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Early Sexual Trauma Exposure and Neural Response Inhibition in Adolescence and Young Adults: Trajectories of Frontal Theta Oscillations During a Go/No-Go Task

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Abstract

Objective—Trauma, particularly when experienced early in life, can alter neurophysiologic and behavioral development, thereby increasing risk for substance use disorders and related psychopathology. However, few studies have empirically examined trauma using well-characterized developmental samples that are followed longitudinally.

Method—The association of assaultive, non-assaultive, and sexual assaultive experiences before 10 years of age with developmental trajectories of brain function during response inhibition was examined by measuring electrophysiologic theta and delta oscillations during no-go and go conditions in an equal probability go/no-go task. Data were drawn from the Collaborative Study of the Genetics of Alcoholism (COGA) prospective cohort, composed of offspring who were aged 12 through 22 years at enrollment from high-risk and comparison families, with follow-ups at 2-year intervals since 2004. In addition, other important predictors of neurophysiologic functioning (eg, substance use, impulsivity, and parental alcohol use disorders) were investigated. Moreover, associations of neurophysiologic functioning with alcohol and cannabis use disorder symptom counts and externalizing and internalizing psychopathology were examined.

Results—Individuals exposed to sexual assaultive trauma before 10 years of age had slower rates of change in developmental trajectories of no-go frontal theta during response inhibition. Importantly, effects remained significant after accounting for exposure to other traumatic exposures, such as parental history of alcohol use disorder and participants' substance use, but not measures of impulsivity. Further, slower rates of change in no-go frontal theta adolescent and young adult development were associated with increased risk for alcohol use disorder symptoms

and internalizing psychopathology, but not for cannabis use disorder symptoms or externalizing psychopathology.

Conclusion—Childhood sexual assault is associated with atypical frontal neurophysiologic development during response inhibition. This could reflect alterations in frontal lobe development, synaptic pruning, and/or cortical maturation involving neural circuits for inhibitory control. These same areas could be associated with increased risk for young adult alcohol use disorder symptoms and internalizing psychopathology. These findings support the hypothesis that changes in neurocognitive development related to early sexual trauma exposure could increase the risk for mental health and substance use problems in young adulthood.

Keywords

sexual abuse; inhibition; event-related oscillations; alcohol dependence; internalizing

Approximately 1 in 4 adolescents in the United States is exposed to a traumatic event before 16 years of age.[1] Those who experience early life trauma have greater lifetime risk for substance use disorders and related mental health problems (ie, depression and anxiety[2–4]). Researchers have suggested that trauma, particularly when experienced early in life, might alter neurobiological and behavioral development, thereby increasing the risk for later onset of psychopathology,[5] including substance use disorders.[6,7] Several cross-sectional studies have reported associations between childhood trauma exposure and neurobiological and cognitive alterations.[8–10] Further, many of these same neurocognitive alterations are correlates of mental health and substance use disorders.[6,7] Although it has been suggested that links between early trauma exposure and later mental health and substance use problems are related to such neurocognitive alterations, few studies have empirically examined this possibility. Therefore, the longitudinal effects of early trauma exposure on neurocognitive development and the impact such effects can have on risk for later mental health and substance use disorders remain largely unknown.

Advances in understanding typical brain development have begun to elucidate why early traumatic experiences can have such a profound influence on neurobiological and behavioral development.[11,12] The brain undergoes its greatest growth and development in the first years of life, with a second phase beginning in adolescence characterized by synaptic pruning, leading to anatomic and functional maturation.[13–16] This second phase of development is most profound in frontal lobe regions of the brain involved in higher-order cognitive functions, including top-down control functions, such as inhibition and other aspects of executive function. This phase also is accompanied by broader developmental changes, including pubertal development, which has been shown to influence cortical maturation and synaptic pruning throughout this period.[17,18] Therefore, it is important to understand whether early trauma exposure predicts differential patterns of brain development during this second maturational phase, a period of great susceptibility to environmental influences, and whether such effects are associated with increased susceptibility to mental health and substance use problems.

Studies examining the effects of early life stress on brain development have mainly implicated neural stress reactivity and emotional processing/regulation pathways,[5,19–23]

indicating that those exposed to early life stress exhibit deficits in cognitive and behavioral control, selective attention, and reward processing.[21,24–27] Cognitive tasks such as the go/no-go (GNG) task, which requires selective attention and behavioral inhibition, could be particularly relevant to the assessment of neural functioning in individuals exposed to early trauma.[28,29] The GNG task requires activation of several brain networks including the executive network,[29] which facilitates the detection, monitoring, and resolution of conflict between 2 competing response tendencies—execution (go) and refraining from execution (no-go) of a motor response—thereby reflecting behavioral execution and inhibition.[30–33] Behavioral inhibition is an essential regulatory executive control that undergoes substantial development during adolescence and persists through young adulthood.[34] This is one developmental process that could be altered in those exposed to early life trauma.[20,35] To date, 2 functional magnetic resonance imagining studies have investigated response inhibition using the GNG task in adolescