per-person income x CAPS-5 total	Spearman rho = −0.406	**0.003**
Per-person income x Avoidance symptoms	Spearman rho = −0.234	0.092
Per-person income x Re-experiencing symptoms	Spearman rho = −0.187	0.180
Per-person income x Negative alterations in cognitions and mood symptoms	Spearman rho = −0.365	**0.007**
Per-person income x Hyperarousal symptoms	Spearman rho = −0.194	0.164
Per-person income x AUDIT score (harmful alcohol use)	Spearman rho = 0.010	0.944
Per-person income x Relative LTL adjusted by age (case group)	Pearson correlation = 0.338	**0.014**
Per-person income x Relative LTL adjusted by age (HC group)	Pearson correlation = −0.094	0.502
AUDIT score (harmful alcohol use) x Relative LTL adjusted by age	Pearson correlation = 0.182	**0.045**

Bold values represent the significant p-values.

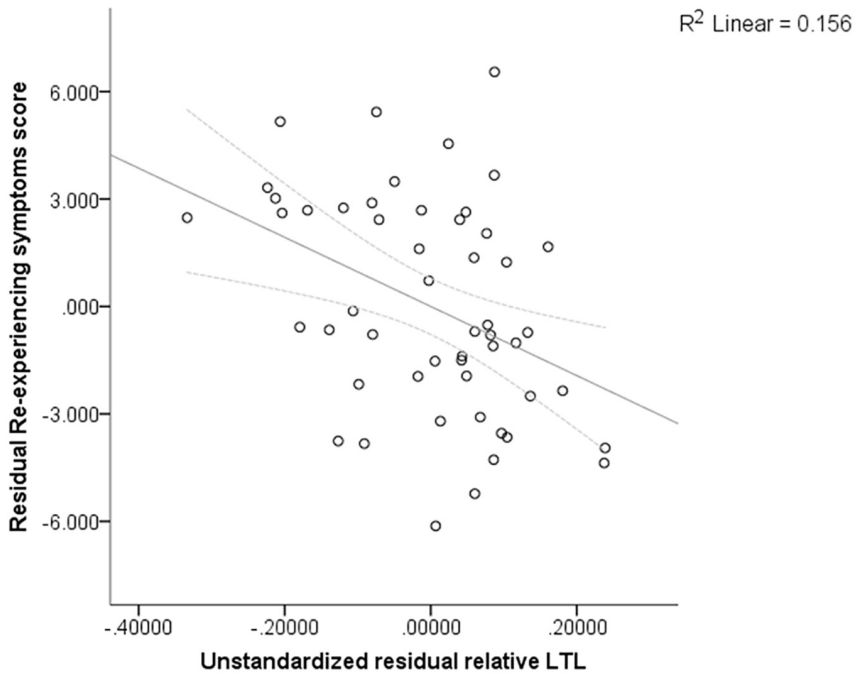

FIGURE 2 | Partial regression plot for the linear regression adjusted by per-person income reflecting the correlation coefficient between PTSD re-experiencing symptoms and relative LTL adjusted by age.

mixed. Contrary to previous research (17), our study found that women with PTSD did not show differences in LTL compared to HC individuals. Our findings suggest that accelerated biological aging as measured through LTL may not be noticeable in young women with PTSD.

Recently, lifetime PTSD symptoms were associated with shorter TL in men and women (12, 15). However, no study investigated the link between TL and PTSD symptom clusters. To the best of our knowledge, this is the first study to show an association between PTSD re-experiencing symptoms and shorter LTL. Re-experiencing symptoms are the most characteristic symptoms of PTSD, denoted by intensive memories of the traumatic event, flashbacks, nightmares, and frightening thoughts (45). We suggest that PTSD re-experiencing symptoms may significantly increase the stress response system and exacerbate dysregulation of the HPA axis, leading to the elevation of concentrations of corticosteroids and immune system alterations accelerating telomere shortening (2, 5, 18, 19, 46–48).

Previous genetic association studies and polygenic risk scores (49–51) showed that re-experiencing symptoms have been associated with the *CRHR1* gene (corticotropin-releasing hormone receptor 1). *CRHR1* is involved in the stress-response system by allostatic load and immune response to stress (52–54). These studies provide additional evidence to our findings suggesting that re-experiencing symptoms may be related to impairment in regulating the immune system, which may cause TL changes. However, the literature lacks studies that investigated the association between PTSD re-experiencing symptoms and TL.

Despite the increasing number of evidence suggesting that re-experiencing and hyperarousal may be linked to biological mechanisms underlying PTSD status, our findings showed no association between hyperarousal symptom severity and LTL, contrary to our hypothesis. Previous studies have shown that hyperarousal symptoms may alter the HPA axis and brain reactivity (55–58); however, these studies have not been able to examine how chronic arousal may influence telomere shortening. Further studies with larger samples are needed to evaluate whether hyperarousal symptoms are linked to mechanisms underlying cellular aging.

Longitudinal analyses revealed no association between telomere shortening and PTSD diagnosis or PTSD symptom severity (avoidance, re-experiencing, hyperarousal, and negative alterations in cognitions and mood) in 24 women who completed the 1-year follow-up. It is important to emphasize that our longitudinal findings were not able to replicate the cross-sectional relationship between shorter relative LTL and higher re-experiencing symptoms. One possible explanation for our no significant findings is perhaps the low statistical power of our longitudinal analysis, as in genetic studies, small biological changes may not be detectable in small sample sizes. Also, understanding the longitudinal changes in TL remains challenging, as there is no evidence of how trauma or PTSD may contribute to TL maintenance.

The present findings must be interpreted in the context of some limitations. First, our study has a relatively small sample size. This may have reduced the statistical power to identify the minor effects of predictor variables in TL. Second, the assessment of TL by qPCR in leukocyte cells depends on the number of leukocytes in the blood, which may be affected by numerous factors, e.g., lifestyle and diseases. Thus, this method gives a relative mean of telomere attrition, i.e., providing information about the shortening rate. Third, the beta coefficient for predicting PTSD re-experiencing symptoms by LTL is relatively small; thus, we need caution to interpret these findings. Fourth, telomere shortening may be affected by genetic (i.e., genetic variants, gene expression) and environmental factors (i.e., lifestyle, smoking behavior, diet), and we were not able to adjust LTL for all variables, as we did not have them available in this study. Last, our analyses are limited to two time points (baseline and 1-year follow-up). Detecting accelerated biological aging may prove difficult after a 1-year period. Further multi-wave longitudinal studies are warranted to verify the effect of PTSD on LTL.

This study provides evidence that shorter baseline LTL may be related to the early stage of PTSD re-experiencing symptoms in recently sexually assaulted women. However, at the 1-year follow-up, we did not observe telomere shortening in both remitters and persistent patients with PTSD. Further, our findings did not replicate the previous association between PTSD diagnosis or trauma exposure and shorter TL. This study also suggests the potential effect of lower per-person income and harmful alcohol use on LTL. Future research should investigate underlying biological mechanisms which interplay TL, trauma, and PTSD, e.g., immune, and endocrine systems.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Research Ethics Committee of Universidade Federal de São Paulo (UNIFESP). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

CMC and SIB participated in the conception and design of this study. CMC drafted the article. CMC, BMC, AFM, VKO, MFM, and SIB participated in data collection, data analysis, and data interpretation. GX, AVGB, TF, MO, and RP aided in the data interpretation. BMC, GX, AVGB, TF, MO, RP, AFM, VKO, MFM, and SIB made critical revisions to this article and agreed on final article before submission. All authors contributed to the article and approved the submitted version.

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Trauma, Mental Health Distress, and Infectious Disease Prevention Among Women Recently Released From Incarceration

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Background: U.S. women recently released from incarceration experience significantly higher rates of trauma and exacerbation of mental health conditions, and the period following release has been identified as a window of heightened risk for mental health distress and human immunodeficiency virus (HIV), sexually transmitted infections (STI) and hepatitis C (HCV) transmissions. Despite these vulnerabilities, and an urgent need for supports, optimal engagement strategies remain unclear. WORTH Transitions is a program made up of two evidence-based interventions focused on improving the health of women returning to the community from incarceration with substance use disorders. Combining the two was designed to reduce HIV/STIs/HCV risks and increase overall health treatment engagement using a community health worker led intervention.

Methods: We examined associations between trauma, mental health symptomology, and HIV/STI/HCV outcomes among women who engaged in the WORTH Transitions intervention ($N = 206$) Specifically, bivariate and longitudinal multivariate models were created to examine associations between trauma and mental health distress (defined as depressive and PTSD symptoms), on (1) types of engagement in HIV/STIs/HCV prevention and behavioral health services; and (2) HIV/STIs/HCV risk outcomes. The women who engaged in the intervention were 18 years and older and some were White, Black and other racial or ethnic minority.

Results: PTSD symptomology and being a Black or indigenous woman of color was significantly ($p = 0.014$) associated with individual or group session engagement. Neither trauma nor PTSD symptoms were associated with higher HIV/STIs/HCV risks. Instead, relative to those who did not engage in HIV/STI/HCV risky behaviors, PTSD symptomology ($p = 0.040$) was associated with more than 3-fold increase in the probability of being lost to follow up (relative risk ratio = 3.722).

Conclusion: Given the impact of PTSD-related symptoms on driving both engagement in HIV/STIs/HCV prevention services and intervention attrition among women leaving incarceration, physical and behavioral health interventions must be both overtly trauma- and mental health-informed. As was the case with WORTH Transitions, physical and behavioral health services for this population must include intentional and active support of the forms of treatment participants endorse to ensure maximal engagement.

Keywords: psychopathology, trauma, PTSD, HIV, hepatitis C, sexually transmitted infections, recently released women

INTRODUCTION

U.S. women recently released from jails and prisons are subject to significantly higher levels of trauma and mental health distress such as post-traumatic stress disorder (PTSD) and depressive symptomology (1). Personal and interpersonal forms of trauma experienced post-incarceration include ones related to adult victimization (2), family (3), alcohol and substance misuse (4), violence from intimate, casual, and paying sexual partners (5), and risky sexual encounters (e.g., transactional sex, condomless sex, sex while high, and/or sex with partners that are known HIV positive) (6, 7). Rates of intimate partner violence as a whole have been found to be ten times levels found in the general population (8), with physical violence as high as 25 percent within the first 6 months after release. This is roughly five to six times higher than among the general population (9). Depressive symptomology and lifetime PTSD prevalence are also high at 44.6 (10) and 53 percent (11), respectively, compared to 12 (12) and 6 (13) percent in the general population. Pervasive levels of trauma are also associated with criminal legal system involvement itself (14) and social and structural determinants of health such as poverty, un- and under-employment, housing insecurity and homelessness, and healthcare stigma (15).

Alongside these significant associations, accumulated trauma and mental health conditions among recently released women are associated with disproportionately high rates of HIV, other sexually transmitted infections (STIs) and Hepatitis C (HCV) (11, 16–19). HIV transmission rates alone are three times levels found among US adults (1.3 vs. 0.5%) (20). The existing literature collectively show high prevalence of exposure to traumatic events and/or recent PTSD across a variety of categories (including childhood and lifetime physical and sexual abuse) among HIV-positive women (21). Severe trauma exposure among women has been associated with HIV risk behaviors such as greater numbers of sexual partners and engagement in transactional sex/sex-trading (22). In addition to domestic violence and sexual victimization, experience of community violence (measured as exposure to violent crime) has also been found to predict sexual risk behaviors among a sample of HIV-positive women (23). Importantly, greater trauma exposure is linked to poor treatment adherence and poor HIV-related health outcomes (24).

Given these intersecting risks, the period following release from incarceration has been identified as a particularly vulnerable window of re-traumatization (25) and HIV/STI/HCV risk behavior re-engagement (26–28). It has also been identified as an opportune time for targeted health and behavioral health treatment interventions (29). And yet, some of these very risk factors (high rates of trauma, mental health symptomology and other comorbid risks such as substance misuse, etc.) have been identified as significant barriers to care (30). Recently released women can be among the hardest to engage in HIV/STIs/HCV prevention services, particularly during the year following release (31). The need for targeted intervention is made especially urgent by steep inclines in the incarceration rates for women in the United States (32, 33). Almost 1.8 million women are released from jails each year and an additional 81,000 transition from state prisons (34). Paradoxically, although ∼80% of women transitioning from jails and prisons report chronic medical, psychiatric, or substance abuse problems, only 15% reported visiting a physician outside of the emergency department in the first-year post release for physical and/or behavioral health care (35). Perceived lack of engagement with physical and behavioral health treatment, such as chronically missed appointments and low adherence to medication regimens, has been linked to having underlying mental health conditions, such as depression and PTSD, and to exposure to traumatic life events (36, 37).

Despite these intersectional risks, and the well-established efficacy of trauma-specific care (38), a significant gap remains regarding optimal trauma-informed physical and behavioral health engagement strategies needed to promote participation in HIV/STIs/HCV prevention services among women recently released from incarceration (32, 39). Similarly, little research has examined accumulated trauma and mental health distress (defined as PTSD and depressive symptoms) on HIV/STI/HCV prevention and treatment engagement, and HIV/STIs/HCV risk outcomes among women released from incarceration. Further complicating this challenge, findings (where available) are somewhat contradictory. Results to date suggest that highly traumatized women transitioning from incarceration possess both higher levels of treatment hesitancy and health- and treatment-seeking behaviors (40). PTSD is associated with low engagement in care among male and female populations transitioning from jail (41). Conversely, depressive symptomology is significantly associated with greater (not less) interest in a pre-exposure prophylaxis (PrEP) intervention (42). Given these associations between incarceration, accumulated trauma, and both depressive and post-traumatic stress symptomology, these latter findings suggest that women transitioning from jails and prisons may encounter

even greater difficulty when attempting to adhere to HIV treatment and engage in care.

In view of these significant gaps, and contradictory findings where available, additional research is needed to extend understanding of associations between trauma, mental health, treatment engagement, and HIV/STIs/HCV outcomes among recently released women to guide efforts to prevent infectious diseases in this especially vulnerable population. To test the hypothesis, we looked at whether trauma has any independent impact on engagement type and/or the likelihood of engaging in risky sexual behaviors. For those who did not complete the study, we examined the impact of trauma on the likelihood of responding to the 6-month survey. Leveraging 6-month longitudinal data collected from cis-gender women ($n = 206$) participating in the WORTH Transitions program, all of whom transitioned from incarceration within 12 months of enrollment in the study, associations were examined between forms and amount of trauma experienced, depressive and PTSD symptomology, and study engagement and HIV/STIs/HCV risk behaviors. Given U.S.' commitment to end the HIV epidemic among marginalized populations and increased reliance on probation, parole, and other forms of community corrections, this study fills a significant research and public health gap. Deepening understanding of these heretofore understudied associations is critical in guiding efforts to sharpen current efforts to address this ongoing public health risk in this highly traumatized population during the especially vulnerable period post-release.

METHODS

Intervention

WORTH Transitions is a multi-site, HIV/STI/HCV prevention and intervention study for high-risk women recently released from incarceration that integrates two evidence-based programs: Women on the Road to Health (WORTH) as well as the version adapted for Black women specifically (E-WORTH: Empowering African-American Women on the Road to Health) and Transitions Clinic. WORTH (43) and E-WORTH (44) is a structured, five-session, multimedia intervention, efficacious in decreasing HIV/STI risks, intimate partner violence, and substance use among women involved in the criminal legal system. WORTH Transitions adaptation was tailored for recently released women, which included specifically addressing trauma experiences. Transitions Clinic is part of a national network of primary care-based programs that focus on the health needs of people returning to the community from incarceration by centering peer community health workers (CHWs) with their own history of incarceration to help patients engage with the health system and address social determinants of health (45). Engagement with Transitions Clinic has been found to reduce acute care utilization, hospitalization for illnesses preventable with access to primary care, and criminal legal system contact (35, 46). A growing body of literature has also demonstrated the effectiveness of peer CHWs in helping to increase access to needed HIV and other prevention and intervention services, while minimizing stigma (47, 48). The use of peer community health agents has also been linked to a decrease in the level of stigma in typical healthcare-related interactions that can interfere with addressing HIV and other STIs, HCV and concomitant risks of substance use disorder and intimate partner violence (49).

WORTH Transitions was adapted to be more trauma-informed, therefore we expect both the transitions clinic and the WORTH sessions to alleviate PTSD symptoms. However, the literature on this population is scarce. Of the available research that exists, it is possible that competing needs may influence their choices of engagement (50). For example, if participants have urgent health care needs they may be more likely to engage in healthcare only. Additionally, some literature does suggest that group sessions, especially with peers, are helpful in working through traumatic experiences and may yield more positive results in those with histories of trauma in need of socialization and support (30). More research is needed to understand these differences.

Study Team

WORTH Transitions was made possible from a collaboration of University of Rochester School of Medicine, Yale University School of Medicine, and Columbia University School of Social Work Social Intervention Group. The University of Rochester Institutional Review Board and then those at the other two institutions approved this study (#00001140).

Recruitment and Enrollment

Participants were recruited, consented, and screened by research assistants or formerly incarcerated community health workers from jails and prisons and multiple other community locations at which recently released women frequent and receive services (e.g., women's transitional housing, homeless shelters, food pantries, public defender offices, courthouses, probation, and substance use disorder treatment programs) in Rochester, New York and New Haven, Connecticut. Indirect recruitment methods were also implemented using social media ads (e.g., Facebook) and flyers posted in frequented locations. Participants could receive a total of $250 in gift card incentives to participate in the study in the following intervals: $10 for screening; $25 for baseline interview; $20 for attending individual and each of the four group WORTH sessions which included HIV/HCV testing in the individual session; $10 for each monthly check-in; $20 for giving a written or video testimonial for our Facebook page; and $30 for 6-month interview.

In addition to being female (cis- or transgender) and recently released from incarceration within 12 months prior to recruitment, inclusion criteria included: English-speaking, being 18 years and older, self-reported recent alcohol and/or substance use disorder histories, agreement to research requirement related to (a) allowing access to medical/mental health/SUD (Substance Use Disorder) treatment records during their participation in the study; and (b) accessing physical and behavioral health treatment. Being able to read was not required. Exclusion criteria included cognitive vulnerability (e.g., scoring < 2 on the Six-Item Screener derived from the Mini-Mental Status Examination) (51), and/or declining HIV/STI/HCV assessment. There were no selection criteria related to race and ethnicity.

A total of 259 women were screened, 208 enrolled (110 from Rochester; 98 from New Haven), and 206 completed baseline measures. Full participation in the study was defined as completion of the study's initial screening, an individual (1:1) WORTH HIV/STI/HCV prevention session including HIV/HCV rapid test and pre/post-test counseling, 4 group sessions, and at least 1 primary care provider (PCP) appointment attended at either the WORTH Transition clinics or their own PCP in Rochester or New Haven. Further HIV/STI/HCV testing and treatment were administered during PCP appointments as required. WORTH Transition personnel and clinic staff received training in trauma-informed care prior to the launch of the study. Participants were referred to substance use and mental health counseling services when such services were deemed clinically necessary or upon participant request.

While participants were encouraged to complete all study activities, as much engagement as participants found comfortable was allowed in view of the high amount of trauma anticipated in the population. In addition, participants who elected to receive physical and behavioral health services from a PCP outside of Transitions Clinic were supported in their decision to do so to minimize trauma associated with a disruption in care. To promote maximum recovery, alternative forms of support were also encouraged such as Twelve Step and other forms of self-help, support groups, or spiritual counseling. WORTH individual and group sessions were delivered by trained, formerly incarcerated CHWs. Outreach activities were also primarily conducted by peers. Transition Clinic appointments were conducted by a lone study PI/co-I at each intervention site trained in trauma-informed, trauma-specific, and culturally-informed care as part of routine care.

MEASURES

All explanatory variables (Trauma, Intimate Partner Violence, and Depression symptomology) were collected at baseline. Outcome variables (Engagement, HIV/STI/HCV risks) were collected during subsequent time points. Engagement was defined as participating in individual and/or group WORTH sessions and/or receiving clinical services from the Transition Clinic post baseline. HIV/STI/HCV risk variables were collected at the 6-month survey timepoint.

Explanatory Variables

Clinical Assessments

Trauma

Traumatic Events. Trauma was modeled in two ways using the Lifetime Stressors Checklist-R (LSC-R) (52). The LSC-R is a 30 item self-report measure that assesses traumatic events over the course of the lifecycle. Items include traumatic experiences with physical abuse/assault, sexual abuse/assault, and others related to medical-, financial-, relationship-, and family-trauma. Questions follow a yes/no response format. In line with previous research (53), a summary variable was computed based on the sum of positive answers in the LSC-R. This computed score most directly reflects breadth of trauma exposure (i.e., higher scores indicate that a participant has experienced many types of traumas); the variable purposefully does not attempt to assign trauma exposures different weights, and thus may not reflect trauma accumulation. As there is no agreed-upon index of trauma severity based on the LSC-R, measuring breadth of trauma exposure seemed to be a reasonable quantification of LSC-R responses.

For the purposes of this study, the item pertaining to experiences with natural disasters was eliminated. In this study, the LSC-R was examined first as a composite variable with values ranging from 0 to 29. A score of 29 indicates that the participant experienced all of the events. Second, we recoded some items of the LSC-R into clusters of trauma types, the first five of which were coded as continuous variables: physical abuse/assault, sexual abuse/assault, family, medical, and system. The remaining four clusters were modeled as binary, single item variables: emotional abuse, financial, relationship, and other events: (e.g., "Are there any events we did not include that you would like to mention?").The LSC-R has been used with criminal legal system populations and has moderate to good test-retest reliability, and good convergent and criterion validity with PTSD symptoms in HIV infected women (54).

Intimate Partner Violence. Intimate partner violence was modeled using the 5-item, yes/no, self-report Ongoing Abuse Scale (OAS) (55) measuring physical (e.g., "Are you presently emotionally or physically abused by your partner or someone important to you?"), sexual (e.g., "Are you presently forced to have sexual activities?"), and emotional intimate partner violence at the present time or presently. The OAS has been tested with women, African Americans, Latino/as and Whites in various settings (Chronbach alpha of 0.59) (55).

Psychopathology

Depressive Symptomology. Depressive symptomology, measured at each time point, was modeled as an ordinal/categorical variable using the *Global Assessment of Individual Needs* (*GAIN)* scale, which is a 113-page validated assessment, usable in shorter subsections, for detailed treatment planning and monitoring of individuals with SUD, yielding a composite score of need, access, and utilization. The reliable and well-validated GAIN Internal Mental Distress Scale (IMDS) component assesses depression and anxiety symptoms over the preceding 90 days and year (severe, none or moderate) (56).

Post-traumatic Stress Disorder Symptoms. PTSD was modeled as a dichotomous variable (negative, positive) using the Trauma Symptom Scale component of the IMDS which reliably measures PTSD ($\alpha = 0.96$).

Covariates

Sociodemographics

The following sociodemographic variables were included in the model: (a) relationship status (single, in relationship, separated/divorced/widowed); (b) age (Under 30, 30–40, over 40), which was chosen based on the distribution of the data (c) educational level [less than High School (HS), HS/General Educational Development (GED), some college, college+]; (d) race/ethnicity (white, non-white); (e) homelessness status

(homeless, not homeless); (f) employment status (unemployed or under, employed full- or part-time, unknown/not reported); and (g) ever in foster care or adopted (no, yes).

External Support Accessed

Modeled as a dichotomous variable, external support accessed during their time in WORTH Transitions was included in the model using a single variable [attended self-help group, attended religious program(s), attended recovery program(s), attend any of the above].

Clinical Measures

Alcohol Use

Alcohol use was modeled as the number of days out of past 90 days during which the patient used alcohol, coded as the following categories: 0 day, 1–30 days, and >30 days.

Substance Use

Substance abuse was modeled as a count of substance used in the past 90 days out of a total of 13 substances (e.g., marijuana, crack, cocaine, heroin, methadone, PCP, hallucinogen, crystal meth, speed, anti-anxiety, downers, painkillers) (none, 1–3, 4 or more -max 8).

Non-clinical Measures

Time Since Released

Using a single item question ("How long has it been since you were released from incarceration?"), time since released from jail or prison was modeled as a categorical variable with four discrete categories: <1 month, 1–3 months, 3–6 months, and >6 months.

Outcome Variables

Engagement

"Engagement" was defined as a categorical variable with four discrete types of possible engagement in WORTH Transitions programming: (a) choosing not to participate in individual or group WORTH sessions or attend Transitions Clinic ("no engagement"); (b) choosing only to participate in WORTH individual or group sessions ("session only"); (c) choosing only to participate in Transitions Clinic services and no WORTH sessions ("healthcare only") (d) choosing to access both WORTH sessions and Transitions Clinic/primary care physician services ("full engagement").

HIV/STI/HCV Risks

Measured at the 6-month mark, HIV/STI/HCV risk outcomes were modeled as a composite variable using self-reported risk behaviors (unprotected sex, risky needle use, sex with someone who injects drugs, sex while high, sex with a male sexual partner who was HIV+) and/or as self-reported HIV/STI/HCV. Any risk behavior endorsed and/or self-reported HIV/STI/HCV was assigned a maximum of one point such that participants who endorsed all risk behaviors and indicated that they received positive diagnosis received a total of one point. Similarly, those reporting only one risk behavior or self-reported HIV/STI/HCV, received a total of one point.

Risk behaviors were measured using the GAIN HIV risk scale ($\alpha = 0.96$).

Self-reported HIV/STI/HCV was measured using yes/no responses to the question: "In the past 6 months, have you been diagnosed with a sexually transmitted disease/HIV/Hep C?" (56).

Statistical Analyses

All statistical analyses were performed using STATA version 15.1 statistics software package.

Bivariate Analyses

Engagement Type

Types of engagement ("engagement none", "engagement: session only", "engagement: healthcare only", and "engagement: full engagement") was similarly analyzed in bivariate analyses on sociodemographic variables (relationship status, age, educational level, race/ethnicity, homelessness status, employment status, ever in foster care or adopted), key variables of interest (trauma, mental health: depressive symptoms, PTSD symptoms) and all other variables in the study (time since release, external support, number of days alcohol used during the past 90 days, count of substance used). Bivariate analyses were carried out via chi-square test of independence for discrete variables and ANOVA for continuous variables.

HIV/STI/HCV Risks

Stratified HIV/STI/HCV risk behavior categories: "no risky behavior", "any risky behavior", and "no 6-month data", were examined in bivariate analyses with engagement type, key variables of interest, controlling for sociodemographic variables and all other variables in the study.

Longitudinal Multivariate Analyses

Engagement Type

Adjusted (model 1a) and unadjusted (model 1a-U) longitudinal multivariate models were built to examine associations between baseline trauma (forms and accumulated), baseline mental health conditions on types of engagement endorsed (no engagement vs. session only; no engagement vs. healthcare only; no engagement vs. full engagement), controlling for all other variables in the study. The accumulated "trauma score" is a continuous variable that can range from 0 to 29. X_i represents the set of control variables, which include the following: whether the patient had any external support (=1 if she attended one or more of self-help group, religious group, or recovery org and 0 otherwise), minority status, screened for severe depression symptoms, screened for PTSD symptoms, relationship status, ever in foster care or adopted, education level, age, time since prison release, count of substances used during the past 90 days. For details on how each of these variables were operationalized in the analysis, refer to the attached XL file. For model 1a [engagement $\text{type}_i = a_1$ (Trauma Score_i) + a_2 (X_i) + e_i], "engagement type" can take 4 discrete outcomes (no engagement vs. session only vs. healthcare only vs. full engagement). Since there are 4 discrete outcomes, Model 1a is estimated via a multinomial logistic regression model, resulting in 3 separate sets of results, using "no engagement" as the reference category: (1) no engagement vs. session only, (2) no engagement vs. healthcare only, and (3) no

engagement vs. full engagement. Unadjusted model 1a (Model 1a-U): $\text{Engagement}_i = \alpha_1(\text{Trauma Score}_i) + e_i$.

HIV/STI/HCV Risks

Finally, adjusted [Model 2a: $\text{RiskyBehaviors}_i = c_1$ (Trauma Score_i) + c_2 (Engagement type_i) + c_3 (X_i) + e_i] and unadjusted models [(Model 2a-U) $\text{RiskyBehaviors}_i = \gamma_1$ (Trauma Score_i) + δ_2 (Engagement type_i) + e_i] were built to examine longitudinal associations between trauma, depressive and PTSD symptomology, engagement type, and HIV/STI/HCV outcomes. Where risky behaviors_i (RiskyBehaviors) can take 3 discrete outcomes as the following: None, Any, or No 6-month data, model 2a is estimated using a multinomial logistic regression model to test the hypothesis that either trauma or engagement type has any independent impact on the likelihood of engaging in risky sexual behaviors (and also on the likelihood of responding to the 6-month survey).

RESULTS

Sample Characteristics

Study participants were disproportionately Black and indigenous women of color (BIWOC) (45.6%), single (55.3%), over 30 years (78.1%), 32.5% of which were 40 and older. Sample characteristics also included high rates of recent homelessness (38.8%), current under- and unemployment (86.4%), recent substance use (59.8%) and non-study help seeking behavior (e.g., self-help groups) (66.5%). Participants were also on the whole evenly distributed across the four time periods since release. Eighty two percent of participants reported lifetime intimate partner violence.

The mean trauma score was 13.9 (out of a maximum of 29). Financial abuse (83%) and emotional abuse (74%) were the most heavily endorsed sub-trauma domains. Women also reported experiencing a high degree of system-trauma (1.18 out of a total possible score of 2), physical abuse/assault trauma across the lifecycle (2.42 out of 5) and medical trauma (1.95 out 2).

Close to three-quarters of women in the sample were identified as having depression symptomology (72.8%) and an even higher amount endorsed post-traumatic stress disorder symptomology (82.0%).

Bivariate Analyses

Engagement Type

Table 1 presents findings of descriptive statistics and bivariate comparisons examining forms of engagement ("engagement none", "engagement: session only" "engagement: healthcare only", and "engagement: full engagement") on sociodemographic variables and study controls. Being BIWOC was significantly associated with visits to the Transition Clinic/receiving health care services. Being un- or underemployed and using alcohol in excess of 30 days was significantly associated with participating in sessions only. Experiencing intimate partner violence was significantly associated with engagement in all study activities (Transition Clinic or PCP and Sessions) whereas experiencing lifetime physical abuse/assault and the overall trauma score was associated with engaging in sessions only.

HIV/STI/HCV Risks

Table 2 presents findings from bivariate comparisons of HIV/STI/HCV risk behaviors ("no risky behaviors", "any risk behaviors", "no 6-month data"), on trauma, study controls and sociodemographic variables. Significant associations were identified between Engagement Type "None" (or not engaging in WORTH Transitions) and HIV/STI/HCV risks ($p = 0.014$). Significant associations were also identified between Age and HIV/STI/HCV risk behaviors (Under 30 years old, $p = 0.014$; Over 40 years old, $p = 0.001$). There was no significant variation in the accumulated Trauma Score across the three HIV/STI/HCV risk behavior outcomes examined ("No Risky Behaviors", "Any Risky Behaviors", "No 6-month Data"). The proportion of study participants who had any Engagement does however vary across risk behavior outcomes. Specifically, those in the "No Risky Behavior" category had the highest proportion of those who were engaged (94.7%), while those in the No 6-month data category had the lowest proportion (75.4%; $p < 0.05$). Moreover, the "No Risky Behavior" category had the highest proportion of participants who were 40 or older (55.3%), while the "Any Risky Behavior" category had the lowest proportion of participants who were 40 or older (14.75; $p < 0.05$).

Longitudinal Multivariate Analyses

Engagement Type

As illustrated in **Table 3**, a 1-point increase in the trauma score is associated with 9.2% higher probability of engaging in session only ($p < 0.05$), and an 8.2% higher probability of engaging in all aspects of the study (session + healthcare) ($p < 0.05$), relative to those with no engagement. After controlling for all the potential confounders (in the adjusted model), these associations are no longer statistically significant, and become smaller in magnitude. In adjusted models, Black or indigenous women of color had a higher odds of engaging in sessions only and in the clinic only when compared with their white peers ($p = 0.014$).

Having PTSD symptomology was significantly associated with participating in sessions only ($p = 0.012$), whereas being out of jail for a longer period of time (>6 months) was significantly associated with attending the Transition Clinic only ($p = 0.029$), as compared with those who did not participate in any study activities after enrollment/baseline.

HIV/STI/HCV Risks

And finally, **Table 4** presents the adjusted and unadjusted longitudinal multivariate models examining associations between baseline trauma, mental health, and engagement type on HIV/STI/HCV outcomes/having self-reported HIV/STI/HCV. There was no statistically significant association—either in the adjusted or the unadjusted models—between the HIV/STIs/HCV risk behaviors and the key explanatory variables: baseline trauma, depressive and PTSD symptomology, and treatment engagement. Similarly, significant risks were not identified between the number of days alcohol was used during past 90 days or the count of substance used in the past 90 days reported at baseline and HIV/STI/HCV risk outcomes. Positive

TABLE 1 | Descriptive statistics by engagement type.

Patient characteristics	All sample	No engagement	Session only	Healthcare only	Full engagement	chi-square test of independence (*p*-value)
N	206	39	85	20	62	
Race/ethnicity						
White	53.9%	69.2%	51.8%	35.0%	53.2%	0.081
Minority	45.6%	28.2%	48.2%	65.0%	46.8%	0.045*
Missing	0.5%	2.6%	0.0%	0.0%	0.0%	0.231
Homelessness						
Not homeless	61.2%	51.3%	67.1%	60.0%	59.7%	0.405
Homeless	38.8%	48.7%	32.9%	40.0%	40.3%	0.405
Depression						
Severe	72.8%	66.7%	75.3%	70.0%	74.2%	0.765
None or moderate	24.3%	28.2%	22.4%	25.0%	24.2%	0.918
Missing	2.9%	5.1%	2.4%	5.0%	1.6%	0.694
PTSD						
Negative	17.5%	30.8%	12.9%	25.0%	12.9%	0.053
Positive	82.0%	69.2%	87.1%	75.0%	85.5%	0.073
Missing	0.5%	0.0%	0.0%	0.0%	1.6%	0.506
Time since release						
<1 month	23.3%	23.1%	30.6%	10.0%	17.7%	0.134
1–3 months	29.1%	41.0%	17.6%	20.0%	40.3%	0.005*
3–6 months	19.4%	20.5%	14.1%	25.0%	24.2%	0.414
>6 months	26.2%	10.3%	36.5%	45.0%	16.1%	0.001**
Missing	1.9%	5.1%	1.2%	0.0%	1.6%	0.428
Relationship status						
Single	55.3%	66.7%	48.2%	60.0%	56.5%	0.265
In relationship	25.2%	17.9%	30.6%	20.0%	24.2%	0.438
Separated/divorced/widow	18.9%	12.8%	21.2%	20.0%	19.4%	0.741
Missing	0.5%	2.6%	0.0%	0.0%	0.0%	0.231
Education level						
Less than HS	27.2%	23.1%	24.7%	35.0%	30.6%	0.662
HS/GED	37.9%	48.7%	38.8%	30.0%	32.3%	0.342
Some college	25.2%	23.1%	23.5%	30.0%	27.4%	0.891
College+	8.7%	2.6%	12.9%	5.0%	8.1%	0.247
Missing	1.0%	2.6%	0.0%	0.0%	1.6%	0.508
Age						
Under 30	19.9%	25.6%	15.3%	30.0%	19.4%	0.358
30–40	44.7%	43.6%	47.1%	40.0%	43.5%	0.936
Over 40	32.5%	28.2%	37.6%	25.0%	30.6%	0.580
Missing	2.9%	2.6%	0.0%	5.0%	6.5%	0.132
Employment status						
Unemployed or under	86.4%	92.3%	91.8%	70.0%	80.6%	0.023*
Employed full or PT	7.3%	0.0%	5.9%	20.0%	9.7%	0.035*
Unknown/not reported	6.3%	7.7%	2.4%	10.0%	9.7%	0.259
Ever in foster care or adopted						
No	80.1%	79.5%	80.0%	80.0%	80.6%	0.999
Yes	18.0%	15.4%	20.0%	15.0%	17.7%	0.911
Missing	1.9%	5.1%	0.0%	5.0%	1.6%	0.189

(Continued)

TABLE 1 | Continued

Patient characteristics	All sample	No engagement	Session only	Healthcare only	Full engagement	chi-square test of independence (*p*-value)
External support						
Attended self-help group	47.6%	46.2%	45.9%	45.0%	51.6%	0.899
Attended religious group	33.0%	20.5%	34.1%	30.0%	40.3%	0.223
Attended recovery org	33.0%	35.9%	30.6%	20.0%	38.7%	0.421
Attend any of the above	66.5%	61.5%	69.4%	55.0%	69.4%	0.538
Count of substance used past 90 days (up to 13 substances)						
None	45.6%	41.0%	43.5%	50.0%	50.0%	0.773
1–3	38.3%	35.9%	41.2%	35.0%	37.1%	0.914
4 or More (max 8)	16.0%	23.1%	15.3%	15.0%	12.9%	0.585
# Days alcohol used during past 90 days						
0 day	62.6%	61.5%	54.1%	75.0%	71.0%	0.122
1–30 Days	25.2%	28.2%	25.9%	20.0%	24.2%	0.913
>30 days	12.1%	10.3%	20.0%	5.0%	4.8%	0.028*

Trauma variable	Variable type (min-max)	All sample	No engagement	Session only	Healthcare only	Full engagement	*p*-value
N		206	39	85	20	62	
IPV (OAS)	Binary	0.82	0.79	0.74	0.85	0.92	0.050*
Abuse: emotional	Binary	0.74	0.77	0.73	0.7	0.76	0.921
Financial	Binary	0.83	0.74	0.86	0.85	0.85	0.403
Relationship	Binary	0.32	0.21	0.31	0.25	0.42	0.126
Other Events	Binary	0.04	0.05	0.01	0	0.1	0.065
Abuse: Physical	Cont (0–5)	2.42 (1.49)	1.97 (1.5)	2.66 (1.44)	1.8 (1.28)	2.56 (1.51)	0.019*
Abuse: Sexual	Cont (0–5)	1.68 (1.53)	1.49 (1.59)	1.81 (1.51)	1.45 (1.57)	1.71 (1.54)	0.637
Family	Cont (0–8)	3.92 (1.76)	3.62 (1.94)	4.15 (1.74)	3.4 (1.64)	3.95 (1.7)	0.222
Medical	Cont (0–4)	1.95 (1.18)	1.56 (1.35)	2.14 (1.11)	1.9 (1.29)	1.94 (1.08)	0.092
System	Cont (0–2)	1.18 (0.45)	1.08 (0.42)	1.24 (0.45)	1.15 (0.49)	1.19 (0.44)	0.323
Trauma Score	Cont (0–29)	13.9 (5.23)	12.28 (5.89)	14.65 (5.02)	12.35 (4.88)	14.4 (4.95)	0.049*

*SD in parentheses; Chi-square test of independence used for binary variables; ANOVA used for continuous variables; *statistically significant at the 0.05 level; **statistically significant at the 0.001 level.*

HIV/STIs/HCV outcomes were solely associated with being in a relationship (lowered risk: relative risk ratio = 0.188; $p = 0.023$).

When comparing those who did not report risk outcomes to those were lost to follow up, those who participated in the study in any way (sessions only: relative risk ratio = 0.075, $p = 0.006$; Transitions Clinic: relative risk ratio = 0.101, $p = 0.035$; WORTH sessions and Transitions Clinic: relative risk ratio = 0.069; $p = 0.004$) had more than 90% lower probability of being lost to follow up. In addition, those participants who were 40 or older were significantly less likely to be in the lost to follow up category (relative risk ratio = 0.079 or more than 90% lower probability; $p = 0.003$), suggesting that the sample attrition was associated with younger patient age. Conversely, relative to those who did not engage in HIV/STI/HCV risky behaviors, those with PTSD symptoms ($p = 0.040$) were associated with more than 3-fold increase in the probability of being lost to follow up (relative risk ratio = 3.722).

DISCUSSION

This study presents multiple important findings related to associations between trauma, mental health, type of treatment engagement, and HIV/STI/HCV risk outcomes among women recently released from incarceration. It also draws attention to what appears to be a highly complex relationship between trauma, PTSD-specific mental health distress, engagement in HIV/STI/HCV prevention services, and HIV/STI/HCV risks. First, although, women transitioning from incarceration have been characterized as among the hardest to engage, study participants on the whole exhibited high rates of engagement

TABLE 2 | Descriptive statistics by HIV/STIs/HCV risks.

Patient characteristics	No risky behaviors ($n = 38$)	Any risky behavior ($n = 34$)	No response ($n = 134$)	*p*-value
Engagement type				
None	5.3%	11.8%	24.6%	0.014*
Session only	47.4%	44.1%	38.8%	0.597
Healthcare only	10.5%	2.9%	11.2%	0.343
TC/PCP and session	36.8%	41.2%	25.4%	0.121
Trauma score	13.5 (5.5)	13.9 (5.3)	14.0 (5.1)	0.858
Race/ethnicity				
White	50.0%	58.8%	53.7%	0.754
Minority	50.0%	41.2%	45.5%	0.754
Missing	0.0%	0.0%	0.7%	0.763
Homelessness				
Not homeless	57.9%	70.6%	59.7%	0.458
Homeless	42.1%	29.4%	40.3%	0.458
Depression				
Severe	26.3%	23.5%	23.9%	0.963
None or moderate	71.1%	73.5%	73.1%	0.948
Missing	2.6%	2.9%	3.0%	0.993
PTSD				
Negative	21.1%	23.5%	14.9%	0.405
Positive	76.3%	76.5%	85.1%	0.301
Missing	2.6%	0.0%	0.0%	0.108
Time since release				
<1 month	28.9%	35.3%	18.7%	0.081
1–3 months	28.9%	20.6%	31.3%	0.468
3–6 months	15.8%	8.8%	23.1%	0.139
>6 months	26.3%	35.3%	23.9%	0.401
Missing	0.0%	0.0%	3.0%	0.334
Relationship status				
Single	42.1%	67.6%	56.0%	0.091
In relationship	34.2%	17.6%	24.6%	0.261
Separated/divorced/widow	23.7%	14.7%	18.7%	0.618
Missing	0.0%	0.0%	0.7%	0.763
Education level				
Less than HS	36.8%	17.6%	26.9%	0.186
HS/GED	36.8%	44.1%	36.6%	0.713
Some college	21.1%	23.5%	26.9%	0.743
College+	5.3%	14.7%	8.2%	0.343
Missing	0.0%	0.0%	1.5%	0.581
Age				
Under 30	5.3%	32.4%	20.9%	0.014*
30–40	34.2%	47.1%	47.0%	0.357
Over 40	55.3%	14.7%	30.6%	0.001**
Missing	5.3%	5.9%	1.5%	0.252
Count of substance used (up to 13 substances)				
None	42.1%	50.0%	45.5%	0.797
1–3	47.4%	29.4%	38.1%	0.292
4 or More (max 8)	10.5%	20.6%	16.4%	0.498
Employment status				
Unemployed or under	81.6%	82.4%	88.8%	0.389
Employed full or PT	13.2%	8.8%	5.2%	0.234

(Continued)

TABLE 2 | Continued

Patient characteristics	No risky behaviors ($n = 38$)	Any risky behavior ($n = 34$)	No response ($n = 134$)	*p*-value
Unknown/not reported	5.3%	8.8%	6.0%	0.795
Ever in foster care or adopted				
No	76.3%	73.5%	82.8%	0.388
Yes	23.7%	23.5%	14.9%	0.301
Missing	0.0%	2.9%	2.2%	0.609
Had any external support	65.8%	64.7%	67.2%	0.959
# Days alcohol used during past 90 days				
0 day	63.2%	67.6%	61.2%	0.783
1–30 days	26.3%	20.6%	26.1%	0.791
>30 days	10.5%	11.8%	12.7%	0.935

**statistically significant at the 0.05 level; **statistically significant at the 0.001 level.*

in WORTH Transitions activities and non-WORTH Transitions self-help programs (e.g., NA, AA, spiritual counseling) despite simultaneously experiencing acute levels of trauma and PTSD symptomatology. Contrary to earlier findings (30), PTSD (vs. depressive) symptomology served as an "engagement catalyst". Specifically, having PSTD symptomology was associated with a significantly higher odds of engaging in peer-led individual and/or group WORTH sessions as was being a Black or Indigenous woman of color (BIWOC). Interestingly, PTSD symptomology was also associated with a significantly higher odds of being lost to follow up in the longitudinal model.

The fact that those with PTSD symptomology turned toward, rather than away from, peer-led activities (at least initially) lends additional support to preliminary findings regarding the efficacy of peer engagement (57). It also underscores the continuing utility of session-based HIV prevention interventions/activities like WORTH Transitions, as compared to asynchronous activities increasingly lauded as less expensive and less time consuming (58–60). Study findings instead suggest that interventions like WORTH Transitions remain highly salient in the arsenal of HIV/STI/HCV prevention interventions. This may be especially true for BIWOC populations. As noted, BIWOC were significantly more likely to engage in all study activities (sessions only, healthcare only, sessions + healthcare), standing in contrast to prior findings categorizing this sub-group as being especially "hard to reach" (31, 61). Although additional research is needed, peer-based prevention interventions like WORTH Transitions may serve to mitigate treatment hesitancy identified among BIWOC (62) and/or challenge the existing narrative of treatment resistance.

These encouraging findings were not true for all participants however as results make clear that a subset of women most at risk for HIV/STI/HCV were less likely to engage and be retained. Specifically, since findings identified significant associations between "not engaging" and HIV/STI/HCV risks/outcomes and PTSD symptomology and a more than 3-fold increase in the probability of being lost to follow up (relative risk ratio = 3.722), additional research is needed to identify which subset of recently released women are not fully reached by the pairing of these two evidence-based interventions (WORTH Transitions) as it is currently designed. As an initial next step, we recommend that qualitative and/or multimethod studies be conducted to identify the total number of group sessions that may be tolerable (or non-exacerbating) for transitioning women exhibiting severe PTSD symptomology. Since findings from this current study also makes clear that significant within-group differences exist among women transitioning from carceral settings, we recommend that future studies utilize the lens of intersectionality (63) to examine trauma and mental health distress, sociodemographic characteristics (race/ethnicity, age, etc.), HIV/STI/HCV risks and engagement in HIV/STI/HCV prevention services in this population. Also through the lens of intersectionality, we recommend that research be conducted with the goal of more finely attuning peer-led HIV/STI/HCV risk prevention interventions by type to highly traumatized women emerging from jails and prisons based on their sociodemographic characteristics and trauma and PTSD symptomology. Given the findings from this current study, it could be the case, for example, that highly traumatized older BIPOC women currently experiencing PTSD symptoms may be more responsive to lengthier peer-led approaches delivered in a group setting, while those who are younger may require individualized peer delivered approaches, regular pre-, during-, or post-group check-ins, and/or groups that are shorter in duration. Developing a typology of peer-led interventions, matched to both trauma and PTSD phenotype and sociodemographic characteristics will significantly advance efforts to prevent new transmissions among this highly vulnerable group who remain at the forefront of HIV/STI/HCV risk. This also has implications in terms of trauma-informed care (TIC) and is consistent with prior calls for patient-centered TIC approaches to mitigate HIV/STI/HCV and other health and behavioral health risks during re-entry (64).

Second, consistent with extant literature (65), only a subset of trauma types were heavily endorsed. Unsurprisingly, high rates of social and structural forms of trauma (e.g., financial-, system-, and medical-) were identified. While peer review literature is replete with references to financial-, system-, and/or medical-related harm experienced by women in the

TABLE 3 | Longitudinal multivariate analysis trauma, psychopathology, and all other variables by engagement type.

Covariate	Model 1a-U				Model 1a			
	Multinomial logistic regression model: unadjusted				Multinomial logistic regression model: adjusted			
No engagement vs. session only	**RRR**	***p*-value**	**(95% CI)**		**RRR**	***p*-value**	**(95% CI)**	
Trauma score	1.092	0.020	1.014	1.177	1.029	0.574	0.930	1.139
Any external support (vs. none)					1.404	0.482	0.546	3.613
Minority (vs. non-minority or unknown)					3.575	0.014*	1.293	9.887
Severe depression (vs. none, moderate, or unknown)					1.632	0.373	0.556	4.789
PTSD positive (vs. negative or unknown)					4.804	0.012*	1.417	16.292
Relationship status								
Single					(referent category)			
In relationship					1.904	0.281	0.590	6.139
Separated/divorced/unknown					1.994	0.310	0.526	7.561
Ever foster/adopted (vs. never or unknown)					0.810	0.729	0.245	2.673
Full or PT employed (vs. not full or PT employed)					0.630	0.339	0.245	1.625
Education level								
Less than HS					(referent category)			
HS/GED					0.888	0.835	0.290	2.716
Some college					1.202	0.777	0.337	4.291
College+ or unknown					3.527	0.192	0.531	23.449
Age category								
Age: 18–29					(referent category)			
Age: 30–40					1.416	0.564	0.435	4.609
Age: >40 or unknown					1.552	0.496	0.438	5.506
Time since release from prison								
<3 months					(referent category)			
1–3 months					0.200	0.011*	0.058	0.690
3–6 months					0.346	0.142	0.084	1.427
>6 months or unknown					1.379	0.635	0.367	5.183
Count of substance used (up to 14 substances)								
None					(referent category)			
1–3					0.978	0.969	0.311	3.078
4 or more (max 9)					0.593	0.468	0.145	2.434
# Days alcohol used during past 90 days								
0 day					(referent category)			
1–30 days					0.760	0.651	0.232	2.492
>30 days					1.268	0.767	0.264	6.105
Constant	0.661	0.441	0.231	1.893	0.165	0.093	0.020	1.353
Covariate	**Multinomial logistic regression model: unadjusted**				**Multinomial logistic regression model: adjusted**			
No engagement vs. healthcare only	**RRR**	***p*-value**	**(95% CI)**		**RRR**	***p*-value**	**(95% CI)**	
Trauma score	1.002	0.963	0.906	1.110	0.970	0.680	0.838	1.122
Any external support (vs. none)					0.839	0.803	0.211	3.330
Minority (vs. non-minority or unknown)					8.298	0.004*	1.962	35.092
Severe depression (vs. none, moderate, or unknown)					2.059	0.353	0.449	9.454
PTSD positive (vs. negative or unknown)					2.244	0.323	0.451	11.168
Relationship status								
Single					(referent category)			
In relationship					1.117	0.894	0.218	5.715

(Continued)

TABLE 3 | Continued

Covariate	Multinomial logistic regression model: unadjusted				Multinomial logistic regression model: adjusted			
No engagement vs. healthcare only	**RRR**	***p*-value**	**(95% CI)**		**RRR**	***p*-value**	**(95% CI)**	
Separated/divorced/unknown					2.779	0.283	0.430	17.957
Ever foster/adopted (vs. never or unknown)					0.599	0.582	0.096	3.717
Full or PT employed (vs. not full or PT employed)					1.460	0.469	0.525	4.062
Education level								
Less than HS					(referent category)			
HS/GED					0.237	0.073	0.049	1.144
Some college					0.781	0.760	0.159	3.831
College+ or unknown					0.439	0.569	0.026	7.465
Age category								
Age: 18–29					(referent category)			
Age: 30–40					0.754	0.730	0.153	3.729
Age: >40 or unknown					0.833	0.832	0.154	4.511
Time since release from prison								
<3 months					(referent category)			
1–3 months					1.005	0.996	0.120	8.389
3–6 months					3.143	0.306	0.351	28.138
>6 months or unknown					10.335	0.029*	1.270	84.096
Count of substance used (up to 14 substances)								
None					(referent category)			
1–3					0.929	0.930	0.184	4.705
4 or More (max 9)					1.866	0.552	0.239	14.561
# Days alcohol used during past 90 days								
0 day					(referent category)			
1–30 days					0.295	0.168	0.052	1.675
>30 days					0.142	0.191	0.008	2.643
Constant	0.498	0.316	0.127	1.948	0.103	0.128	0.005	1.929
Covariate	**Multinomial logistic regression model: unadjusted**				**Multinomial logistic regression model: adjusted**			
No engage vs. session + TC	**RRR**	***p*-value**	**(95% CI)**	**RRR**	***p*-value**	**(95% CI)**		
Trauma score	1.082	0.049	1.000	1.170	1.048	0.373	0.945	1.162
Any external support (vs. none)					1.513	0.405	0.571	4.012
Minority (vs. non-minority or unknown)					3.465	0.018*	1.236	9.710
Severe depression (vs. none, moderate, or unknown)					1.768	0.306	0.594	5.266
PTSD positive (vs. negative or unknown)					2.243	0.191	0.669	7.519
Relationship status								
Single					(referent category)			
In relationship					1.512	0.501	0.453	5.048
Separated/divorced/unknown					1.476	0.580	0.372	5.848
Ever foster/adopted (vs. never or unknown)					0.709	0.580	0.210	2.398
Full or PT employed (vs. not full or PT employed)					1.262	0.578	0.555	2.871
Education level								
Less than HS					(referent category)			
HS/GED					0.518	0.242	0.172	1.558
Some college					0.832	0.772	0.239	2.897
College+ or unknown					1.522	0.672	0.218	10.618
Age category								
Age: 18–29					(referent category)			

(Continued)

TABLE 3 | Continued

Covariate	Multinomial logistic regression model: unadjusted			Multinomial logistic regression model: adjusted			
No engage vs. session + TC	**RRR**	***p*-value**	**(95% CI)**	**RRR**	***p*-value**	**(95% CI)**	
Age: 30–40					1.232	0.732	0.374 4.064
Age: >40 or unknown					1.427	0.580	0.405 5.031
Time since release from prison							
<3 months					(referent category)		
1–3 months					0.957	0.945	0.271 3.374
3–6 months					1.402	0.647	0.331 5.942
>6 months or Unknown					1.356	0.683	0.315 5.846
Count of substance used (up to 13 substances)							
None					(referent category)		
1–3					1.134	0.832	0.353 3.640
4 or more (max 8)					0.740	0.676	0.180 3.040
# Days alcohol used during past 90 days							
0 day					(referent category)		
1–30 days					0.504	0.264	0.151 1.677
>30 days					0.210	0.107	0.031 1.399
Constant	0.554	0.297	0.183 1.681		0.161	0.087	0.020 1.305

**statistically significant at the 0.05 level.*

criminal legal system pre-, during and post incarceration (66), to our knowledge, only one peer reviewed manuscript has examined associations between "social and/or structural trauma" on HIV/STI/HCV risks among recently released women (67). None to date have examined how these forms of trauma may impact the ways in which women transitioning from incarcerated settings (or women in the criminal legal system as a whole) may engage in and/or are retained in HIV/STI/HCV prevention interventions. Additional research is needed to fill this gap. We specifically recommend that future researchers examine how social and structural trauma may be proximally or distally associated with PTSD-related mental health distress, engagement, and/or HIV/STI/HCV outcomes. In addition, while the efficacy of trauma-informed care for incarcerated populations has been well documented in scholarly literature (68), far less is known regarding how (1) to target recently released women in particular (29); and (2) HIV/STI/HCV prevention services and trauma-informed services should be differently structured and/or delivered based on social and structural trauma histories.

Third, results suggest that longer windows of time since release are associated with significantly higher odds of engagement in Transition Clinic health services and as such may serve as a "critical time" for optimal engagement. While these findings are on the whole unsurprising given the preponderance of peer reviewed literature pointing to the need for targeted support during this especially vulnerable period of transition and risk (69), they nevertheless speak to the importance of optimally timed interventions. Building on this body of literature, the Transitions Clinic program specifically aims to reach individuals within 2 weeks of release and includes peer in-reach to jails and prisons prior to release (29). This study offers insight on future directions of research in order to deepen scholarly and practitioner understanding of how these interventions should be structured and optimally timed. It may be that more flexibility is needed in addressing women's varied mental health, physical health, and structural priorities, depending on their level of mental health distress and PTSD symptomology as they transition from carceral settings.

Lastly, the findings from this study suggest that neither trauma nor mental health symptomology was associated with higher amounts of HIV/STI/HCV risks. Conversely, being in a relationship was found to be protective. While a small handful of peer reviewed studies have pointed to a potentially protective role of having a committed partner (25), HIV/STI/HCV risks have instead overwhelmingly been attributed to risky male sexual partners (70). We therefore recommend that additional research be conducted with recently released women to determine if and/or how the level of protection offered may change over time. For example, given afore referenced findings pointing to the saliency of the window post release, it may be possible that the more time recently released women spend with their partners, partner-related HIV/STI/HCV risks may increase.

Additional qualitative quantitative, and mixed methods studies from this data will explore several of these themes including depression, trauma and other factors associated with differences in levels of engagement and the implementation, fidelity, and adherence of the study.

STRENGTHS AND LIMITATIONS

Strengths of this study includes its novel use of two evidence-based interventions, WORTH (and E-WORTH) which has been deemed highly efficacious in preventing

TABLE 4 | Longitudinal multivariate analysis trauma, psychopathology, and all other variables by HIV/STIs/HCV risk behaviors.

Covariate	Model 2a-U				Model 2a			
	No risky behaviors vs. any risky behaviors (no interaction): unadjusted				No risky behaviors vs. any risky behaviors (no interaction): adjusted			
	RRR	*p*-value	95% CI		RRR	*p*-value	95% CI	
Engagement type								
None	(referent category)				(referent category)			
Session only	0.400	0.332	0.063	2.543	0.240	0.214	0.025	2.279
Healthcare only	0.124	0.140	0.008	1.986	0.062	0.086	0.003	1.487
Full engagement	0.481	0.443	0.074	3.118	0.422	0.443	0.047	3.823
Trauma score	1.014	0.759	0.925	1.112	1.074	0.299	0.939	1.229
Any external support (vs. none)					1.039	0.952	0.298	3.622
Minority (vs. non-minority or unknown)					0.757	0.656	0.222	2.580
Severe depression (vs. none, moderate, or unknown)					0.821	0.770	0.220	3.072
PTSD positive (vs. negative or unknown)					2.137	0.345	0.442	10.329
Relationship status								
Single					(referent category)			
In relationship					0.188	0.023	0.044	0.796
Separated/divorced/unknown					0.282	0.133	0.054	1.470
Ever foster/adopted (vs. never or unknown)					0.873	0.851	0.211	3.609
Full or PT employed (vs. not full or PT employed)					1.168	0.754	0.443	3.076
Education level								
Less than HS					(referent category)			
HS/GED					3.809	0.069	0.899	16.141
Some college					3.435	0.136	0.678	17.417
Less than HS					9.960	0.054	0.959	103.466
Age category								
Age: 18–29					(referent category)			
Age: 30–40					0.159	0.052	0.025	1.016
Age: >40 or unknown					0.025	0.000**	0.004	0.178
Time since release from prison								
<3 months					(referent category)			
1–3 months					0.457	0.331	0.094	2.216
3–6 months					0.684	0.702	0.098	4.774
>6 months or unknown					1.991	0.359	0.457	8.677
Count of substance used (up to 13 substances)								
None					(referent category)			
1–3					0.426	0.252	0.099	1.834
4 or more (max 8)					1.187	0.865	0.164	8.577
# Days alcohol used during past 90 days								
0 day								
1–30 days					1.785	0.476	0.362	8.795
>30 days					2.896	0.309	0.373	22.469
Constant	1.700	0.601	0.232	12.435	5.843	0.289	0.223	152.928

(Continued)

TABLE 4 | Continued

Covariate	No risky behaviors vs. no 6-mo data (no interaction): unadjusted				No risky behaviors vs. no 6-mo data (no interaction): adjusted			
	RRR	*p*-value	95% CI		RRR	*p*-value	95% CI	
Engagement type								
None	(referent category)				(referent category)			
Session only	0.157	0.019	0.033	0.734	0.075	0.006*	0.012	0.481
Healthcare only	0.224	0.105	0.037	1.366	0.101	0.035*	0.012	0.846
Full engagement	0.133	0.012	0.028	0.641	0.069	0.004*	0.011	0.430
Trauma score	1.041	0.277	0.968	1.121	1.084	0.121	0.979	1.201
Any external support (vs. none)					1.167	0.760	0.434	3.142
Minority (vs. non-minority or unknown)					1.292	0.589	0.509	3.278
Severe depression (vs. none, moderate, or unknown)					0.872	0.788	0.321	2.372
PTSD positive (vs. negative or unknown)					3.722	0.040*	1.060	13.066
Relationship status								
Single					(referent category)			
In relationship					0.434	0.135	0.145	1.297
Separated/divorced/unknown					0.440	0.192	0.128	1.512
Ever foster/adopted (vs. never or unknown)					0.402	0.102	0.135	1.198
Full or PT employed (vs. not full or PT employed)					0.887	0.758	0.414	1.902
Education level								
Less than HS					(referent category)			
HS/GED					1.625	0.355	0.581	4.548
Some college					2.092	0.221	0.642	6.811
College + or unknown					5.913	0.075	0.833	41.949
Age category								
Age: 18–29					(referent category)			
Age: 30–40					0.311	0.180	0.056	1.713
Age: >40 or Unknown					0.079	0.003*	0.014	0.433
Time since release from prison								
<3 months					(referent category)			
1–3 months					1.280	0.691	0.378	4.333
3–6 months					3.519	0.088	0.829	14.932
>6 months or Unknown					2.569	0.127	0.764	8.640
Count of substance used (up to 13 substances)								
None					(referent category)			
1–3					0.678	0.505	0.216	2.127
4 or More (max 8)					1.370	0.706	0.266	7.047
# Days alcohol used during past 90 days								
0 day								
1–30 days					1.409	0.580	0.418	4.744
>30 days					1.915	0.445	0.362	10.125
Constant	10.233	0.006	1.970	53.142	11.532	0.076	0.774	171.787

**statistically significant at the 0.05 level; **statistically significant at the 0.001 level.*

HIV/STIs/HCV among women in the criminal legal system, and Transitions Clinic which effectively uses peers to increase engagement.

Limitations include sample size limitations impacting the level of power needed to detect true effect sizes in some longitudinal models and the use of self-reported HIV/STIs/HCV

risk data and biological outcomes. Self-reported data has proven reliable in research studies however (71) and respondents across studies have demonstrated high recall for HIV and health-related outcomes (72). In addition, having an English-speaking requirement may have limited the number of Latina participants who were less proficient in English.

CONCLUSION

This manuscript presents important findings regarding the impact of trauma and mental health symptoms on HIV/STI/HCV engagement in a highly efficacious HIV/STI/HCV prevention intervention among recently released women. Results underscore the extent to which this group may be health seeking, desirous of support and reachable by services that are appropriately tailored, contradicting prior research. Through this lens, this study also provides insight regarding how to best tailor HIV/STI/HCV prevention and intervention services for this highly vulnerable population of women in the U.S. criminal legal system who remain among the most vulnerable to new transmission.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

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

AUTHOR CONTRIBUTIONS

KJ served as primary author in preparing the manuscript and contributed to research design. DM, TH, and LP edited extensively and contributed to research design. AN, AL, ZS, RC, JW, and RJ contributed significantly to the literature review, outline, and introduction. DM ran all analyses. All other authors provided critical review. All authors contributed to the article and approved the submitted version.

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SYSTEMATIC REVIEW
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Neurobiological Alterations in Females With PTSD: A Systematic Review

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Most females experience at least one traumatic event in their lives, but not all develop PTSD. Despite considerable research, our understanding of the key factors that constitute risk for PTSD among females is limited. Previous research has largely focused on sex differences, neglecting within group comparisons, thereby obviating differences between females who do and do not develop PTSD following exposure to trauma. In this systematic review, we conducted a search for the extent of existing research utilizing magnetic resonance imaging (MRI) to examine neurobiological differences among females of all ages, with and without PTSD. Only studies of females who met full diagnostic criteria for PTSD were included. Fifty-six studies were selected and reviewed. We synthesized here findings from structural MRI (sMRI), functional MRI (fMRI), diffusion tensor imaging (DTI), and resting state functional connectivity (rs-FC MRI) studies, comparing females with and without PTSD. A range of biopsychosocial constructs that may leave females vulnerable to PTSD were discussed. First, the ways timing and type of exposure to trauma may impact PTSD risk were discussed. Second, the key role that cognitive and behavioral mechanisms may play in PTSD was described, including rumination, and deficient fear extinction. Third, the role of specific symptom patterns and common comorbidities in female-specific PTSD was described, as well as sex-specific implications on treatment and parenting outcomes. We concluded by identifying areas for future research, to address the need to better understand developmental aspects of brain alterations, the differential impact of trauma types and timing, the putative role of neuroendocrine system in neurobiology of PTSD among females, and the impact of social and cultural factors on neurobiology in females with PTSD.

Keywords: PTSD, females, sex differences, neuroimaging, MRI

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INTRODUCTION

Nearly 90% of adults in the U.S. report lifetime exposure to at least one potentially traumatizing event, while only 8.3% go on to develop posttraumatic stress disorder (1). Females report slightly lower rates of overall trauma exposure as compared to males, but are twice as likely to meet diagnostic criteria for PTSD (2). Females' proclivity to develop PTSD more frequently than

males may be partially explained by greater exposure to specific types of trauma relative to males (e.g., intimate partner violence). However, such an explanation is too glib and fails to consider relevant biological (sex) and psychosocial (gender) substrates of PTSD in females that could provide further clarification as to why females develop PTSD at higher rates than males, and why some females develop PTSD while others do not.

Over the past decade, scholars have begun to examine neurobiological markers of PTSD more closely. A growing body of evidence reflects differential neurological and clinical manifestations of trauma exposure according to sex [e.g., (3)]. Females appear to exhibit specific symptom patterns that vary according to trauma type, timing, and duration (4). For example, adult female victims of severe abuse, particularly sexual abuse, may display higher rates of dissociation than victims of other types of trauma (5, 6). Varying rates of PTSD among females have also been related to the neuroendocrine system, wherein estradiol regulation through the hypothalamus has been identified as a protective factor against developing PTSD following a traumatic event (7–9). Thus, the likelihood that females develop PTSD following trauma exposure may partially dependent on the phase of the menstrual cycle at the time of exposure. The extent of a female's risk of experiencing symptoms of PTSD may also be associated with learned coping styles influenced by social and cultural factors in the environment.

Psychosocial and cultural factors influencing symptom severity in PTSD in females pertain to gender socialization, social support, and cultural definitions of self and femininity, and ascription to traditional gender norms (10–13). Researchers have long posited that females process emotional information differently from males and that there is significant within-group variability that may be attributed to the aforementioned constructs (14, 15). For example, females who ruminate more demonstrate less cognitive flexibility and are thus more vulnerable to negative psychological outcomes, including exacerbated PTSD symptoms (15, 16). Such coping styles may be learned as part of cultural socialization to gender, wherein socialized masculinity is associated with more problem-oriented coping styles and femininity with emotional coping (15). Some, such as rumination, have been associated with poor psychological outcomes and distinct neural correlates (17). Culture may also influence the adaptation of personality traits associated with poor neurological and psychological outcomes, such as neuroticism, found to have its own neural correlates (16). In sum, it is likely that females' distinct risk for PTSD and subsequent severity is comprised of social, environmental, and biological factors. Despite the evidence that such covariates might cause substantial within group variability, few authors have reviewed existing neuroimaging literature regarding the difference between trauma exposed females who do an do not develop PTSD.

Literature reviews examining the role of biological sex in PTSD highlight the influence of the human and animal female neuroendocrine system on PTSD symptoms, fear responses, and extinction [e.g., (8, 18, 19)]. They report mixed findings in the literature, noting that varied impacts of estradiol and progesterone on fear extinction and PTSD symptoms underscore the need for a greater understanding of differences among females with PTSD. Seligowski et al. (19) similarly make important contributions to the current body of literature, highlighting differences between neural correlates of PTSD in males and females while also emphasizing the need for greater understanding of differences among females. A review of neuroimaging findings specific to trauma exposed female samples with and without PTSD would complement this literature, and elucidate future directions for both between and within group comparisons of females with PTSD.

The goal of the present review is therefore to examine and summarize the extant body of research relevant to within-group neuroimaging exploration of females with a diagnosis of PTSD. We hope to clarify neurobiological symptoms of PTSD in females, their prognosis for recovery, and areas for future research. We refer to the female sex throughout the review in order to accurately portray the literature and associated findings for a number of reasons. First, sex, defined as a dichotomous variable stipulated at birth by biology and genetics, encompasses the underlying neural mechanisms of PTSD and the neuroendocrine system. Conversely, gender is a nonbinary, socially defined construct that influences concepts of femininity and masculinity (19). While gender undoubtedly influences PTSD outcomes, there is ample evidence that the influence of such psychosocial factors on the development of PTSD may vary by sex (19). Additionally, in many of the studies summarized participants' gender identity is not consistently reported in the literature, term "female" may be a more accurate description of the relevant literature. While we use the term female and mainly refer to biological differences between PTSD and trauma exposed controls in the aftermath of exposure to trauma, it is important to note that these differences are not necessarily innate only and may interact with environmental factors.

METHODS

Database searches in PubMed, PsychInfo, and EBSCOHost were conducted to find peer-reviewed scholarly works exploring neural mechanisms and brain morphology related to PTSD in females, elucidated by neural imaging through MRI. We did not limit the timeframe of publications to allow for breadth in results. Search criteria included female samples of who had undergone MRI scans related to PTSD. Search terms included "neuroimaging," "sex differences," "PTSD," "women," "females," "MRI" and "fMRI." The initial search returned 87 articles, the abstracts of which were subsequently screened to determine whether they met inclusion and exclusion criteria. Only studies that included MRI scans (sMRI, fMRI, rs-FC) of female samples who met the full diagnostic criteria for PTSD were included. No animal studies met inclusion criteria. Studies including male samples were included as long as there were within-group analyses among females. Relevant articles were imported into Covidence, a software system designed to assist in systematic literature reviews, and submitted to other reviewers for their opinion. Of the initial articles, 24 were deemed irrelevant, leaving a total of 63 articles for full-text review. Following the review of the full-text, ten additional studies were removed because they

did not meet the inclusion criteria. Subsequent to the initial search, a complementary manual search was conducted to ensure that the authors captured the full breadth of literature on PTSD in females. An additional search was conducted using the keywords "pediatric PTSD," "MRI," and "females." This search returned 18 articles, of which only three were eligible for review according to inclusion criteria. As such, a total of 56 studies were included, as shown in **Table 1**.

RESULTS

In this literature review, we present putative factors impacting neurobiological and clinical presentations of PTSD in females. We review the role of key external determinants including trauma timing and trauma type, intrapersonal considerations and neural correlates that place females particularly at risk of developing PTSD, and conclude with the ways that these may culminate in the clinical presentations of PTSD in females. We then address the impacts PTSD has on both mothers' abilities to relate to their children, the neural substrates of mothers with PTSD, and the subsequent effects that has on their children. Finally, we end with a discussion of treatment outcomes among females with PTSD.

The Role of Trauma Characteristics in Neurobiological Presentation

Trauma Timing

Trauma that occurs early in life severely influences brain development (70). The extent and location of the impact is modulated by the timing, type, and duration of the traumatic exposure during childhood (4, 68, 71). Because male and female brains mature differently due to sex differences endogenous to the neuroendocrine system, it is important to understand the effects of childhood trauma on the brain of females. One of the types of childhood maltreatment studied most frequently in the PTSD literature en masse is childhood sexual abuse (CSA) (66, 72). Surprisingly, there were few neuroimaging studies that met the inclusion criteria for our review. This section of the review presents the immediate and the long-term neurobiological impacts of CSA in females with PTSD documented in the neuroimaging literature.

Neurodevelopmental outcomes of female victims of CSA with PTSD appear to differ from those of healthy controls. Areas of activation in the brain associated with CSA can be seen in **Figure 1**. In adolescence, female victims of CSA showed compromised BOLD activity using reinforcement learning fMRI tasks showed compromised activity and increased cortical thickness within the frontoparietal network (FPN) (68, 69, 73). As survivors develop into adulthood, such impacts to the FPN may translate into compromised neurological and cognitive functioning (63, 74).

Adult female victims of CSA that occurred before the age of twelve may exhibit decreased gray matter volume (GMV) in the visual cortex and right basolateral and cortical amygdala, in addition to smaller splenium than healthy controls (63, 75). Similarly, they continue to exhibit alterations in the FPN and somatosensory network sizes in resting state fMRI tasks, which vary according to symptom severity (59, 68). We interpret these findings of the protraction of deficits in the FPN, together with reduced GMV in the amygdala and visual cortex, to suggest that female adult survivors of CSA may struggle with aspects of executive functioning, including visual memory, attention shifting, and learning.

The severity of these deficits is likely influenced by the timing of CSA. For example, the literature has established that sexual abuse between 10 and 11 years is likely to damage the amygdala (59). Other critical periods have been established for the hippocampus (3–5 years), corpus callosum (9–10 years), and the prefrontal cortex (14–16 years) (4). The ways that these neurobiological presentations manifest as clinical symptoms of PTSD will be discussed further in a following section of the review.

Additional literature about childhood maltreatment and abuse pertains to samples of adolescents and adult females with mixed types and histories of physical, emotional, and sexual abuse in childhood, which we will refer to as childhood maltreatment. There is expanding evidence to support the notion that female adolescent brain development is affected by childhood maltreatment. For example, in adolescent victims of mixed types of childhood abuse, brain volumes are compromised in the insula, splenium, hippocampal, and frontal lobe suggesting an increased rate of myelination in comparison with healthy controls (67). This may lead to alterations in executive functioning and processing of self-referential information (5, 30). The deviation from normative development in the splenium, otherwise one of the fastest-developing parts of the corpus callosum in normative samples between 4 and 18, can debilitate visual focus and the modulation of visual information in the thalamus (76). In all, these varied pathways of neurological growth due to childhood abuse have the potential to impact development across the lifespan.

As females develop into adulthood, these deficits appear to continue throughout the brain, manifesting as overall reduced GMV and cortical thickness (CT) in some areas (i.e., the amygdala, visual cortex, midcingulate cortex, subiculum and presubiculum; see **Figure 1**) and increased CT in others (i.e., FPN) (5, 59, 63, 64, 69, 72, 74). Resting state functional connectivity appears interrupted between the visual, frontoparietal, and default mode networks (59). Similarly, adult females with a history of childhood abuse show more activity in the amygdala in response to fearful stimuli than healthy controls, which may suggest challenges in top-down regulation (49). In some female survivors of childhood maltreatment, such neurobiological profiles may result in challenges with executive functioning, self-referential processing, social relationships, and emotional regulation [e.g., (5, 57, 67)].

As with CSA, the nature and extent of the neurobiological and subsequent psychological impact of childhood maltreatment appears to be associated with its severity and duration (59, 67, 69, 72–74). For example, dissociation severity has been negatively correlated with GMV in the ventral attention network (VAN) (59). The duration of childhood maltreatment and CSA and corresponding severity of neurological alterations in males and

TABLE 1 | List of studies included.

References	Sample size	Sample mean age and SD when available	Trauma type	Trauma timing	Imaging type
Adult samples					
Aupperle et al. (20)	14	40.07 (SD = 7.44)	IPV	Adulthood	fMRI: Cued anticipation task
Aupperle et al. (21)	22	34.60 (SD = 9.40)	IPV	Adulthood	fMRI: Stop/signal Task
Berman et al. (22)	62	25.21	Sexual assault	Adulthood	MRI, fMRI- rsFC
Berman et al. (23)	62	25.21	Sexual assault	Adulthood	MRI
Brown et al., (24)	70	32	Interpersonal violence	Adulthood	fMRI: Implicit emotional interference/conflict task
Brown et al. (16)	61	31.05	Interpersonal violence	Adulthood	fMRI: Emotion interference/conflict matching task, rsFC
Buchholz et al. (17)	39	31.33 (SD = 9.38)	Interpersonal violence	Adulthood	fMRI: Emotion interference task
Cisler et al. (25)	16	33.8 (SD = 10.8)	Interpersonal violence	Adulthood	fMRI: trauma memory recall task
Cisler et al., (26)	40	33.26	Interpersonal violence	Adulthood	fMRI: trauma memory recall task
Cisler et al., (25)	16	33.8 (SD = 10.8)	Interpersonal violence	Adulthood	fMRI: trauma memory recall task
Crombie et al. (27)	121	33.15	Interpersonal violence	Adulthood	MRI
Felmingham et al., (28)	86	Not indicated	Mixed (accidents and interpersonal violence)	Adulthood	fMRI: fear perception task
Fonzo et al. (29)	24	Not indicated	IPV	Adulthood	fMRI: emotional face-matching task, rsFC
Fonzo et al. (30)	33	Not indicated	IPV	Adulthood	fMRI: emotional face processing task, rsFC
Graziano et al., (31)	21	31.9 (11.04)	Mixed interpersonal violence	Adulthood	DTI
Graziano et al., (32)	78	31.45	Mixed interpersonal violence	Adulthood	DTI
Jovanovic et al. (33)	41	39.2	Mixed, specific type not indicated	Not indicated	fMRI: Go/No go task
Landre et al. (34)	34	24.8	Sexual abuse	Adulthood	MRI
Moser et al. (35)	35	33.49	Interpersonal violence	Adulthood	fMRI: separation task
Moser et al. (36)	48	33.6 (5.4)	Interpersonal violence	Adulthood	fMRI: separation task
Neumeister et al. (37)	36	26.47	Interpersonal violence	Adulthood	fMRI: trauma-related picture processing task
Neumeister et al. (38)	38	26.84	Interpersonal violence	Adulthood	fMRI: trauma related word-processing task
New et al. (39)	42	36.3	Sexual abuse	Adulthood	fMRI: explicit emotion regulation task
Philippi et al. (40)	71	31.93 (9.39)	Interpersonal violence	Adulthood	fMRI: Self-related impact coding task, rsFC
Privratsky et al., (41)	65	33.7 (9)	Not indicated	Not indicated	fMRI: fear conditioning and extinction task
Ross et al. (42)	29	31.17	Interpersonal violence	Adulthood	fMRI: reinforcement learning task
Sartin-Tarm et al. (43)	43	30.8 (8.2)	Interpersonal violence	Adulthood	fMRI: fear conditioning and extinction task
Satterthwaite et al. (44)	105	31.22	IPV	Adulthood	fMRI: rsFC
Schechter et al. (45)	45	26.18	Interpersonal violence	Adulthood	fMRI: maternal separation task
Schechter et al. (46)	59	34.2 (5.7)	Interpersonal violence	Adulthood	fMRI: maternal separation task
Simmons et al. (47)	30	35.73	IPV	Adulthood	fMRI: cued anticipation task
Simmons et al. (48)	30	34.58	IPV	Adulthood	fMRI: cued anticipation task
Stevens et al. (49)	40	38.4	Mixed	Adulthood	fMRI: emotion regulation fear and neutral face processing task
Strigo et al., (50)	38	35.62	IPV	Adulthood	fMRI: experimental pain paradigm task
Vatheuer et al. (51)	99	29.38	Not specified	Not specified	MRI
Weaver et al., (52)	19		Interpersonal violence	Adulthood	fMRI: emotional conflict task
Weaver et al., (53)	61	32.34	Interpersonal violence	Adulthood	fMRI: reward-punishment contingency task
Bluhm et al., (54)	32	38.53	Childhood maltreatment	Childhood	fMRI: Free thinking task
Chalavi et al., (55)	61	42	Childhood maltreatment, Adult IPV	Childhood	MRI
Chalavi et al., (5)	65	39.48	Childhood maltreatment	Childhood	MRI

(Continued)

TABLE 1 | Continued

References	Sample size	Sample mean age and SD when available	Trauma type	Trauma timing	Imaging type
Frewen et al. (56)	30	37.22 (7.00)	Childhood maltreatment, interpersonal violence	Childhood	fMRI: emotional imagery/numbing task
Frewen et al. (57)	44	30.86	Childhood maltreatment	Childhood	fMRI: visual-verbal self-other referential processing task
Kitayama et al., (58)	18	37.3	Childhood maltreatment	Childhood	MRI
Lebois et al. (59)	65	34.37 (12.2)	Childhood maltreatment	Childhood	fMRI: interference, masked faces, and rest tasks
Ludascher et al. (60)	25	28.38	Childhood maltreatment	Childhood	fMRI: Dissociation-script task
Sierk et al. (61)	42	40.12	Childhood maltreatment	Childhood	fMRI Diffusion MRI
Steuwe et al. (62)	32	32.06 (12.03)	Childhood maltreatment	Childhood	fMRI: eye contact task
Steuwe et al., (62)	32	32.06	Childhood maltreatment	Childhood	fMRI: eye contact task
Tomoda et al. (63)	37	19.75	Childhood sexual abuse	Childhood	MRI
Veer et al. (64)	24	27.5	Childhood maltreatment	childhood	MRI
Child/adolescent samples					
Cisler et al., (65)	34	13	Childhood maltreatment	Childhood/ Adolescence	fMRI: implicit threat processing
DeBellis and Keshavan (66)	183	11.72	Childhood maltreatment	Childhood/ Adolescence	MRI
Klabunde et al. (67)	59	13.9	Interpersonal violence	Childhood	MRI
Letkiewicz et al. (68)	60	15.3	Interpersonal violence	Adolescence	fMRI: reinforcement learning task
Ross et al., (69)**	253	14.7 (1.9)	Childhood maltreatment	Adolescence	MRI

fMRI, functional Magnetic Resonance Imaging; MRI, Magnetic Resonance Imaging; IPV, Intimate Partner Violence; DTI, Diffusion Tensor Imaging.
*** Included adolescents and adults.*

females is also likely a combination of biological and psychosocial considerations. For example, if a child feels safe disclosing abuse to a caregiver then the continuance of the abuse might be less. In such cases, the child's social environment would therefore have facilitated a lesser duration of abuse, perhaps leading to improved neurobiological outcomes (77). This again underscores the probable relationship between environment and biology in the development of PTSD and potential neurological impact (77). Further neuroimaging research is needed to examine the specific interaction of nonbiological and biological factors on neurobiological outcomes of childhood maltreatment and sexual abuse in females.

Trauma Timing Summary

Female survivors of CSA and other forms of childhood maltreatment have distinct neurobiological profiles when compared to healthy controls, with modified aging in various parts of the brain associated with emotion regulation, executive functioning, and learning. Specifically, the literature accentuates differences in the connectivity and cortical thickness of FPNs between healthy controls and survivors of sexual abuse. Concurrently, it indicates varying outcomes in GMV in the visual cortex, frontal lobe, corpus callosum, and the VAN in survivors of other types of childhood maltreatment. Because much of the literature on childhood maltreatment works with samples who have suffered different types of abuse, it is likely that some of the results in the literature pertaining to general childhood abuse overlap with those specifically examining CSA. Type of abuse notwithstanding, the impact of the abuse on brain development is directly correlated with the age at which the abuse occurred, its severity, and duration (4, 66). The literature also highlights the distinct severity of the neurobiological impact of abuse prior to the age of 12 [e.g., (63)], thereby providing support for critical periods of neurological development in females. The extent of the modifications in neurobiological presentations resulting from abuse is likely also a function of environmental and social factors.

Trauma Type

Females are more vulnerable to interpersonal violence than males (78, 79). Broadly, interpersonal violence is emotional, physical, or sexual violence by a perpetrator who may or may not be an intimate partner. The literature describes two types of interpersonal violence that are more commonly directed toward females: intimate partner violence (IPV) and sexual assault. IPV is defined as physical, sexual, or emotional violence at the hands of a romantic partner or significant other (78, 80). In the literature, sexual assault is also examined without specification as to whether the perpetrator is an intimate partner. Other studies investigate interpersonal violence using samples that combine types of interpersonal violence (e.g., physical, sexual, emotional abuse). Therefore, a neural typology of specific types of interpersonal violence is difficult to ascertain. We will explore the evidence for existing patterns in the following sections.

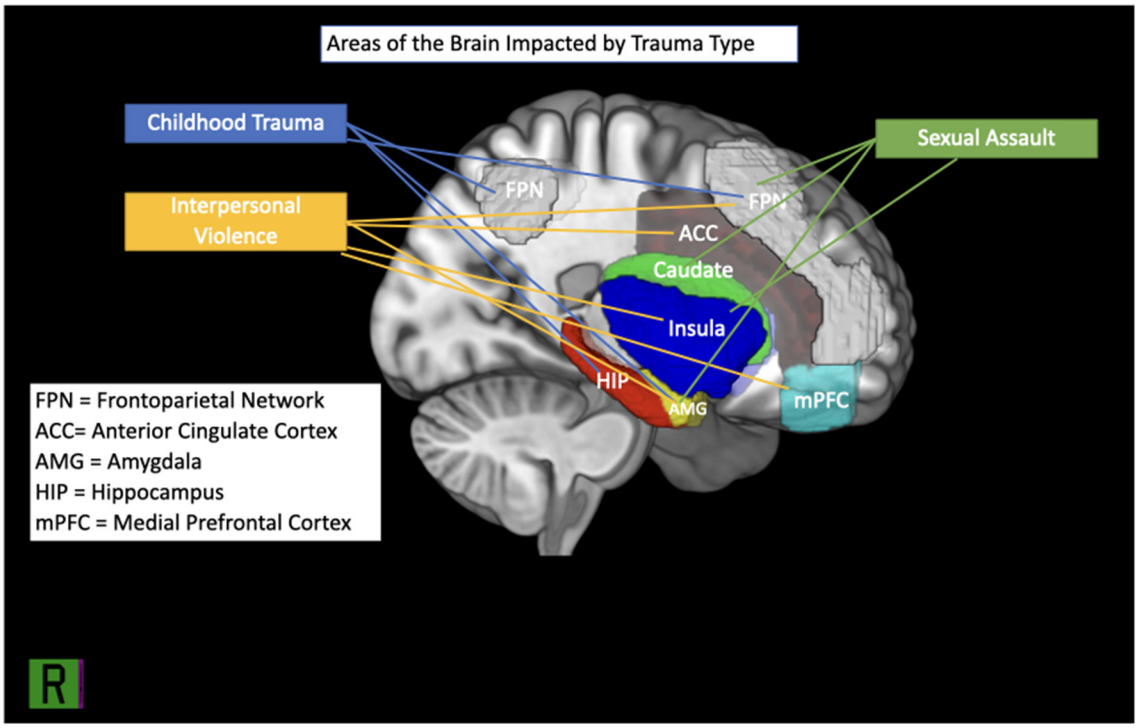

FIGURE 1 | Brain regions implicated in IPV, childhood trauma and sexual assault.

Intimate Partner Violence

Adult females are more likely than males to experience and report being victims of intimate partner violence in their lifetime than males (78), yet only eight of the neuroimaging studies reviewed specifically address neural correlates of IPV. Although scarce, existing literature suggests that female survivors of IPV with PTSD exhibit neurobiological changes relative to healthy controls. Aberrations from healthy controls manifest in various ways across the frontoparietal, default, and salience networks, and translate into difficulty with executive functioning, emotional regulation, and hypervigilance [e.g., (29, 81)].

Within-group comparisons suggest divergence among females with IPV-PTSD from healthy controls in activity in the amygdala, anterior cingulate cortex, insula, dorsolateral prefrontal cortex, and medial prefrontal cortex (21, 29, 82). In general, it appears that some female survivors of IPV may struggle to accurately appraise situations as threatening or not and, in turn, to adjust neural responses to task demand (29, 82). Challenges with top-down regulation are reflected in trends toward increased activity in the medial and dorsolateral PFC, anterior ACC, and insula evaluating social and emotional stimuli in comparison to healthy controls (21, 29, 35, 82–84). Conversely, a proclivity toward hypoactivation of the frontal and parietal lobes when neural activation is required suggest further challenges modulating arousal, perhaps leading to avoidance and numbness often reported in PTSD (29, 50, 82). In some females, such issues may be further compounded by hyperactivity in the anterior cingulate cortex and dorsolateral prefrontal cortex, suggesting deviations from normative abilities to focus and integrate contextual information into emotional responses (35). Some female survivors of IPV-PTSD exhibit disorganized connectivity between the frontal and limbic systems, resulting in sustained periods of heightened arousal that may cause them to misdirect and fixate their attention on nonthreatening stimuli (82).

Taken together, these deficits may leave females with PTSD vulnerable to further neural dysregulation in the face of future trauma. Clinical presentations of PTSD in female survivors of PTSD may also be impacted by social and environmental variables, such as lack of perceived social support and cultural messages about blame in intimate partner violence (10, 81). The magnitude of the effect of these and other environmental and social covariates on neurobiological presentations in female survivors of IPV remains to be explored in the neuroimaging literature examined for the present review.

Sexual Assault

Adult females are more vulnerable to SA than males (79), making the neurobiological profiles of female survivors of SA with PTSD of particular interest. Of the studies reviewed, five directly examined survivors of sexual assault. Similar to IPV survivors, the female samples of sexual assault presented with varying alterations of GMV, activity and functional connectivity in the brain areas frequently implicated in PTSD (e.g., the insula, amygdala, right caudate, prefrontal cortex, and medial occipital cortex). The composite of the neural correlates found in the literature suggest hyperactivity in the insula and prefrontal

cortex, in addition to aberrant GMV in the amygdala, right caudate, and insula in female survivors of SA as compared to healthy controls (22, 23). Similar to IPV survivors, the female samples of SA survivors also presented with changing degrees of activity and resting-state functional connectivity (rsFC) in the brain areas frequently implicated in PTSD (e.g., the insula, amygdala, right caudate, and medial occipital cortex) (22, 23, 34). Hypoactivation in the prefrontal cortex provides further support for challenges with emotional regulation and the executive functioning required for attention shifting (39). Collectively, female survivors of SA who have PTSD may face greater difficulties in the realms of information processing related to self and others, hyperarousal, and executive functioning than healthy controls. As a result, they may be more susceptible to PTSD symptoms of greater severity if faced with subsequent traumatic events.

Given the paucity of studies specifically examining the neural correlates of IPV-PTSD due to sexual assault in female samples, it is difficult to determine how females with IPV and sexual assault might be distinct in their neurobiological presentation. Results suggest similar presentations wherein there may be compromised ability to manage arousal in the amygdala and insula, thereby engendering deficits in automatic emotional processing. Such alterations may necessitate greater activation of the prefrontal cortex, perhaps reflecting the brain's attempt to overcompensate for a lack of control in the amygdala and insula. Relative to healthy controls, differences in social processing are fairly common in female survivors of sexual abuse, perhaps due to smaller volumes of the right caudate. There is also research to suggest that there are sociocultural elements that may predispose females to sexual assault, such as living in poverty and prior history of abuse (85). Additional research is needed to determine whether there is a difference in neural underpinnings of sexual assault and IPV, and the ways that society and culture may influence outcomes and neurobiological symptoms of PTSD in female survivors of sexual assault and IPV.

Mixed Samples of Interpersonal Violence

Remaining studies addressing interpersonal violence in females combine types of interpersonal violence, diluting the impact of each type of interpersonal violence on the female brain. It is therefore difficult to establish a unique neurobiological profile for female survivors of interpersonal violence with PTSD based on extant literature. However, results echo those discussed in prior sections, with deviations from healthy controls in GMV in addition to variations in subcortical activity and rsFC. Different findings from those already reported provide insight into the role of the corpus callosum in the brain, specifically the genu (31). Others have found increased right caudate volumes, perhaps leading to difficulty managing social expectations and threat appraisal (26, 27). Increased GMV in this region of the brain have been associated with other forms of psychopathology, including psychosis (86), further emphasizing the degree of compromised functioning in females with PTSD. Because most are studies examining fMRIs related to specific symptoms of PTSD, they will be reviewed in further detail when we examine clinical presentations of PTSD and their neural correlates.

Other Trauma Types

There is a gap in the neuroimaging literature surrounding the neural correlates of PTSD in females related to types of trauma other than those described above (i.e., medical trauma, natural disasters, or other). Our literature search rendered only three neuroimaging studies examining the neural correlates of PTSD stemming from other types of trauma in females meet our inclusion criteria. One examines the neural correlates of PTSD among breast cancer survivors, finding no significant differences in amygdala and hippocampal brain volume as compared to healthy controls (87). One did not clearly specify the types of trauma that the females in their samples had experienced, and another mixed trauma from accidents with interpersonal violence. The results of these studies are discussed in later sections in which we identify neural correlates of specific symptom clusters of PTSD in females.

Trauma Type Summary

Although it is difficult to determine the association between the type of interpersonal violence females incur and neurobiological deficits in functioning, the literature appears to establish that interpersonal violence impacts females' brains (see **Figure 1**). More specifically, it seems to cause weakened regulation of arousal by impacting GMV in the amygdala and insula, while creating a deficit in rsFC between the insula, amygdala, and prefrontal cortex that weakens executive, cognitive, and social functioning. What remains unknown is the extent to which this impact is influenced by individual differences within samples, such as variability among subjects' trauma load, symptom severity. Further, study designs are largely cross-sectional and sample sizes are generally small, thereby reducing the generalizability of the results found. Finally, as we highlighted in each of the sections above, the extent of the interaction between trauma exposure and sociocultural factors on neurobiological presentations in females with and without PTSD remains largely unexplored by neuroimaging research.

Underlying Purported Mechanisms

In addition to differential susceptibility to specific types of gendered trauma, there are individual determinants that influence neurobiological presentations in females with PTSD. In the present section, we will examine some of these, including the neuroendocrine system, coping mechanisms, and behavioral mechanisms of PTSD in females.

The Neuroendocrine System

The impact of the neuroendocrine system on fear circuitry in the brain is well-documented among healthy females. Specifically, due to the high amount of estrogen and progesterone receptors in the amygdala and hippocampus, these areas are particularly susceptible to differential functioning and volume throughout the female menstrual cycle (8). These fluctuations can manifest as more frequent and severe symptoms of reexperiencing intrusive memories, negative alterations in mood (e.g., increased anxiety and depression), and difficulty with memory and executive functioning. For example, extinction recall is negatively impacted during the early luteal phase of the menstrual cycle (8, 88).

Despite the abundant evidence that the neuroendocrine system influences individual PTSD symptoms in female humans and rodents, only one study met our inclusion criteria of a diagnosis of PTSD. Sartin-Tarm et al. (43) examined the impact of estradiol on fear habituation in females with and without PTSD and found that estradiol was positively correlated with activation in the anterior cingulate cortex and dorsomedial prefrontal cortex during fear habituation responses. Low levels of estradiol negatively predicted the ability to habituate to fear extinction among those with PTSD. These results further stress the importance of the timing of the traumatic event on neurological susceptibility to trauma responses and the development of PTSD.

Emotion Regulation and Gendered Coping Mechanisms

Challenges with emotional regulation among females with PTSD reflect changes in several regions of the brain, presumably impacted by posttraumatic stress. The neuroimaging literature posits that females' implicit and explicit emotional regulation is affected by altered neural connectivity. Broadly, it suggests hypoactivity in the vmPFC and hyperactivity in the amygdala (49, 89). This hyperactivity may result in excess physiological and emotional arousal in females with PTSD and, in turn, lead to deficits in executive functioning required for emotion regulation. This is particularly true when females diagnosed with PTSD are faced with tasks of increasing cognitive demand or emotional load (21, 39, 52, 89).

Emotion regulation is also affected by the positive or negative evaluation of stimuli and its relevance to the initial traumatic event. Among females with PTSD, more threatening stimuli are associated with increased activation in the hippocampus and amygdala and decreased connectivity between the insula, the dACC, and the amygdala relative to healthy controls (29, 53). Challenges with emotional regulation are also evident in bottom-up regulation wherein females show hypoactivity of the vmPFC in response to positive stimuli (56). Taken together, it appears that females with PTSD exhibit distinct modifications in neurobiology that result in greater emotional dysregulation relative to healthy controls, often as a function of cognitive load. These neurobiological alterations may interfere with the executive functioning required for emotion regulation (21, 33). Overall, these patterns in the literature reflect a neural hypoactivity when faced with positive events, and hyperactivity and an attentional bias when faced with negative events. It is likely that the negative attention bias, together with the gendered coping mechanisms previously discussed (i.e., rumination and neuroticism) contribute to the other symptoms of hyperarousal and create a unique profile of arousal in females with PTSD.

Some of the challenges with emotional regulation discussed may be related to socialization to more gendered coping styles and, in turn, impact neurobiological presentations in females with PTSD. Certain emotion-focused coping styles and personality traits may leave females more vulnerable to developing psychopathology when faced with stressors or traumatic events (15). Perhaps two of those most documented are rumination, relevant to the PTSD symptom of reexperiencing (90), and neuroticism, a personality trait related to general psychopathology at large (15, 16).

Rumination

Researchers have found that females ruminate more than men and that rumination, an emotion-focused coping style defined as self-referential thought focused on negative outcomes, is a transdiagnostic consideration in psychopathology (15). The tendency to ruminate has been correlated with sociocultural considerations such as identification with femininity, as well as biological sex factors like estradiol levels (12, 91). As the other constructs reviewed, rumination and its impact on PTSD symptoms is therefore likely the product of nature and nurture.

Extant literature characterizes rumination as the function of potential deficits with executive functioning, including memory (92), attentional shift (16), emotional processing, and coping (15). These correlate with hyperconnectivity between the right amygdala and the mPFC, PCC, precuneus, and the orbital cortex, reflecting the need to make a greater cognitive effort to shift attention sets (21). Conjointly, such weaknesses may cause those who ruminate to fixate on negatively-valenced emotional information, thereby leading to exacerbated outcomes among females with PTSD. For example, rumination in females with PTSD has been positively correlated with the frequency and intensity of reexperiencing symptoms, corresponding to increased GMV in the left isthmus cingulate (40, 90, 93).

Neuroticism

Much like rumination, neuroticism, a personality construct defined as one's proclivity toward experiencing negative emotional states, is associated with poor psychological outcomes (16, 94). Those who endorse higher levels of neuroticism may experience high levels of anxiety, have difficulty coping with challenging situations, and display poorer emotion regulation than others 16). Females with PTSD who display more neurotic tendencies experience PTSD symptoms of greater severity (95), making it important to understand the neural correlates of neuroticism.

Like rumination, neuroticism interferes with the ability to objectively evaluate environmental stimuli, due to an overactivation of brain regions associated with fear, self-referential processing, and value judgments needed to make accurate decisions. Neuroticism is positively correlated with hyperactivation in the amygdala, right PFC, dmPFC, and parahippocampus (16). Together, rumination and neuroticism leave females with PTSD more vulnerable to reexperiencing, negative alterations in mood, difficulty with memory, and accurate fear-based learning.

Behavioral Mechanisms

Behavioral mechanisms of PTSD involve fear-based learning, such as extinction, value expectation, and inhibition. Fear extinction is an important part of PTSD symptom reduction and recovery and is therefore a large part of APA-recommended PTSD treatments like exposure therapy (96, 97). Fear extinction requires the ability to accurately assess potentially fearful future events, to inhibit fear responses when they arise and decrease

arousal, and the eventual ability to learn from experiences (98). The neuroimaging literature suggests that females diagnosed with PTSD present with deficits in the neural underpinnings of each of these processes, contributing to rigid thinking and learning styles which thereby hinder their recovery (21).

Accurate assessment of future events requires application of prior knowledge and experiences to future situations and their possible outcomes. The literature suggests that many females with PTSD may struggle to integrate prior experiences into their expectations and responses to situations and tasks at hand, in threatening and nonthreatening situations (42). Because females with PTSD may have difficulty incorporating lessons learned into decision making and problem solving, they may resort more to trial and error in problem solving tasks (68). This may be due to a propensity to prediction errors, combined with an attentional bias in the brain toward negative information that is consistent with inaccurate value expectations (26, 48). Females with PTSD are more neurologically reactive to anticipated negative events and less so to anticipated positive events than healthy controls, thereby further complicating the formation of expectations (47). Neuroimaging results suggest that these outcomes are associated with deficits in the FPN, and hypoconnectivity in the ACC and dmPFC (26, 68).

Inhibition is also an important part of reversing fear-based learning, involving the ability to monitor one's own mental and physiological state and to purposefully react to the same (21, 99). The literature reviewed reflects the notion that females with PTSD may struggle with inhibition, such that they may find it difficult to regulate arousal in response to external stimuli. These challenges are reflected in hyperactivation of the insula, dmPFC, the striatum, the amygdala, and hypoactivation of the vmPFC (21, 33, 48). Such abnormalities may result in difficulties with cognitive control, attention shifting, and processing of self-referential information, all processes required to inhibit arousal (47, 99). Such deviations from normative social learning, expectation formation, and inhibition may contribute to the documented mixed outcomes of exposure therapy in among females with PTSD.

Successful extinction has been negatively correlated with activation in the vmPFC and bilateral amygdala (96). However, females with PTSD display the opposite neurological profile when engaging in extinction learning tasks. Another important factor that is not often considered by the neuroimaging literature is the impact of individual estradiol levels on extinction learning, frequently overlooked by extant neuroimaging evidence (43). Although previously discussed, it is important to highlight it here as a factor that may make females more vulnerable to varying results in behavioral treatments of PTSD.

Underlying Mechanisms Summary

Females have distinct coping styles and ways of regulating their emotions, corresponding to personality (e.g., neuroticism), cognition, (e.g., rumination), and behavior (e.g., fear processing). These are each associated with a specific neural presentation and may be linked to both gender and sex. Although each has specific neural correlates, they appear to reflect a common pattern of decreased connectivity between the insula and dmPFC. In addition, the literature reflects patterns of hyperactivity in the amygdala, insula, dmPFC, and striatum with deficits in connectivity between the amygdala and the vmPFC. The mechanisms reviewed may leave females more vulnerable to worsening trauma symptoms and unique presentations of PTSD and comorbid disorders. In the following section, we examine the literature surrounding neural correlates of clinical presentations of PTSD in females, including symptom types, severity, and comorbidity.

Presentation

The DSM-5 classifies PTSD according to criteria across four symptom clusters: reexperiencing, or experiencing unwanted memories of the traumatic event; hyperarousal, evidenced by symptoms such as being startled easily or hypervigilance; avoidance of stimuli that are reminders of the traumatic event; and increased negative affect across several domains, including irritability, anhedonia, and feelings of alienation from others (100). As previously noted, these symptoms often differ in severity and duration, often according to the type and timing of trauma. For females, clinical and neurobiological presentations may also be a function of the phase of their menstrual cycle in which the trauma occurs, together with age (8). In the present section we will review the different types of clinical presentations that arise in females with PTSD, according to symptom cluster.

Reexperiencing

A hallmark of PTSD is reexperiencing the traumatic event through intrusive thoughts, memories, or nightmares, which may be triggered by direct or indirect reminders of the traumatic event (100). The neuroimaging literature on females with PTSD examines reexperiencing through fMRI imaging of subjects being exposed to direct or indirect reminders of the traumatic experience [e.g., (35)], or through the correlation of self-report of reexperiencing with GMV and rsFC [e.g., (27)]. In general, the evidence suggests that females who indicate higher rates of reexperiencing symptoms exhibit altered neural correlates associated with visual memory and inhibition, and increased activity between the limbic and default networks.

Among females with PTSD, reexperiencing is associated with reduced CT in the left inferior and mid temporal gyrus and increased GMV in the lingual gyrus (22, 27). Diffusion Tensor Imaging (DTI) similarly suggests compromised white matter volumes (WMV) of the postcentral gyrus in the corpus callosum. The alterations of WMV in the corpus callosum may suggest deficits in the processing and communication of visual information between hemispheres (21, 31). The increased GMV of the lingual gyrus, also associated with inhibition and top-down regulation, may lead to difficulties in preventing memories from surging to conscious awareness. This may lead females with PTSD to feel flooded by visual memories of their traumatic event, thereby increasing overall arousal (101).

Distress associated with reminders of traumatic events is reflected in an increased rsFC between the right and left amygdala, the right inferior frontal gyrus, the right hippocampus, and the visual and dorsomedial cortex (27, 37, 38, 102). It is concurrently associated with hypoconnectivity between the

lingual cluster and the fusiform cortex, responsible for the voluntary and involuntary processing of trauma memories (22). The combination of hyper- and hypoactivity in these areas of the brain may reflect the brain's altered ability to assimilate traumatic memories and prevent hyperarousal when confronted with reminders of the same.

Hyperarousal

Hyperarousal among individuals with PTSD manifests as irritability, impulsivity, hypervigilance, difficulty sleeping, inability to concentrate, and exaggerated startle responses (102). These symptoms may indicate deficits in emotion regulation, often described in PTSD as part of a "feedback loop" that leads to further arousal, thereby creating challenges with concentration and reliable evaluation of environmental stimuli (101).

Hypervigilance can generally be defined as a sense of constant awareness of one's surroundings, even in situations one knows to be safe. Surprisingly, we found the neural correlates of hypervigilance to be largely understudied in females with PTSD. However, the little evidence that exists describes a pattern of hyperconnectivity between the amygdala, insula, ACC and the superior colliculus and locus cereleus in females with PTSD (102). These areas of the brain, responsible for visual and auditory processing and arousal, suggest overactivation which, together with the negative attention bias previously discussed, may lead to appraisals of otherwise neutral stimuli as threatening (21, 102).

Negative Affect

Negative affect and changes in mood are often reflected in self-blame, exaggerated negative perceptions of self and others, anhedonia, and detachment or estrangement from others (102). Extant literature reports that many females with PTSD have an overwhelmingly negative self-image coupled with tremendous guilt relative to those without PTSD. They may find themselves debilitated in their ability to modify such negative cognitive distortions, due to rigidity in thinking, which has been connected to poor psychological outcomes (48, 57). Neural correlates reflect a greater preoccupation with the self than others as well as a negative attention bias toward their own qualities, relative to healthy controls. This attention bias may manifest as a tendency to accept more negative qualities about themselves, while also endorsing more positive qualities about others. Examinations of neural activity suggest greater activity of the visual cortex when imagining the self as opposed to others, in addition to greater activation in the mPFC when considering negative qualities about themselves (57). The correlates of self-blame mirror those of reexperiencing, exhibiting reduced GMV in the lingual gyrus, such that self-blame may involve an aspect of reexperiencing among females with PTSD (21, 57). Cumulatively, these results may suggest difficulty regulating emotions in relation to the self and negative cognitive distortions about the self, with favorable biases toward others.

Avoidance

Among males and females, avoidance is associated with heightened global PTSD symptom severity (103). Females with PTSD who engage in avoidance with greater frequency show reduced CT in the occipital gyri, as well as the left lateral fissure and right posterior cingulate (27). The posterior cingulate cortex has been found to mediate information between emotions and memory (104), while the lateral fissure and occipital gyri have been associated with visual and working memory. The reduction in CT may suggest a decreased capacity to process emotional memories and uncertainty about the safety of their surroundings due to prediction errors. In turn, individuals with PTSD may develop avoidance as a coping skill to escape overwhelming feelings that may be associated with their inability to accurately process emotional and environmental stimuli.

Specifiers: PTSD With Depersonalization or Derealization

The most recent diagnostic classification for PTSD includes a specifier for a dissociative subtype (PTSD-D) to identify the presence of persistent symptoms of depersonalization or derealization. DSM-5 defines depersonalization as "persistent or recurrent experiences of feeling detached from, and as if one were an outside observer of, one's mental processes or body," and derealization as "persistent or recurrent experiences of unreality of surroundings" (105). PTSD-D can therefore be summarized as a presentation of PTSD in which there is a disconnection, or dissociation, from one's lived experience.

Extant neuroimaging literature comparing females with PTSD-D to healthy controls suggests that dissociative experiences relate to hyperactivity in the somatomotor network (i.e., the right superior temporal gyrus, involved in auditory processing) and frontoparietal lobes, specifically in the left inferior, precentral, and medial gyri (59, 60). Higher rates of dissociation severity are negatively related to activation in the parahippocampal gyrus, associated with memory formation and spatial location of objects, and hypoactivity in the ventromedial prefrontal cortex (59, 60, 106). Accordingly, the neurobiological profile of females with PTSD-D suggests difficulties with emotion regulation, likely caused by a sense of sensory and emotional overwhelm. Altered activity in the vmPFC may suggest deficits in amygdala regulation (89), leading to challenges in downregulating excessive arousal, and hypervigilance among some females with PTSD. This presentation is heightened by deficits in synchronization between key brain regions including the amygdala, hippocampus, thalamus, and the brain stem (61), proposed to be linked to the experience of dissociation.

Presentation Summary

Females with PTSD present with altered GMV and WMV in areas of the brain responsible for emotion and visual processing. These deviations from volumes in healthy controls correspond to hypoactivity of brain structures involved in top-down and bottom-up emotion regulation (i.e., the vmPFC) and executive functioning (i.e., the dmPFC), in addition to hyperactivity of areas related to arousal (i.e., the amygdala) and sensory processing (i.e., the right superior temporal gyri).

Comorbidities

A review of clinical presentations of PTSD in females would be incomplete without a discussion of the literature related to

comorbidities. As many as 83% of males and females diagnosed with PTSD present with a comorbid disorder, and female gender has been identified as a risk factor for the same (107, 108). As such, it is important to review the neuroimaging literature regarding specific comorbidities that occur with PTSD. PTSD rarely occurs by itself, and it is frequently associated with comorbidities such as Major Depressive Disorder (MDD), Dissociative Identity Disorder (DID), Borderline Personality Disorder (BPD), and Substance Abuse Disorder (55, 109, 110). Past literature has studied neural correlates of each of the aforementioned comorbidities with PTSD in females except Substance Abuse Disorder.

PTSD and Major Depressive Disorder

Reports on the incidence of PTSD-MDD vary, but the literature reports it as one of the most commonly occurring comorbidities among patient populations with PTSD. Recent statistics show that up to 89% of males and females with PTSD present with PTSD-MDD (108–110). Despite the high prevalence of depression among PTSD populations, there is little neuroimaging research that specifically investigates the neural correlates of PTSD-MDD in females. The only study we found that met the inclusion criteria for this review implicated a hypoconnectivity between the amygdala and the frontal and temporal lobes in PTSD-MDD (44). These results replicate others found in literature that examined PTSD, perhaps because so many studies contain samples with mixed presentations of PTSD in females, including PTSD-MDD [e.g., (49)]. Despite these findings, there is still not enough information to clearly establish a neurobiological profile for PTSD-MDD.

PTSD and Borderline Personality Disorder

A comparison of the symptoms of BPD and PTSD in the DSM-5 reveal an overlap of symptoms. Patients of BPD and PTSD both present with difficulty with emotion regulation; an unstable sense of self, marked by negative self-image; dissociative symptoms; and a proclivity toward impulsivity or behaviors that might incur self-harm (100). As such, one might expect that the literature would reflect similarly impacted areas in the brain, both in GMV and rsFC, perhaps on a larger scale due to the presence of a dual diagnosis. However, the study that met the inclusion criteria for the present review actually found no significant differences between GMV of the amygdala, vmPFC, or bilateral ACC when comparing females with BPD and PTSD to those with PTSD alone (51). The dearth of neuroimaging literature surrounding BPD and comorbid PTSD, en masse with these results that suggest insignificant differences between neurobiological profiles, suggests the need for further investigation of this comorbidity.

PTSD and Dissociative Identity Disorder

PTSD-DID has been examined largely as it pertains to differences in morphology between females afflicted with the disorder and healthy controls. Results are again insufficient in volume to reveal a specific neurobiological profile of PTSD-DID, but portray interesting findings surrounding subcortical GMV in females with PTSD-DID. More specifically, PTSD-DID has been associated with reduced hippocampal GMV with concurrent increased GMV in the right putamen, pallidum, and striatum as a function of the severity of dissociative symptoms (5, 55). It is unclear from the current body of literature whether these neural correlates also correspond to those with PTSD-D.

Summary of Comorbidities

In general, there is a lack of information surrounding comorbidities with PTSD and associated neural correlates in female samples that precludes conclusions about specific neurobiological profiles of each. Perhaps one of the most challenging components of studying such comorbidities is that PTSD symptoms are shared among so many psychiatric disorders, such that determining specific neural correlates is particularly challenging (44). It is perhaps this overlap in symptoms and variety of presentations that lead to differing outcomes and prognoses among females with PTSD.

Sex Related Outcomes of PTSD

We turn now to an examination of the outcomes of PTSD among females, looking at some of the ways that trauma further impacts them specifically. We begin by reviewing literature on the ways that PTSD impacts mothering and corresponding neural correlates and end with a review of treatment outcomes.

Parenting Outcomes: Mothers With PTSD and Their Children

Children of mothers with PTSD are more likely to experience traumatic events than children of healthy mothers (111). The literature documents one possible explanation as lower levels of attunement and maternal sensitivity among mothers with PTSD, particularly if a mother endured severe childhood trauma [e.g., (45, 112)]. Parenting requires the ability to mentalize (i.e., take another's perspective by identifying their emotions), empathize, and respond sensitively to a child's needs (36). As we have documented, PTSD may result in emotional dysregulation and a proclivity toward interpreting neutral social information as threatening, resulting in a state of persistent hyperarousal. In mothers, it is likely that such constant hyperarousal complicates their ability to respond sensitively to their young.

Evidence for heightened arousal when faced with stress in relation to their young can be found in decreased activation of the vmPFC among mothers with PTSD relative to healthy controls (36, 46). Altered emotion regulation may cause mothers with PTSD to respond differently to separation from their children than healthy controls, manifesting as heightened arousal and increased activity in the dmPFC (36). Thus, mothers with PTSD may have more difficulty engaging in parental reflective functioning relative to healthy controls, thereby complicating the formation of a secure attachment with their children.

Children of mothers who suffered childhood abuse exhibit patterns that mirror their mothers' emotion regulation, evidenced by decreased vmPFC activity. Relative to children of healthy controls, the literature points to a higher probability that children of mothers with PTSD endure a traumatic event or develop psychopathology, perhaps related to emotion regulation and arousal (46, 111). Together, the neuroimaging literature

reflects the detrimental impacts of intergenerational trauma on youth when a mother has PTSD, making it imperative that the field move toward a greater understanding of the etiology, presentation, and treatment of PTSD in females.

Treatment Outcomes

Results of clinical trials of treatment in females with PTSD suggest that outcomes are largely dependent upon trauma severity, independent of age or clinical approach. Few approaches have been examined solely in female samples, emphasizing the challenge in coming to conclusions regarding best practices specifically for females with PTSD. No treatment was reviewed more than once in the literature reviewed, such that results have not been replicated among more than one sample of females.

Extant neuroimaging literature investigates the impact of Trauma-Focused Cognitive Behavioral Therapy (TF-CBT), Exposure Therapy (ET), and Cognitive Processing Therapy (CPT) on rsFC (20, 21, 25, 65). Results suggest that, regardless of the modality, effective treatments improve connectivity between the amygdala, the insula, the right hippocampus, and the right superior frontal gyrus (21, 25, 65). Therapy for PTSD among females has also been correlated with an increase in WMV in the splenium and left cingulate gyrus, thereby rehabilitating communication between the left and right hemispheres (32). Symptom reduction from treatment is therefore likely observed in increased emotional and physiological regulation, thereby granting patients a sense of greater self-control and reduced fear.

Such outcomes appear to be predicted by trauma type and severity more than other individual factors, such as age (20, 25). As previously established, these covariates moderate the degree to which neural correlates change as a result of trauma, and treatment outcomes are often a function of pretreatment neurobiology. For example, the success of TF-CBT appears to be a function of pre-existing amygdala connectivity with the dACC in threatening situations (65). Similarly, pretreatment levels of activation in the amygdala and the insula, corresponding to anticipation of negative events, predicted CPT outcomes (20). Outcomes in the corpus callosum are similarly predicted by the extent of the damage that existed pretreatment (32).

As a whole, there is evidence to suggest that current evidence-based treatments are efficacious in repairing certain neurological impacts of PTSD in females, particularly for those who present with mild to moderate trauma loads. However, little is known about meaningful interventions for victims of more severe types of trauma, highlighting an area for further research.

DISCUSSION

This review addresses the neurobiological presentation of females with PTSD and potential covariates that may contribute to the higher incidence of PTSD reported among females. The significance of the type and timing of the traumatic event, the neuroendocrine system, gendered coping styles, and outcomes of trauma in females are discussed. Where possible, we highlighted the likely relationship of biological and nonbiological factors on PTSD outcomes in females. We identify areas of further research pertaining to females with PTSD.

In general, females with PTSD present with altered GMV, WMV, and connectivity between the amygdala and prefrontal cortex. Females are more vulnerable to specific types of traumatic exposures than males, but based on the current body of research, it is difficult to establish a specific neurobiological profile in females with PTSD according to the type of traumatic event. Many of the studies examining interpersonal violence use samples with survivors of different types of interpersonal violence, complicating the ability to make clear conclusions. Prior literature underscores the impact of sexual assault on females, noting its potential to modify DNA expression (113, 114). Such results emphasize the need for further research that clearly distinguishes between trauma types in samples. Additionally, as with most neuroimaging literature, the generalizability of the results is limited by small sample sizes, convenience samples, mixed trauma histories within samples, and cross-sectional designs. Because neuroimaging studies largely do not focus on cultural factors affecting clinical outcomes, the findings presented do not adequately consider cultural factors that may influence brain development and outcomes in PTSD.

The present review summarized the impact of the type and timing of trauma on PTSD outcomes in females. Type of trauma notwithstanding, it appears that trauma is most detrimental when it occurs in childhood, modifying the naturally occurring aging process in the brain. In females, childhood trauma is associated with specific symptoms of PTSD, such as dissociation (5). The severity of these symptoms varies as a function of the duration and severity of abuse, which is likely related to social factors in the victim's environment. The susceptibility of victims of childhood abuse to adverse neurobiological outcomes is consistent with prior literature suggesting that there are critical periods for neurological development in which the brain is more vulnerable to the effects of stress and trauma (4, 83). The literature makes a distinction between childhood abuse before the age of 12, partially due to the onset of menstruation in females.

Our findings suggest that the type of trauma sustained is perhaps less influential on the brain than a victim's age upon initial trauma exposure. This may be due to the relative lack of comparison between trauma types among females in the neuroimaging literature. Nonetheless, there are unique factors to consider when examining the influence of trauma type on brain development that are not necessarily addressed by extant neuroimaging literature. For example, IPV is distinct from interpersonal violence because of the unique dynamic in which a victim knows and has a close, intimate relationship to their assailant (10). This experience is uniquely accompanied by betrayal trauma, in addition to specific subtleties related to disclosure and subsequent emotional and psychological impacts of the same (11). Such contextual factors create nuances in the experience of trauma exposure and type that are not reflected in the current body of literature, such that trauma type may be more influential on the brain than current neuroimaging findings suggest.

Another factor that was ostensibly absent from the neuroimaging literature examined in the present review was the female neuroendocrine system. Although the literature reviewed acknowledges the impact of menstrual phase on

female presentations, it offers little insight regarding the effect of the neuroendocrine system on neurological and symptom presentation of PTSD in females. Other reviews have documented that the phase of the menstrual cycle correlates to memory, fear responses, reexperiencing, and negative mood in females with and without PTSD (8, 115). Similarly, the timing of trauma in relation to the onset of puberty has also been found to predict severity of PTSD symptoms (116). Consistent with other literature examining the impact of estradiol on learning, the present review found one study that suggested a positive association between estradiol and fear extinction (43). Female hormones of estradiol and progesterone fluctuate throughout the menstrual cycle, and this variation is moderated by the hippocampus (8). The hippocampus itself has been shown to fluctuate in volume throughout the menstrual cycle and has been associated with positive treatment outcomes [i.e., (117, 118)]. It would therefore seem logical that further research investigate the impact of the neuroendocrine system on females' presentation of PTSD and neurobiological substrates throughout the menstrual cycle. Because it is largely ignored by the neuroimaging literature, it is likely that the field is missing information necessary to establish a complete typology for females with PTSD. Put simply, it appears that hormonal fluctuations are a covariate that many authors have failed to consider in extant neuroimaging research on females diagnosed with PTSD.

However incomplete due to the lack of studies examining the neuroendocrine system, there is evidence that females engage in specific types of emotion-based coping that may, in turn, influence the severity of their neurological and psychological symptoms. Neuroticism and rumination may be rooted in societal beliefs that problem-oriented problem solving and coping is masculine (17, 40, 119, 120). Such coping styles and traits have been correlated to negative emotional outcomes which, when combined with PTSD, may leave females particularly vulnerable to developing further psychopathology. Neurobiological profiles associated with these traits highlight increased GMV in the temporal lobe and hyperactivation in the prefrontal cortex (17, 90). These alterations lead to more frequent incidences of reexperiencing and hyperarousal, thereby further debilitating already compromised emotion regulation and executive functioning in some females with PTSD (90). Such exacerbated presentations create mixed outcomes for females with PTSD, particularly as it pertains to maternity and treatment.

Females with PTSD may have more difficulty establishing secure attachments with their children than healthy controls (121). Although not exclusively focused on females, prior studies have found that dismissive and fearful attachment styles correlate with dismissive or fearful adult attachment styles (122). Mothers with dismissive attachment styles may be less sensitive to their children's needs, reflecting a deficit in mentalization and parental reflective functioning (36, 45, 46, 123). The neuroimaging literature suggests that these deficits are correlated with increased arousal and activity in the prefrontal cortex when faced with stress in the parent-child relationship. It is likely that cultural and societal factors are also important in parenting outcomes among females with PTSD, but this is largely unexplored in the present neuroimaging literature pertaining to mothers.

Although the presentation of symptoms for females with PTSD appears bleak and compounded by the unique types of traumatic events they may experience, there is reason for hope. Treatment outcomes suggest moderate efficacy among those with mild to moderate PTSD. Like the remaining body of literature, studies are limited by small sample sizes, mixed sources of trauma, comorbidities, and overlapping symptoms. Further research is needed to understand ways of reaching females with more severe symptoms of PTSD, in addition to the effect of cultural and societal factors and their interaction with neurobiology on symptom severity and prognosis.

Limitations

Perhaps the most important limitation of our review is that a focus on neurobiological substrates of PTSD in females detracts from the worthwhile examination of societal and cultural factors influencing PTSD symptom presentation and severity in females. For example, gender norms often impact the way females manifest psychopathology [e.g., (14)]. While we attempted to address this shortcoming by discussing gender norms surrounding emotional coping styles, there are certainly other nonbiological factors that impact PTSD in females, such as perceived social support and peer reactions to trauma disclosure (10). We posit that this weakness is also a reflection of the biological focus of neuroimaging literature, and suggest that future neuroimaging research consider more thoroughly the impact of cultural and societal influences on the neurobiological presentation of females with PTSD.

By including only studies that used MRI imaging, we did not report on several studies that use PEG and EEG methods in female samples with PTSD that may have been relevant to our review, of which there are several. Including studies that used other forms of neuroimaging may have provided a more complete picture of females with PTSD, symptom clusters, and their neural correlates. Many MRI studies use convenience samples, such that the participants within the studies reviewed do not likely represent all females with PTSD. Most samples consisted of predominantly white females, thereby limiting the generalizability of the findings presented to females of color or those who are nonbinary.

By excluding studies in which subjects had probable instead of confirmed PTSD, we likely failed to include valuable information about females' presentation and recovery from PTSD. To that end, PTSD is not the only clinical outcome of a traumatic event as many females present with Major Depressive Disorder as their primary diagnosis. Such studies are equally important to the present body of literature, but were not included in this review for the sake of cohesiveness. Similarly, by including only studies that make comparisons of females with and without PTSD, we cannot specify whether the findings described here are sex-specific or sex-related. Findings in mixed sex samples point to sex similarities

and differences in neural connectivity in PTSD. Findings in mixed sex samples point to sex similarities and differences in neural connectivity in PTSD. For example, both females and males with PTSD show increased activation in the dACC in tasks of extinction (124). On the other hand, Helpman et al. (125) found that females with PTSD displayed rs-FC patterns that were the opposite of males and healthy females, pointing to sex-specific neural patterns in PTSD. Such mixed findings underscore the need for further research examining females with and without PTSD. Finally, as the neuroimaging literature does not consistently report the gender identity of participants, the impact of gender, rather than sex, cannot be teased out. Moreover, the pertinence of the findings to persons across the gender spectrum may be limited. Further research is needed to address the relevance of findings to those across the gender spectrum, in addition to the replicability of prior outcomes.

To summarize the literature, we grouped samples according to trauma type and timing. In doing so, we may have overlooked the fact that many with PTSD experience multiple traumas in childhood and adulthood. This, however, is also reflected in the current body of literature that amalgamates trauma types and timings in an effort to comprehend the neural underpinnings of PTSD of females. Similarly mirroring the neuroimaging literature which often presents mixed findings, the neurobiological outcomes discussed may differ from those previously found by other authors. However, fMRI studies in particular are frequently scrutinized for limited replicability based on imaging methodology, ROI used, and fMRI tasks involved (126, 127). Therefore, these differences may also be the result of varying study designs and procedures. Finally, due to the amplitude of studies included and the varying methods they used, we synthesized information about some regions of the brain more broadly instead of referring to specific brain regions, such as the prefrontal cortex and anterior cingulate. Many studies examine different areas of each, such that results were grouped according to their larger brain region for clarity. We suggest that future reviews focus specifically on the impact of PTSD on these brain regions in females, thereby providing an opportunity for richer discussion of the workings of the prefrontal cortex and anterior cingulate cortex.

CONCLUSION

The present review highlights biopsychosocial factors that may make females vulnerable to PTSD, clinical presentations of PTSD in females, and their neural correlates. Clinical presentations in females reflect deficits in the brain related to executive functioning (i.e., dmPFC), emotion regulation (i.e., amygdala), and inhibition (VAN). The differences between females with and without PTSD highlighted in this review reflect important considerations for future research, particularly as it pertains to the impact of the neuroendocrine system on clinical presentations of PTSD. Similarly, we highlight the need for more consistency in samples of females with PTSD, especially as it pertains to comorbidities, trauma type, and timing. We are hopeful that, in years to come, there will be more representation of females in PTSD literature such that their needs are more specifically considered by psychology and psychiatry.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

AUTHOR CONTRIBUTIONS

EE-M: literature search, writing-original draft, and revisions. XZ and MB: writing-review and editing. CF: literature search and writing—editing. LH: conceptualization and writing-review and editing. YN: conceptualization, funding acquisition, supervision, and writing-review and editing. All authors contributed to the article and approved the submitted version.

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A Promotive Process of Resource Gain Against Harsh and Inconsistent Discipline in Mothers Coping With Breast Cancer: A Serial Mediation Model

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Breast cancer is a life-threatening disease and a source of enduring stress. The Family Stress Model posits that psychological distress provoked by stressful conditions may spill over and intensify harsh and inconsistent parental discipline. However, the Conservation of Resources theory posits that having more resources may lead to further resource gain, which may promote adaptive coping with adversities. Therefore, this study examined a serial mediation model in which financial resources (income) are predicted to be associated with more interpersonal resources (paternal involvement). The latter is expected to be linked with less maternal post-traumatic stress symptoms, which, in turn, should be associated with less harsh and inconsistent discipline in mothers coping with breast cancer. A sample of 100 Israeli mothers receiving breast cancer treatments was recruited through social media. The participants completed online self-report questionnaires. Structural Equation Modeling indicated significant serial mediation, in which a greater income level was associated with more paternal involvement, which was linked to a lower level of maternal post-traumatic symptoms. The latter, in turn, was associated with less harsh and inconsistent maternal discipline practices. We controlled for illness severity and the time since diagnosis, which did not predict maternal discipline practices. The study suggests that although breast cancer is a stressful condition for any family, having more financial resources can be a significant promotive factor predicting a cascading process by which paternal functioning facilitates better mental health of mothers, and, in turn, better maternal parenting practices.

Keywords: resource gain, income, paternal involvement, post-traumatic symptoms, maternal parenting practices

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INTRODUCTION

Breast cancer (BC) has been identified as the most common cancer and the most frequent cause of cancer mortality in women. In 2020, about 2.3 million BC diagnoses and 685,000 deaths were documented worldwide. BC is more prevalent in older ages (1), but some women may face it at a young age (2). Young women are more likely to have at least one minor child living at home (3), and are more willing than non-parent patients to receive aggressive treatments to increase their likelihood of survival (4, 5). BC patients with

dependent children cope not only with intensive treatments [i.e., surgery, radiation therapy, endocrine therapy, chemotherapy, or targeted biologic therapy; (6)] and their side effects (e.g., pain, fatigue) but also with childcare (7). Because mothers are typically the primary caregivers, they experience more parenting concerns than fathers who are cancer patients (8). Mothers with BC report a range of problems related to parenting, including physical limitations (e.g., fatigue) and difficulty in maintaining the child's routine [for a review, see (9)]. They also report lower parental self-efficacy and satisfaction compared with healthy mothers (10, 11). Moreover, their children tend to experience more emotional distress, externalizing, and internalizing behavioral problems compared with children of non-ill mothers (12, 13).

Long-standing research emphasizes that parenting is a major protective factor for healthy child development in the face of adversity (14). For example, while illness characteristics (e.g., cancer site, stage, time since diagnosis) were not found to be associated with the physical, emotional, and social wellbeing of children whose parents had cancer (7), supportive caregiving was associated with lower child anxiety levels (15). It is therefore imperative to identify promotive processes (e.g., resources gain) for maternal parenting practices while coping with BC, which is the focus of the current study. Specifically, we tested whether financial resources are indirectly associated with less harsh and inconstant maternal discipline through a serial mediation process involving greater paternal involvement, which in turn is linked with less maternal post-traumatic stress symptoms (PTSS). The findings of this study may facilitate the development of interventions designed to improve parenting practices for mothers with BC, which may ultimately benefit their children's adjustment.

A Theoretical Framework

The Family Stress Model (FSM) posits that stressful conditions may intensify emotional distress, which may deplete the psychological resources of parents, making them more inclined to use harsh or inconsistent disciplinary practices (16, 17). Harsh discipline is defined as coercive acts directed toward children, expressed by verbal (e.g., yelling) or physical aggression (18). Inconsistent discipline refers to a lack of adherence to rules and standards related to children's behavior (19). Such negative parent-child interchanges were postulated to result in behavioral problems in children (16, 17). To date, research on the parenting quality of cancer patients has focused mostly on communication about the disease and empathic responses to children [for a review see (12)], but not much is known about harsh and inconsistent discipline practices while undergoing BC treatments.

The FSM was supported in several stressful conditions, including economic hardship (16, 17, 20) and traumatic stress (21–23). BC is a life-threatening disease, which may trigger traumatic psychological reactions (24). Cancer patients may experience fear of cancer recurrence and fear of death (25), and they are at risk for post-traumatic stress disorder [PTSD; for reviews see (26, 27)], even more than other types of cancer [for a review see (28)]. The prevalence of PTSD in BC patients varies from 3 to 32.3% across studies, and it is more prevalent at younger ages (25, 29). Although PTSS have been linked with more harsh and inconsistent discipline practices (23, 30), it was not studied in the context of BC. The research on BC patients shows that greater psychological distress is associated with more difficulties in parental (11, 31) and family functioning (32). Hence, the current study aims to expand the scope of the literature by focusing on the associations between PTSS and harsh and inconsistent discipline in mothers dealing with BC treatments.

The Promotive Role of Resource Gain When Facing BC

The FSM posits that even under stressful conditions, promotive factors (i.e., factors that directly predict positive outcomes) may facilitate better psychological and interpersonal functioning of family members (33). The Conservation of Resources theory [COR; (34)] further illuminates a mechanism by which promotive factors operate to enhance better adaptation to trauma. Specifically, in the wake of trauma, individuals seek to secure, retain, and gain resources, but they often lose them, which may lead to further loss of resources (35). Personal (e.g., personality traits), social (e.g., support), and material resources (or lack thereof) determine the extent to which a situation is perceived as stressful vs. manageable (36). Thus, a major loss of crucial resources may lead to a traumatic response (35). In contrast, having more resources may lead to a spiraling process of resource gain (36), which provides a sense of security, a basic foundation for one's survival, and thus strengthens the psychological resilience for traumatic stress (34). Relying on the COR theory, we were interested in examining a promotive process of resource gain in mothers coping with BC. Specifically, we aimed to examine whether their material resources (i.e., income) are associated with more social resources (i.e., paternal involvement), which in turn predict lower PTSS and sequentially less harsh and inconsistent discipline.

Income as a Promotive Resource for Families Facing BC

Income is a vital resource for family functioning and more so when dealing with illness, a situation that often requires paying for costly medical, psychological, or instrumental services (37, 38). Hence, besides health concerns and demands, families dealing with BC may face economic strains (39). The FSM posits that under economic strains, psychological resources may dampen, resulting in disrupted co-parenting relations (16). Indeed, economic strains have been negatively associated with co-parenting quality (40). Fathers are particularly sensitive to financial problems, which may impair their co-parenting relationships (41). In this study, we focused on the association between economic resources and paternal involvement. Paternal involvement is defined as cooperative co-parenting, specifically by support provision in caregiving tasks (42), and it is interrelated with co-parenting relations (43).

While economic stress may hinder co-parenting relations through psychological distress (16), the COR theory posits that having more financial resources can help parents cope better with

stressors by providing a greater sense of security that facilitates psychological adaptation (34, 36). In fact, parents with greater resources such as higher income tend to invest more time in childrearing and co-parenting activities than those with fewer resources (44). As such, it could be that when dealing with BC, more economic resources may help fathers be more engaged in paternal tasks.

The amount of support provided by fathers with wives diagnosed with BC tends to depend on their partner's level of physical impairment (45). While coping with their partner's cancer, fathers often experience strains related to their caregiving roles while still handling other tasks of work and finance (46, 47). Research on BC indicates that more frequent BC demands are associated with greater depressive mood, which is associated with lower marital quality (48). However, the effect of financial resources on paternal involvement and their cascading effect on maternal harsh and inconsistent discipline in families facing BC has not been studied.

Paternal Involvement as a Promotive Factor Against PTSS

When coping with BC, the support provided by a spouse is a major resource that predicts a better quality of life for women (49). In contrast, having an unsupportive or unhelpful partner predicts a higher level of anxiety in women with BC (50). Because cancer treatments may impede maternal functioning (7), and because mothers are often the primary caregivers, paternal involvement can serve as an interpersonal resource. Greater resources are postulated by the COR theory to promote a greater sense of security that facilitates psychological resilience in the face of trauma (34).

Social support has been found to be a protective factor against the development of PTSS following potentially traumatic events (51, 52), such as a cancer diagnosis (25, 53). More social support also predicts greater post-traumatic growth and better quality of life in women survivors of BC (54, 55). Similarly, a higher quality of co-parenting relations predicts lower levels of depressive symptoms and stress in mothers expecting their second child (56). As such, it could be that greater paternal involvement, as a form of support, will be associated with lower PTSS in mothers coping with BC.

The involvement of fathers may lead to less harsh and inconsistent maternal practices troughs lower PTSS levels in mothers. Given that social support and marital relations are associated with better family functioning and higher levels of parenting confidence when coping with cancer (48), and that lower PTSS are associated with lower harsh and inconsistent discipline (23), it could be that greater paternal involvement will be negatively associated with harsh and inconsistent discipline practices in mothers with BC, mediated by lower maternal PTSS levels.

In sum, the FSM postulates that psychological symptoms associated with stress may spill over and increase harsh and inconsistent parenting (16, 17). However, promotive factors may facilitate better psychological and family functioning (33). The COR theory further explains that resources can be accumulated and thereby promote better psychological adjustment to traumatic stress (36). Research evidence supports the FSM in the context of trauma (23), and points to various promotive factors for families facing adversity (33). However, evidence regarding the association between PTSS and harsh and inconsistent discipline in women fighting BC is lacking. Moreover, the promotive role of resource gain for mental and parental resilience in mothers battling BC has not yet been studied. These gaps are addressed in the current study.

The Current Study

The present study aims to examine a resilience process, by which promotive factors, namely, economic resources, are serially linked to less harsh and inconsistent discipline of mothers coping with BC through more paternal involvement and lower maternal PTSS. Relying on the FSM and COR theory, we tested whether more economic resources (i.e., income level) are associated with more interpersonal resources (i.e., paternal involvement), which are related to lower maternal PTSS, and in turn, less harsh and inconsistent discipline in mothers coping with BC treatments.

Research Hypotheses

1. Lower family income levels will be associated with more harsh and inconsistent discipline of mothers coping with BC.
2. The association between income level and harsh and inconsistent discipline will be serially mediated by paternal involvement and maternal PTSS levels. Within this hypothesis, we hypothesized that: (a) paternal involvement will mediate the link between income level and maternal PTSS levels, and (b) maternal PTSS levels will mediate the link between paternal involvement and harsh and inconsistent discipline.

METHOD

Participants

The sample included 100 Israeli mothers who have been diagnosed with BC and were undergoing BC treatments. The participants were mothers of children aged 6–17. We focused on this age group because it has been recognized to be at risk for the development of emotional and behavioral problems when parents are dealing with cancer [for a review, see (57)]. The mean age of mothers was 46.02 ($SD = 6.06$). Most of the mothers were married (88%). The rest indicated they are cohabiting with a partner (4%), involved in a relationship (1%), or divorced (7%). Women reported an average of 17.58 years of marriage or current intimate relationship ($SD = 6.23$) and a mean of 2.94 children ($SD = 1.01$). The majority of participants earned at least a Bachelor's degree (66%) and reported an average of 15 years of education ($SD = 2.75$). The majority of the mothers (65.6%) worked at least part-time (68.7%). The vast majority of mothers were born in Israel (90%) and considered themselves secular (67%) and Jewish (99%). All were native Hebrew speakers. The family income of the participants varied between 0 and 5,000 ILS (1%), 5,000–10,000 ILS (18.6%), 10,000–15,000 ILS (20.6%), 15,000–25,000 ILS (41.2%), 25,000–30,000 ILS (15.5%), 30,000 or

higher (3.1%). For comparison, the mean family income in Israel in 2018 was 24,872 ILS ($7765) (58).

Most of the mothers reported being diagnosed within the past 12 months (66%). Disease stages were zero (2.1%), one (13.8%), two (37.2%), three (27.7%), or four (19.2%). During the study, mothers reported receiving cancer treatments, including chemotherapy (40%), biological therapy (37%), hormonal therapy (35%), radiation (25%), or other treatments (6%).

Procedure

After receiving IRB approval from [The Paul Baerwald School of Social Work and Social Welfare at the Hebrew University in Jerusalem], the data were collected between July 2018 to September 2019. Participants were recruited using a convenience sampling method. The first author advertised the study in closed online BC groups on social media. First, mothers who were interested in participating were asked to fill out a short, online screening questionnaire assessing their compatibility with the research criteria. Namely, participants had to be native Hebrew speakers, mothers to children aged 6–17 and diagnosed with BC who are currently undergoing cancer treatments. Mothers who have met the screening criteria were automatically referred to an online survey. Next, mothers consenting to participate were asked to complete an anonymous online self-report questionnaire.

Measures

Income

Mothers were asked to indicate their total family income including salaries or any other income (e.g., social security) by choosing between the following options: 0–5,000 ILS, 5,000–10,000 ILS, 10,000–15,000 ILS, 15,000–25,000 ILS, 25,000–30,000 ILS, 30,000 ILS or higher.

Posttraumatic Symptoms

The Hebrew version of the Post-Traumatic Stress Checklist for DSM-5 [PCL-5; (59)] is a 20-item standardized and clinically validated self-report measure assessing PTSD as defined by the DSM-5. We used the Hebrew version of the PCL-C 5, which has been widely used and has shown good psychometric properties [e.g., (60, 61)]. Mothers completed the Hebrew version of the PCL-C (civilian version), in which the items refer to PTSS related to a traumatic experience. Respondents were asked to rate the extent to which they were bothered by each PTSD symptom in the past month using a 5-point scale ranging from 1 (*not at all*) to 5 (*extremely*). Higher sum scores indicate greater PTSS. Cronbach's alphas indicated good internal consistency ($\alpha = 0.95$).

Paternal Involvement

The Hebrew version (62) of the Co-parenting Relationship Scale [CRS; (63)] is a 35-item measure assessing seven co-parenting domains, from which we utilized two subscales reflecting the perceived involvement of fathers in parenting tasks, including (a) the 7-item Endorsement of Partner's Parenting subscale, which assesses the perceived parenting of one's partner (e.g., "My partner is willing to make personal sacrifices to help take care of our child"), and (b) the 2-item Division of Labor subscale, which assesses the perceived division of labor in parenting tasks (e.g., "My partner likes to play with our child and then leave dirty work to me"). Mothers rated each item on a scale ranging from 0 (*not true of us*) to 6 (*very true of us*). A total score of paternal involvement was computed by averaging the items after reversing negatively keyed items (Cronbach's $\alpha = 0.87$).

Harsh and Inconsistent Discipline Practices

The Alabama Parenting Questionnaire [APQ; (64)] is a parent-report measure that includes 42 items assessing five dimensions of parenting practices used on children ages 6-17. We used two subscales assessing harsh and inconsistent discipline practices, including the 6-item Inconsistent Discipline subscale (e.g., "You threaten to punish your child and then you do not actually punish him/her") and the 3-item Corporal Punishment subscale (e.g., "You yell or scream at your child when he or she has done something wrong"). A total sum score was computed, with higher scores indicating more harsh and inconsistent discipline (Cronbach's $\alpha = 0.69$). The APQ has demonstrated discriminant and predictive validity (65). The APQ was translated to Hebrew by the first author. The Hebrew version was translated back to English by a scholar not related to this paper and the resulting translation was examined by the first author for accuracy.

Socio-Demographic Background

Mothers completed a brief questionnaire assessing socio-demographic factors, including the age of the mother, country of birth, marital status, economic status, education, religious affiliation, health status, number of children, and number of years married or cohabiting.

Disease and Treatment

Mothers were asked to report whether they were diagnosed with BC ($0 = No$, $1 = Yes$), the stage of the disease (0–4), the time since diagnosis ($1 = up\ to\ 12\ months$, $2 = more\ than\ a\ year$), and current treatments, including chemotherapy, biological therapy, hormonal therapy, radiation, or other treatments.

Data Analysis Plan

A preliminary analysis was conducted using SPSS 25. We then specified a path model using structural equation modeling (SEM) *via* Amos 25 (66) to test the serial mediation model. Missing values occurred across variables and participants, but Little's Missing Completely at Random (MCAR) test indicated that the data were missing at random [$\chi^2(33) = 33.76$, $p = 0.43$]. We, therefore, tested the model using Full Information Maximum Likelihood (FIML) estimation, which uses all available information from the observed data to generate parameter estimates (67). Indirect effects were assessed using Bayesian estimation (68). In this approach, confidence intervals are calculated based on the posterior distribution of the indirect effect as obtained through computerized simulation [Markov Chain Monte Carlo—MCMC; (69)]. When zero falls outside of the 95% confidence interval, it indicates a significant indirect effect.

Power analysis was conducted using Monte Carlo simulation with 1,000 repetitions in Mplus version 8.5. (70). The simulation indicated that we had sufficient power to detect the paths constructing the indirect effect (ranging from 0.81 to 0.99).

The power to detect the serial indirect effect with bootstrap confidence intervals (k = 5,000) was 0.79.

RESULTS

Descriptive statistics and zero-order correlations for the study variables are presented in **Table 1**. Harsh and inconsistent discipline was negatively associated with income level and paternal involvement but positively associated with PTSS. Income level was positively associated with paternal involvement and negatively associated with PTSS of mothers. Paternal involvement was negatively associated with PTSS. Lastly, mothers who were diagnosed more than a year before participating in the study had a more advanced (higher) BC stage and reported lower levels of paternal involvement.

We conducted additional preliminary analyses to examine the relations between other demographic variables and the outcome variable, harsh and inconsistent discipline. Pearson correlations computed to examine links with maternal age and the number of children, and Spearman correlations computed to examine links with education level, employment, and marital status, yielded non-significant associations with harsh and inconsistent discipline. Hence, we did not include these demographic variables in our models.

Next we specified a serial mediation path model in which family income is associated with harsh and inconsistent discipline directly and indirectly through paternal involvement and maternal PTSS levels. In this model, income level was also specified to predict PTSS and paternal involvement, and PTSS was specified to predict harsh and inconsistent discipline. We controlled for cancer stage and time since diagnosis. Results are shown in **Figure 1** in the form of standardized beta coefficients. This model was saturated (i.e., $df = 0$).

As predicted, family income was associated with lower levels of paternal involvement, which was associated with greater PTSS in mothers. PTSS, in turn, were associated with more harsh and inconsistent discipline practices. The model explained 17% of the variance of paternal involvement, 34% of the variance of PTSS, and 22% of the variance of maternal harsh and inconsistent discipline. A more advanced stage ($\beta = 0.21$, $p < 0.05$) and less time since diagnosis ($\beta = -0.24$, $p < 0.01$) was also associated with lower PTSS. However, neither paternal involvement nor harsh and inconsistent discipline was significantly predicted by stage and time since diagnosis. The direct effect of family income on maternal harsh and inconsistent discipline, above and beyond paternal involvement, maternal PTSS, stage, and time since diagnosis, was not significant (see **Figure 1**).

Next, we tested the indirect, direct, and total effects of income level on harsh and inconsistent maternal discipline using Bayesian confidence intervals (see **Table 2**). Several indirect effects in the model emerged as significant. Specifically, the 95% confidence interval of the indirect path between income level and maternal PTSS through paternal involvement did not include 0, indicating significance at the $p < 0.05$ level. As predicted, a greater income level was associated with more paternal involvement, which in turn was associated with lower PTSS in mothers ($\beta = -0.14$, CI [−0.26, −0.05]). The indirect effect of paternal involvement on harsh and inconsistent discipline through PTSS was also significant ($p < 0.05$), such that greater paternal involvement was associated with lower PTSS in mothers, which in turn was associated with lower harsh and inconsistent maternal discipline ($\beta = -0.14$, CI [−0.28, −0.03]). Finally, the serial indirect effect of family income on the mother's harsh and inconsistent discipline through parental involvement and the mother's PTSS was significant at the $p < 0.05$ level. As anticipated, a higher income level was associated with more paternal involvement, which was associated with lower levels of maternal PTSS, which, in turn, were associated with lower harsh and inconsistent maternal discipline ($\beta = -0.06$, CI [−0.13, −0.01]). The total indirect effect of family income on harsh and inconsistent discipline, which includes all indirect paths, significant or non-significant, from family income to harsh and inconsistent discipline, was significant ($\beta = -0.15$, CI [−0.29, −0.04]). However, the total effect, which includes all direct and indirect paths from family income to harsh and inconsistent discipline, failed to reach significance, despite the significant zero-order correlation between these variables.

Because psychological distress may affect perceived support (45), we also tested an alternative model in which the order of the mediators was reversed (maternal PTSS predicting paternal involvement). This model did not yield a significant indirect effect.

DISCUSSION

BC is a potentially traumatic event (24) that may adversely affect maternal functioning [for a review, see (71)]. Relying on the FSM (16, 33) and COR theory (34), the current study aimed to examine a process by which promotive factors (i.e., economic resources and engagement of fathers in parenting) serially predict lower PTSS and in turn less harsh and inconsistent discipline in mothers coping with BC treatments. In line with our hypotheses and theory, we found a serial mediation process in which economic resources promote more paternal involvement, which was linked with lower maternal PTSS, and in turn, with less harsh and inconsistent discipline practices in mothers undergoing BC treatments.

The present study indicates that during BC treatments, having greater PTSS levels places mothers at risk for engagement in ineffective parenting practices. These findings support the FSM (16) and research showing that under stressful conditions, distressed parents tend to have more negative interchanges with their children (23, 33). The current study, however, expands the scope of the extant literature by focusing on the effect of PTSS on harsh and inconsistent discipline in the context of BC. Individuals with PTSS tend to display more anger and hostile behaviors (72). PTSS may deplete the mental resources of mothers, making it more difficult to tolerate intense mother-child interactions (73), which may lead to coercive and inconsistent patenting behaviors (16, 17). It should be noted that our study indicated that the effect of PTSS on maternal practices is above and beyond the severity of the disease and the time since it

TABLE 1 | Means, standard deviations, and zero-order correlations of the study variables.

	1	2	3	4	5	6	*M*	*SD*
1. Harsh and inconsistent discipline	–						16.11	3.61
2. Income level	−0.27**	–					4.51	1.27
3. Paternal involvement	−0.30**	0.43***	–				5.00	1.35
4. PTSS	0.45***	−0.38***	−0.51***	–			40.65	16.35
5. Stage	−0.12	0.12	0.09	−0.18	–		3.48	1.02
6. Time since diagnosis	−0.06	0.09	−0.23*	0.19	0.46***	–		

*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$.

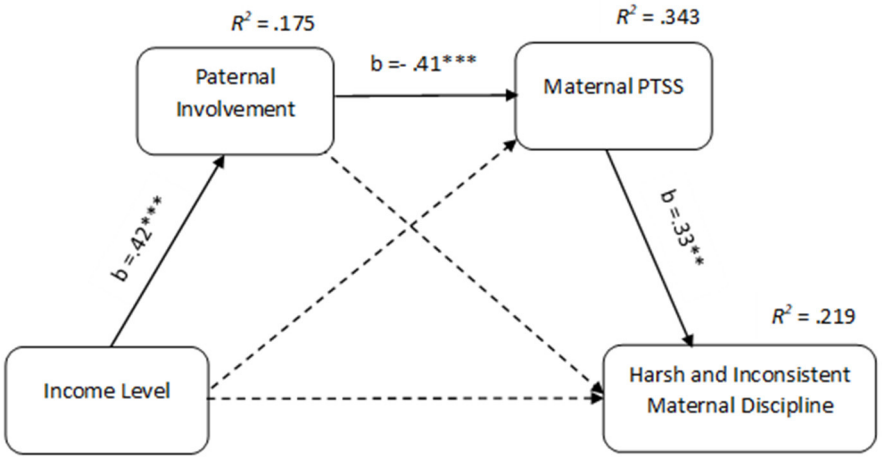

FIGURE 1 | Serial mediation model for the effect of family income on harsh and inconsistent maternal discipline *via* paternal involvement and PTSS of mothers coping with breast cancer. PTSS, Post Traumatic Stress Symptoms. Control variables: cancer stage and time since diagnosis. Entries are standardized structural coefficients. Dashed paths were not found to be significant. **$p < 0.01$. ***$p < 0.001$.

was diagnosed. Consistent with previous research, these findings highlight that the psychological response to trauma rather than the traumatic event itself is the main predictor of engagement in negative parental practices (74).

The study sheds light on a less studied parental behavior in the context of BC: harsh (e.g., yelling) and inconsistent discipline. Research on the parenting of mothers with BC is focused mostly on cancer-related parental tasks such as communicating about the disease (75). Harsh and coercive practices have been repeatedly found to predict behavioral problems in children and adolescents [for a review, see (33)]. Given that children of cancer-patient mothers are at risk to develop psychological and behavioral problems (12, 13), and given that parenting is a central protective factor for children exposed to adversity (14), more attention should be given to this topic.

The present study further points to a possible process of maternal resilience during BC treatments. Specifically, greater financial resources may be particularly important for fathers and promote their greater involvement in parenting tasks, which may then lead to better mental health and parenting outcomes in mothers. This finding suggests a chain of resource gain. The COR theory posits that existing resources may serve as a substrate for the gain or loss of other resources (34–36). In the context of BC, fathers and mothers are required to deal with multiple tasks, challenges, and changes [for a review, see (75)]. This may require out-of-pocket financial investments to cover mounting costs, in addition to caregiving support, often while losing income due to work reduction (39). When confronting uncertain stressful conditions, material resources facilitate a greater sense of security and better capacity to handle stress, thereby promoting better psychological adaptation (34, 36). Psychological security may, consequently, increase fathers' availability to engage in parenting tasks.

We found that in families with more financial resources, fathers were more likely to take part in parenting, which in turn, was associated with lower levels of PTSS in mothers. The COR theory (34–36) explains that having more resources facilitates successful coping with stress. Indeed, previous research indicated that having fewer economic resources predicts PTSD following exposure to trauma (76), including BC (29). Our study points to an indirect pathway by which economic resources promote better mental health in terms of PTSS, through paternal involvement. Social support has long been recognized as a protective factor against PTSD. However, while the extant research focused on general support (51, 52), the present study showed that support in the form of paternal involvement may

TABLE 2 | Total, direct and indirect effects of income, paternal involvement, PTSS and maternal harsh and inconsistent discipline.

Path	Coefficient	SE	Lower CI	Upper CI
Income > PI > HID	−0.03	0.001	−0.14	0.07
Income > PTSS > HID	−0.05	0.001	−0.14	0.02
Income > PI > PTSS	**−0.14**	**0.001**	**−0.26**	**−0.05**
PI > PTSS > HID	**−0.14**	**0.001**	**−0.28**	**−0.03**
Income > PI > PTSS > HID	**−0.06**	**0.001**	**−0.13**	**−0.01**
Income > HID				
Total effect	−0.26	0.003	−0.45	0.05
Direct effect	−0.11	0.001	−0.32	0.15
Total indirect effect	**−0.15**	**0.001**	**−0.29**	**−0.04**

PI, Paternal Involvement; PTSS, Post Traumatic Stress Symptoms; HID, Harsh and Inconsistent Discipline. Significant paths are bold.

be uniquely beneficial to the mental health of mothers during BC treatments.

While undergoing intensive cancer treatments with significant side effects, mothers may fail to maintain a family routine and perform their parental roles (77). BC is a condition in which mothers are required to shift their attention to their own recovery, which may disrupt day-to-day maternal functioning. Mothers are very often the primary caregivers of children and may struggle to balance their own and their children's needs [for a review, see (75)]. The inability to effectively carry out their maternal role is a major source of distress for mothers with cancer (78). For example, mothers are worried about the effects of their cancer on their children's wellbeing and feel guilt, shame, and loss of control [for a review, see (75)]. Thus, having a partner who takes an active part in parenting can facilitate a sense of security, a fundamental protective factor against PTSS when encountering threatening situations such as cancer (34).

Overall, our model suggests a cascading process by which economic resources facilitate a sequence of adaptive behaviors and coping, culminating in better maternal functioning when coping with BC. The current model adds to prior findings regarding the effects of economic hardship, trauma, social support, and PTSS on parenting [e.g., (20, 22, 23)] by examining a comprehensive process combining these factors. The model illuminates a promotive process for maternal functioning at the intersection between cancer and economic condition. Specifically, although cancer may be a stressful condition for any family, good financial status is a significant resource that may lead to a chain of reactions resulting in better paternal functioning and improved maternal functioning and mental state. On the other hand, the findings also suggest that a lack of sufficient financial resources places women with BC at risk of losing additional resources such as paternal involvement. Poor resources may signify the situation as more threatening and hence may intensify PTSS and, in turn, intensify harsh and inconsistent discipline.

Limitations and Future Directions

Several limitations should be taken into consideration when interpreting the results of the current study. First, this is a cross-sectional, correlational study, and therefore no causality or chronological order can be inferred. Given the correlational design, it cannot be concluded that greater economic resources *cause* greater involvement of fathers and subsequently lower levels of PTSS and better maternal functioning. In addition, although an alternative model ruled out that maternal PTSS mediates the relationship between income level and paternal involvement, only a longitudinal design could delineate the temporal sequence of the variables examined in the model.

Second, the exclusive use of self-report measures may be vulnerable to various biases and statistical artifacts (e.g., self-presentation, common method variance). Thus, future studies should incorporate other types of measures and sources of information (e.g., observations, multi-informant surveys). Third, this study used a relatively small sample of 100 women recruited in closed social media groups for women with BC and included only Jewish Israeli women. Therefore, it may not be representative of the entire population of women dealing with BC. It is important to replicate the model in more culturally diverse populations where gender roles in parental tasks may differ. Another issue concerning the generalizability of the findings is related to the specific social policy in Israel. Israel provides universal public health services. Cancer patients also qualify for social security benefits and supportive psychosocial interventions for the target patient and the family without out-of-pocket costs. Perhaps the support provided by the social and healthcare systems in Israel weakened the effects in the model, which accounted for only 22% of the variance in harsh and inconsistent discipline. More research is needed in diverse societal contexts, for instance, in societies that do not have effective universal social and healthcare systems. Another limitation is related to the relatively low reliability of the harsh and inconsistent measures. This finding is consistent with previous findings describing the psychometric properties of the APQ (64). However, the low alpha coefficient may have reduced the effect sizes in the model. Finally, the present study examined family income level as an indicator of family economic resources. Future research should examine the effect of economic recourses in a more detailed way, for example, by testing the serial effect of being above vs. below the poverty line on fathers' and mothers' functioning. These findings may broaden the understanding of the impact of family economic resources on families dealing with BC.

Clinical Implications

A BC diagnosis is often perceived by mothers as the most distressing event in their lives (79), and brings about a range of challenges that may alter mother-child relationships (71). Beyond the physical and emotional difficulties experienced during cancer treatments, a cancer diagnosis may undermine mothers' identity as effective parents [for a review, see (75)]. It is therefore imperative to develop interventions designed to the unique needs of mothers with BC. The present study points to possible promotive resources against PTSS and harsh and inconsistent discipline in mothers coping with BC. Our findings suggest that interventions should incorporate a systemic approach when assisting families coping with BC. At the societal level, interventions should focus on providing financial aid (e.g., disability benefits). At the family level, the model suggests that family interventions aimed at strengthening paternal functioning and co-parenting relationships may sequentially lead to better adaptation of mothers coping with BC. At the individual level, interventions designed to prevent post-traumatic distress may help mothers in their maternal role and ultimately promote their children's wellbeing.

CONCLUSION

BC is a stressful condition that may adversely impact mental health and parental functioning in mothers. This study examined a process by which resource gain is linked with more negative maternal practices during BC treatments. In line with the FSM and COR theory, the study highlights a cascading process by which, when coping with BC, having more financial resources may promote more paternal involvement, which may lead to lower maternal PTSS levels and, in turn, to less harsh and inconsistent maternal discipline. This is important because such harsh and inconsistent parenting practices have been implicated in the development of children's psychological and behavioral problems.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary materials, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

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

AUTHOR CONTRIBUTIONS

OZ is the principal investigator; she contributed to the research design, collection and analysis of the data, and writing all the parts of the manuscript. GB and YH contributed to the conceptualization of the model. All authors contributed to the article and approved the submitted version.

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Post-traumatic-stress in the context of childhood maltreatment: pathways from attachment through mentalizing during the transition to parenthood

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Introduction: This study aimed to clarify the role of mentalizing in pathways from attachment to Post Traumatic Stress Symptoms (PTSS) in survivors of childhood maltreatment (CM). We focused on the transition to parenting, a critical period for reworking parenting representations to reduce intergenerational maltreatment cycles.

Method: Study participants included 100 pregnant CM survivors. We assessed PTSS with the SCID and attachment and mentalizing with the Adult Attachment Interview (AAI), which was rated for Attachment and Reflective Functioning (RF).

Results: Regarding Re-experiencing trauma symptoms, the results of the path analysis were consistent with mediation. CM survivors' mentalizing about their early relationships with their parents (RF-Other) directly impacted Re-experiencing trauma symptoms, and attachment had an effect on Re-experiencing trauma symptoms through mentalizing (RF-Other). Regarding Arousal/Reactivity symptoms, the results of the pathways analysis were consistent with partial mediation by mentalizing about early relationships with parents (RF-Other). In addition to the pathway from attachment via mentalizing (RF-Other) to Arousal/Reactivity, the pathway between attachment and Arousal/Reactivity also remained significant.

Discussion: This study provides new evidence of a mentalizing and attachment model of PTSS in CM survivors. The findings indicate that increased mentalizing about early relationships with parents is an important process associated with lower PTSS. Finally, we discuss the implications of developing interventions for CM survivors to reduce PTSS. Scaffolding the development of mentalizing regarding attachment relationships in which CM occurred may help CM survivors reduce the intrusion of traumatic memories and decrease trauma-related arousal and reactivity symptoms. Interventions to help CM survivors mentalize regarding parents and attachment relationships in which trauma occurred may be particularly important during the transition to parenting when activation of representations of parenting can trigger PTSS.

KEYWORDS

attachment, mentalizing, RF, trauma, pregnancy, PTSS/PTSD

Introduction

Childhood maltreatment (CM) is a pressing public health concern impacting 25–55% of the population, depending on country and measurement (Moody et al., 2018). There is rapidly expanding evidence of the negative impacts of CM across the life course. Post-Traumatic Stress Disorder (PTSD) is the most frequent Axis I disorder associated with CM (Cloitre et al., 1997; Macpherson et al., 2021), with a 30–37% lifetime prevalence in adults with CM (Widom, 1999) compared to 5–10% in the community (Yehuda et al., 2015). For some CM survivors, Post-Traumatic Stress Symptoms (PTSS) can persist, unremitting, for years and decades. PTSS include intrusive recall of aspects of the event, avoidance of reminders, hyperarousal and hypervigilance, and dysphoria or anhedonia. In terms of a heuristic model, a dual-lens focusing on mentalizing and attachment in addition to trauma can elucidate risk and resilience processes for CM-associated PTSS (Lieberman and Amaya-Jackson, 2005; Pynoos et al., 2009; Ensink et al., 2021). As conceptualized by Fonagy et al. (2002), mentalizing references capacities involved in understanding attachment relationships and others, as well as oneself, in terms of mental states, affects, and intentions, thus enabling a mental perspective. In addition, mentalizing is a resilience factor in the context of trauma (Ensink et al., 2017; Duval et al., 2018). During pregnancy and the transition to parenthood, CM survivors are at heightened risk of PTSS (Muzik et al., 2013; Martinez-Torteya et al., 2014; Stacks et al., 2014; Choi et al., 2015; Christie et al., 2017). Further research is needed to inform theory and interventions with CM survivors to reduce PTSS and the intergenerational transmission of CM (Christie et al., 2017; Berthelot et al., 2018). However, there are few studies on the relationship between attachment, mentalizing, and CM-associated PTSS, especially during the transition to parenthood. To address current gaps in knowledge, we aimed to examine pathways involving attachment, mentalizing, and PTSS in pregnant women with CM.

The clinical fall-out of maltreatment: PTSS

CM-associated impacts are evident across the lifecycle, including social difficulties, health-harming behaviors, mental and physical illness, increased allostatic load, reduced telomere length, and shorter lifespan (Rogosch et al., 2011; Bellis et al., 2019). In the context of CM, prolonged exposure to fear and anxiety triggers chronic and extreme activation of the stress response system (Heim et al., 2008; O'Donovan et al., 2011). Consistent with our focus on mentalizing regarding self and others, new PTSD diagnostic practices also include a focus on negative alterations in self-referential and other-referential cognitions in addition to symptoms (American Psychiatric Association, 2013; Friedman, 2013; Cox et al., 2014).

Pregnant women endure increased vulnerability to PTSS, and pregnant CM survivors are at even higher risk (Seng et al., 2010; Yildiz et al., 2017; Narayan et al., 2018, 2019). Increased PTSS vulnerability during pregnancy is likely because preparation for the caregiver role activates memories of the parenting they received (Slade et al., 2009; Ammaniti et al., 2013). In the context of CM, memories of abuse by caregivers were abusive is potentially re-traumatizing. However, pregnancy is also a critical period during which there are opportunities for reworking traumatic experiences and representations of parenting. Developing mentalizing regarding relationships with maltreating parents may promote better adjustment during this developmental transition by reducing PTSS so CM survivors can use the present to prepare for their future role as parents (Berthelot et al., 2018). However, there is a paucity of research to inform interventions to address CM and PTSS and help prepare future parents to reduce the risk of repeating patterns of abuse.

Attachment and trauma

Parental responsiveness to infant distress establishes secure or insecure attachment (Bowlby, 1980) and calibrates the child's developing stress regulation system (Shai and Belsky, 2011, 2017; Mikulincer et al., 2015). Expectancies regarding the parent's availability to respond to distress become embedded in cognitive schemas and internal working models (Bowlby, 1973). For example, secure attachment involves representations of the self as deserving of care and others as available to help (Mikulincer et al., 2006; Fonagy et al., 2007).

Attachment and trauma impact similar physiological pathways involving fear and its regulation (Pynoos et al., 2009; Ensink et al., 2021), and attachment influences recovery after exposure to trauma. Consistent with this, secure attachment is associated with less severe PTSS in CM survivors, including adults (O'Connor and Elklit, 2008; Escolas et al., 2012; Ortigo et al., 2013), children (Ensink et al., 2021) and adolescents (Jardin et al., 2017). Conversely, insecure attachment is associated with more severe PTSS (Ogle et al., 2015; Woodhouse et al., 2015) and mediates (Muller et al., 2012) and moderates (Kanninen et al., 2003; Stovall-McClough and Cloitre, 2006; Sandberg, 2010; Ensink et al., 2021) the relations between CM and PTSS.

Maltreatment activates the attachment system so that children continue to seek out maltreating attachment figures, placing them in a situation of fear without resolution. This double bind leads to the approach/avoidance behaviors characteristic of disorganized attachment. In adults, disorganization is the mental state associated with CM (White et al., 2020), hypothesized to contribute to Unresolved Trauma and increased PTSS. For example, in CM-exposed psychiatric patients, Unresolved Trauma is associated with a seven-fold increase in PTSD (Stovall-McClough and Cloitre, 2006).

Mentalizing: a potential mechanism

Mentalizing, operationalized as reflective functioning (RF) for research purposes, facilitates interpersonal functioning by making the reactions of others understandable and predictable (Fonagy et al., 2002) and aids stress regulation at a physiological level (Borelli et al., 2018). Difficulties in mentalizing are a transdiagnostic risk factor for psychopathology (Katznelson, 2014). Mentalizing

develops optimally in relationships where children feel safe, and parents treat them as psychological agents whose behavior is motivated by mental states (Fonagy and Target, 2006; Ensink et al., 2017). Maltreatment stunts the development of mentalizing (Ensink et al., 2015, 2017). Furthermore, maltreatment likely installs an aversion to considering the minds of others, given the frankly destructive intentions toward them that the child must infer from the abusive act. Consisting with this theorizing, sexual abuse is associated with lower mentalizing regarding others (RF-Other; Ensink et al., 2015). Mentalizing regarding relationships with attachment figures (RF-Other) mediated the relationship between childhood sexual abuse and child depressive symptoms, as well as externalizing difficulties (Ensink et al., 2016a). In addition, mentalizing characterized by uncertainty about the reactions of others is associated with maltreatment and mediated the relationship between CM and personality disorder symptoms in adolescents (Duval et al., 2018).

In the context of CM, mentalizing and imagining their parents' psychological experiences and personal histories may help CM survivors gain a perspective that reduces the intrusion of past traumatic memories into the present. In line with this, Fonagy et al. (1991) showed in a seminal study that CM survivors who were able to mentalize regarding their attachment figures could establish secure attachment relationships with their infants. We replicated these findings in CM survivors and found that higher mentalizing regarding childhood maltreatment (RF-Trauma) was associated with a lower likelihood of infants having a disorganized attachment style (Berthelot et al., 2015). Furthermore, the relationship between CM and the quality of relationships with romantic partners and parenting behaviors was mediated by mentalizing about themselves (RF-Self: Borelli et al., 2020). In sum, different dimensions of mentalizing are associated with critical outcomes in the context of trauma.

Current investigation

The present study aims to advance research literature by analyzing the relationships between attachment, mentalizing, and PTSS in CM survivors during the transition to parenthood. Within a cross-sectional design, we examined whether mentalizing regarding their early relationships with their parents empirically linked CM-exposed expectant mothers' attachment representations to their PTSS. Consistent with Fonagy's mentalizing model of attachment and mentalizing, we hypothesized that attachment would be associated with mentalizing regarding relationships with attachment figures (RF-Other). In turn, mentalizing would have a direct association with PTSS. This pathway, where attachment is linked to PTSS symptoms via mentalizing, would be consistent with mediation by mentalizing of the association between attachment and PTSS.

Method

Participants and procedure

This study used a subset of data from a longitudinal study regarding the intergenerational transmission of CM-related risk. We recruited pregnant women at the obstetrics clinic of a large metropolitan hospital in Canada and obtained informed consent for study participation. The hospital's ethics committee approved the study. Prospective participants ($n = 809$) were first screened at the hospital using the Parental Bonding Instrument (PBI; Parker et al., 1979) to identify women who had experienced inadequate parenting and maltreatment in childhood. Eligible mothers were over 18, were free from psychotic disorder or acute drug addiction, and lived within a 100 km range of the city. Of the 131 eligible participants, 101 women consented to study participation. We used the Childhood Experience of Care and Abuse (CECA) interview (Bifulco et al., 1994) to confirm CM. Participants completed the CECA, the SCID, and the AAI at their homes or the hospital. Postgraduate clinical psychology students and clinical psychologists conducted interviews. We recorded interviews for coding and reliability purposes and transcribed AAI interviews for subsequent coding.

The participants ranged in age from 18 to 41 years ($M = 28.46$, SD = 5.58). All women were pregnant at the time of the study; more than half (60%) had other children ($M = 0.81$, SD = 0.90). The sample was predominantly French-Canadian (73%), with the remainder being African–American (10%), Hispanic (6%), North African (4%), other Caucasian (4%), Asian (2%), and Native Canadian (1%). Approximately half (52%) of the sample were cohabiting, 34% were married, and 14% were single. Regarding education, 55% had post-secondary education, and 41% had been to university. The majority were employed (67%). Still, approximately half of the sample had an annual family income below $30,000, considered below the poverty index of roughly $34,000 for a Canadian family of one child.

Regarding CM, 58% reported physical abuse, 40% sexual abuse, 78% neglect, and 79% antipathy. A biological parent or primary caregiver perpetrated 79% of physical abuse, 38% of sexual abuse, 100% of neglect, and 100% of antipathy. Regarding the severity of CM, 59% of physically abused women experienced moderate to severe CM, 72% of sexually abused women experienced moderate to severe CM, 66% of neglected women experienced moderate to severe CM, and 67% of women who reported antipathy experienced moderate to severe CM.

Measures

Screening measures

Parental care

The Parental Bonding Instrument (PBI; Parker et al., 1979) is a 25-item self-report questionnaire developed to assess adults' perception of parental care and the protection/control they received during the first 16 years of childhood. Respondents are questioned about their experiences with each parent separately to obtain care and protection scores for each parent. The instrument's psychometric properties have been extensively evaluated and shown to have good retest reliability, internal consistency, and validity (Parker, 1989, 1990), with demonstrated stability over twenty years (Murphy et al., 2010). The present study used the PBI as a screening instrument to identify pregnant women who had experienced low parental care from both parents in childhood.

Standard PBI cut-off scores were care scores of 27 for maternal and 24 for paternal figures.

Child abuse

The Childhood Experiences of Care and Abuse interview (CECA; Bifulco, Brown and Harris,1994) is a semi-structured interview to measure adverse childhood experiences retrospectively. The CECA assesses different domains of childhood maltreatment experiences, including physical and sexual abuse, neglect, and antipathy. Ratings are made for each maltreatment type on a 1–4 scale (little/none, some, moderate, and marked) using a manual that provides explicit examples of the type of parental behavior considered to represent different levels of severity. The investigator-based format of the CECA has the advantage of not depending on participants to categorize their childhood experiences as abusive. In addition, the CECA has good psychometric properties, including inter-rater reliability and validity (Bifulco et al., 2005). In the current study, all CECA interviews were audiotaped and subsequently coded by trained raters. Doctoral students in clinical psychology administered and videotaped the CECA interviews. Two rates evaluated CECAs to confirm CM. All the mothers who screened positive on the PBI had confirmed cases of child maltreatment using the CECA.

Key study measures

Attachment. The Adult Attachment Interview (AAI; George et al., 1985) is a semi-structured interview designed to assess adults' state of mind regarding attachment relationships with their parents during childhood. Based on their general strategy evident in discussing attachment relationships, participants are categorized as secure-autonomous (F), insecure-dismissing (Ds), insecure-preoccupied (E), or cannot classify (CC), using Main et al. (2002) coding manual. Secure-autonomous individuals provide relatively clear, coherent, concise, and consistent responses. Individuals with adverse childhood experiences can be classified as secure-autonomous if they provide coherent accounts of adverse experiences showing that such experiences are processed. Insecure-dismissing participants, by contrast, give highly positive and idealized descriptions of their parents, contradicted later in interviews, and insist that they cannot remember experiences with their attachment figures. For insecure-preoccupied individuals, questions provoke excessive activation of attachment-related memories and confused, angry, or passive preoccupation with attachment figures. Participants who have experienced CM are assessed to determine whether they are unresolved/disorganized regarding CM (U/d). Lack of resolution is coded using a scale (1–9), with scores of 5 and higher considered to reflect lack of resolution (Main et al., 2002). Lack of resolution manifests in lapses in the monitoring of reasoning or discourse when individuals discuss traumatic experiences. We combined the Unresolved/disorganized and Cannot Classify classifications because of potential commonalities in etiology and sequelae (Bakermans-Kranenburg and van IJzendoorn, 2009). The AAI has good psychometric properties evidenced in high test–retest reliability, validity, and stability over time (Bakermans-Kranenburg and Van IJzendoorn, 1993; Benoit and Parker, 1994; Sagi et al., 1994).

In the present study, a rater trained to be reliable to the coding standards of the Berkeley laboratory of Mary Main and Erik Hesse coded AAI transcripts. The rater was naive to information regarding CM exposure. We used a three-way classification; Secure, Insecure (Including Dismissing and Preoccupied), and Unresolved/disorganized.

Reflective functioning. AAI transcripts were coded for RF using the RF manual (Fonagy et al., 1998). The RF coding system has good psychometric properties, including high inter-rater reliability and good discriminant, divergent, and predictive validity across samples (Fonagy et al., 1998; Taubner et al., 2013). RF is scored on a scale of −1 to 9, with higher scores indicating higher mentalizing. In addition, questions that explicitly demand an appreciation of mental states (e.g., "Why did your parents behave as they did during your childhood?") are scored for RF. Two experienced raters trained by the developers of the RF coding system coded RF. Inter-rater reliability computed on the ten most complex cases (10% of the total sample) showed intraclass correlations of 0.79 for the RF ratings indicating good reliability on challenging transcripts. Mentalizing evident in the AAI can be scored in terms of participants' RF regarding early relationships with their parents (RF-Other), RF regarding self (RF-Self), and RF regarding trauma (RF-Trauma; Berthelot et al., 2015: Ensink et al., 2016b). We were specifically interested in RF-Other, as we hypothesized that RF regarding early relationships with parents would have the most significant implications for PTSS related to maltreatment by parents.

Post-traumatic stress symptoms. The Structured Clinical Interviews for DSM-IV Disorders I (SCID-I; First et al., 1997) was used to assess PTSS. Exposure to a traumatic event, re-experiencing the trauma, avoidance of the trauma-related content or situations, and hyperarousal/reactivity are assessed. Symptoms are rated on a three-point scale (not present, unsure, and present). The SCID has established reliability and validity (Zanarini and Frankenburg, 2001; Weertman et al., 2003). A clinical psychologist trained in SCID administration and rating conducted the interviews.

Data analysis

First, we calculated descriptive statistics and correlations using IBM SPSS v.26. We intended to use the dimensions of RF significantly correlated with PTSS at the bivariate level in the path analysis. Next, we conducted a path analysis using Mplus 8.6 (Muthén and Muthén, 2017) in which we examined whether participants' attachment predicted their RF-O, which in turn predicted their PTSS. Specifically, we entered attachment using a three-level variable (secure, insecure, unresolved). For mentalizing, we selected participants' RF-Other, as the variable hypothesized to be the most relevant and the only RF dimension significantly correlated with PTSS. Next, we used PTSS Re-experiencing and PTSS Arousal scores assessed with the SCID for the outcome variable. Finally, using the maximum likelihood estimation method (ML), our model tested the indirect effects, which started from the predictor (attachment) to the PTSS outcomes (Re-experiencing and Hyperarousal) through mothers' RF-Other as a potential indirect effect. The indirect effects were bootstrapped 1000 times with 95%

confidence intervals (CIs). To evaluate the fit of the model, we used the chi-square test, the Comparative Fit Index (CFI), the Tucker-Lewis Index (TLI), the root mean square error of approximation (RMSEA), and the standardized root mean square (SRMR).

Missing data were handled using the Full Information Maximum likelihood method (FIML). FIML enables using complete and incomplete observations and automatically adjusts the model estimation (Kline, 1998). FIML is superior to other missing data techniques, such as multiple imputations (Larsen, 2011).

Results

Descriptive statistics

Regarding attachment, participants were classified as Secure (n = 37, 36.7%), Insecure (n = 27, 26.7%), and Unresolved (n = 37, 36.7%). Correlations between the key study variables are presented in Table 1. Only RF (Other) significantly correlated with PTSS. Means and standard deviations for RF and PTSS by attachment type are presented as supplementary material.

Path analysis

We conducted a path analysis to test the mediational effect of RF-Other. In other words, the analysis tested whether attachment predicted RF-Other, which predicted PTSS.

The results of the path analysis showed that RF-other indirectly linked attachment (Secure, Insecure, Unresolved) and PTSS Re-experiencing and Hyperarousal/Reactivity symptoms. Fit indices indicated that the hypothesized model was a good representation of the observed data, χ^2 (1) = 0.002, p = 0.999, χ^2/df = 0.002, CFI = 1.00, TLI = 1.04, RMSEA = 0.00 and SRMR = 0.00. Because of the 3-level attachment variable, regression coefficients reflect the mean slope from one level to another (mean of the slopes between 1 and 2 and between 2 and 3). The full results of the path analysis are reported in Figure 1. Regarding attachment and RF-Other, results showed that more insecure and disorganized attachment were associated with lower levels of RF-Other (β = −0.286, p = 0.001). The model explained 8.2% of the variance of RF-other. Only RF-Other, not attachment, was significantly associated with Re-experiencing symptoms (β = −0.262, p < 0.001). The indirect effect of attachment on Re-experiencing symptoms through RF-other was also significant (b = ***0.0***75, 95% CI [.022, 0.162]). The indirect effect (b = 0.075) accounted for 34.2% of the total effect of attachment on Re-experiencing symptoms. Once RF-other was included in the model, the direct effect of attachment was no longer significant (β = 0.144, p = 0.100). This is consistent with full mediation by RF of the relationship between attachment and Re-experiencing symptoms. The model explained 11.2% of the variance in Re-experiencing symptoms. The Re-experiencing symptoms curve was flat from secure to insecure attachment, with a steeper increase from insecure attachment to unresolved trauma. However, the direct effect of attachment was not significant.

Concerning Hyperarousal/Reactivity symptoms, both attachment (β = 0.366, p = 0.015) and RF-Other (β = −0.299, p = 0.033) were associated with PTSS. More insecure and Unresolved/disorganized attachment (where attachment was rated as Secure, Insecure, and Unresolved/disorganized) and lower RF-Other were associated with higher Hyperarousal/Reactivity symptoms. Furthermore, the indirect effect of attachment on Hyperarousal/Reactivity through RF was significant (b = ***0.0***86, 95% CI [.033,0.140]). The indirect effect (b = 0.086) accounted for 18.7% of the total effect. The direct effect of attachment (β = 0.366) on hyperarousal remained significant. The model explained 9.4% of the Hyperarousal/Reactivity symptoms variance. The Hyperarousal/Reactivity symptoms curve was flat from secure to insecure attachment with a steeper increase from insecure attachment to unresolved attachment, suggesting that the latter attachment type contributes the most to the significance of the observed coefficients.

Discussion

The present study aimed to investigate pathways to PTSS involving mentalizing and attachment in pregnant CM survivors. As hypothesized, higher PTSS was associated with lower mentalizing regarding early attachment relationships (RF-Other). Furthermore, the findings of the path analysis were consistent with mediation via RF-Other of the effect of attachment on Re-experiencing symptoms and partial mediation of the effect of attachment on Hyperarousal/reactivity symptoms. The study provides new evidence supporting a mentalizing and attachment model of CM-associated PTSS. The findings have important clinical implications suggesting that increasing mentalizing about attachment relationships, including those in which maltreatment occurred, may decrease PTSS.

The study findings lend further credence to the now robust observation that mentalizing is frequently deficient in the context of PTSS and CM (Nietlisbach et al., 2010; Mazza et al., 2012; Nazarov et al., 2015; Palgi et al., 2016). In addition, it adds to the growing body of research showing that mentalizing is a resilience factor in the context of CM that may reduce the risk of subsequent psychological difficulties (Berthelot et al., 2015; Ensink et al., 2016a, 2017; Duval et al., 2018). The findings regarding mediation by RF-Other extend previous research by Huang et al. (2020), who, using self-report measures, found that mentalizing difficulties characterized by uncertainty and attachment insecurity mediated the effect of childhood trauma on PTSS. By using observer-based measures of PTSS, mentalizing, and attachment, the current study revealed the salience of mentalizing regarding attachment relationships (RF-Other) for CM-associated PTSS.

Regarding attachment and Hyperarousal/Reactivity symptoms, mediation by mentalizing was partial, and the effect of attachment remained significant. To understand the effect of attachment on PTSS further, we examined the attachment and PTSS curve. The curve was flat from secure to insecure attachment, with a steeper increase from insecure attachment to unresolved trauma, suggesting that unresolved trauma contributes the most to explaining variance in PTSS symptoms. These findings are consistent with research by Stovall-McClough and Cloitre (2006), showing that unresolved trauma was associated with a seven-fold increase in PTSS in hospitalized CM survivors.

TABLE 1 Correlation between attachment, mentalizing (measured as RF), and post-traumatic stress symptoms.

	RF-self	RF-other	RF-trauma	PTSS Re-experiencing	PTS avoidance	PTS hyperarousal
Attachment (AAI)	−0.21*	−0.29**	0.738**	0.22*	0.23*	0.26*
RF-self	1	0.87**	0.10	−0.05	0.09	0.00
RF-other	–	1	−0.04	−0.31**	−0.06	−0.24*
RF-trauma	–	–	1	0.17	0.20	0.232
PTS Re-exp	–	–	–	1	0.80**	0.92**
PTS avoidance	–	–	–	–	1	0.85**
PTSHyperarousal	–	–	–	–	–	1

Note: Adult Attachment was assessed as Secure, Insecure, Unresolved. Mentalizing was assessed as RF-Self, RF-Other and RF-Ttrawna, PTSS was assessed with the SCID, Re-experiencing, Avoidance of trauma related content or situations, Hyperarousal *p <0.05. **p <.O1.

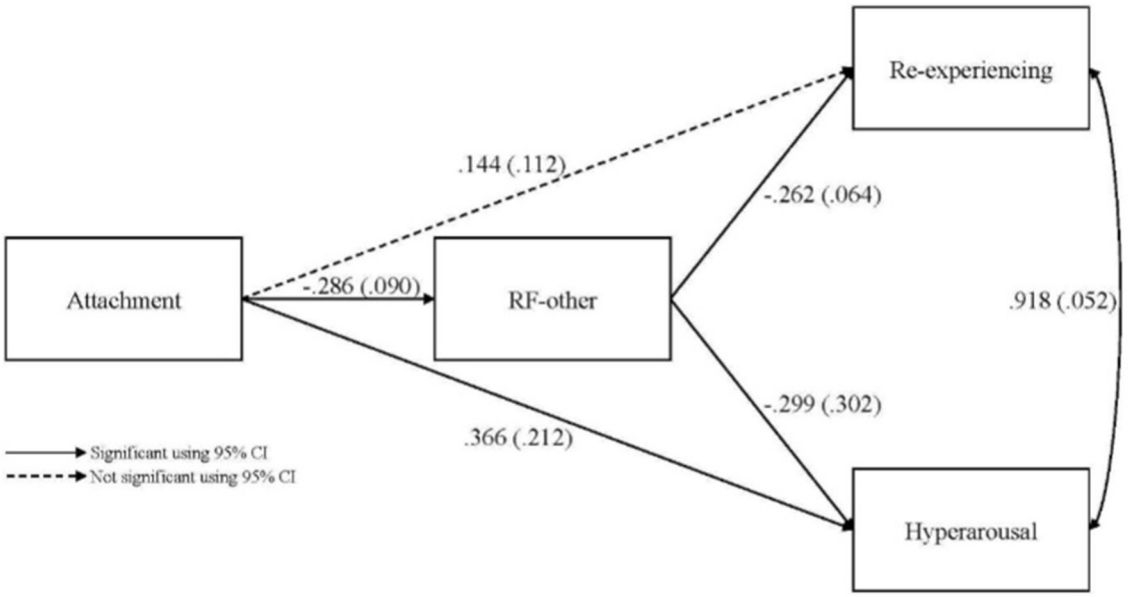

FIGURE 1
Path analysis from attachment to post-traumatic stress symptoms with mentalizing (RF-other) as a mediator.

Our findings have important implications for intervention and suggest that improving mentalizing about early attachment relationships may reduce Re-experiencing and Hyperarousal/reactivity in pregnant CM survivors. Mentalizing about early attachment relationships with parents may help CM survivors reduce the intrusion of traumatic memories and hyperarousal. During pregnancy, CM survivors may benefit from interventions that help them look back and rework traumatic relationships without becoming re-traumatized. Such intervention may help reduce the intrusion of memories of past trauma into the present so that CM survivors can use the present to prepare for the future and becoming parents themselves (Berthelot et al., 2018).

While we did not examine Complex PTSD, our findings regarding long term CM-associated PTSS are consistent with a Complex PTSD framework. The findings expand our understanding of PTSS, mentalizing, and attachment processes in CM survivors and show the importance of mentalizing about early attachment relationships (RF-Other), especially those in which abuse occurred, in pathways to PTSS. This extends previous research showing that, in CM survivors, RF-Other mediated the relationship between sexual abuse and psychological difficulties (Ensink et al., 2016a). We did not find associations between PTSS and mentalizing regarding trauma (RF-Trauma) nor mentalizing regarding self (RF-Self). However, previous research shows that RF-Trauma has implications for other outcomes in CM survivors, such as investment in their pregnancy (Ensink et al., 2014) and infant attachment organization (Berthelot et al., 2015).

Furthermore, RF-Self was previously shown to mediate the relationship between insensitive care in childhood, romantic relationships with partners, and maternal behavior in CM-exposed parents (Borelli et al., 2020). While our findings highlight the importance of mentalizing about attachment relationships (RF-Other) for reducing PTSS in CM survivors, it complements previous research showing that mentalizing about self (RF-Self) and trauma (RF-Trauma) also affect psychological adjustment, romantic and attachment relationships, intergenerational

transmission of risk, and resilience in CM survivors. The complementary findings are consistent with mentalizing being a multicomponent construct, with some mentalizing difficulties contributing to psychological difficulties and other mentalizing difficulties impacting relationships with partners and infant attachment.

The finding that lower mentalizing was associated with more PTSS is also in line with existing evidence that among CM survivors mentalizing difficulties are transdiagnostic risk factors for a range of psychological difficulties, including personality disorder features (Chiesa and Fonagy, 2014; Duval et al., 2018), depressive symptoms, dissociation, externalizing and sexualization (Ensink et al., 2016a, 2017). To date, empirically supported treatments such as mentalization-based treatment (MBT; Bateman and Fonagy, 2008) are effective for patients with personality disorders (Storebo et al., 2020; Stoffers-Winterling et al., 2022). MBT is being adapted for treating CM-associated PTSD to address the difficulties CM survivors experience in emotion regulation and interpersonal relationships. Furthermore, Berthelot et al. (2018) have developed prenatal interventions to facilitate mentalizing about parenting and past trauma specifically for CM survivors.

The study has definite strengths, such as observer-rated measures of attachment and RF and PTSS. However, the study has limitations that need consideration before generalizing based on the findings. The sample size is adequate given the low number of latent variables and indicators, the absence of missing data, and Monte Carlo analyses showed that the sample size provided sufficient power. However, further studies using larger samples are needed. All study participants were pregnant women and replication with a gender-diversified sample would enable testing whether the findings apply to men. We were particularly interested in understanding the relations between PTSS, mentalizing, and attachment during pregnancy to inform interventions during this critical preparation period of transition and preparation to becoming parents. Including measures of pregnancy-specific processes, such as attachment to the fetus, could have enhanced the study further. Also, the sample was diverse regarding socio-economic status, but replication in higher-risk samples is needed. Many study participants experienced moderate to severe physical and sexual abuse. However, replication in a larger sample is required before we can generalize the findings to different CM types and severity.

Furthermore, our focus on PTSS advances our understanding of CM's long-term impacts and is consistent with a complex PTSD framework, but including a measure of complex PTSD can enhance the contribution of future studies. Finally, we cannot optimally establish mediation, given that we simultaneously assessed our independent variable, mediator, and dependent variables. To optimally test the proposed theoretical models offered within this study, one would need to assess attachment at the first time point, RF at the first and subsequent time points, and the dependent variable at the second and third time point. The statistical model would need to incorporate the final time points of all measures while controlling for prior assessments of these measures.

Conclusion

This study provides new evidence supporting a mentalizing and attachment model of PTSS in CM survivors. For CM survivors, mentalizing about early attachment relationships (RF-Other) may be particularly important for reducing Re-experiencing and Hyperarousal/reactivity. The findings have important clinical implications. Interventions to scaffold mentalizing about their parents and attachment relationships in which abuse occurred (RF-Other) could help CM gain mental perspective and reduce the intrusion of traumatic memories and hyperarousal.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

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

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.

Publisher's note

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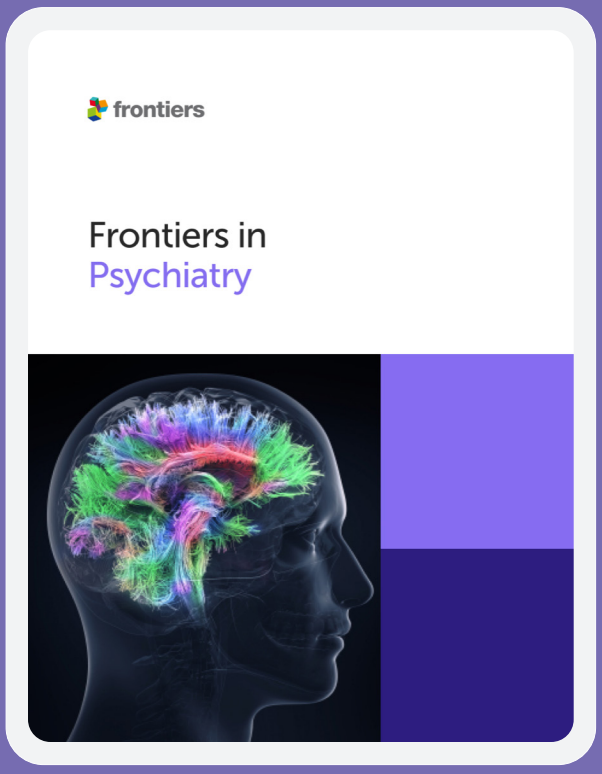

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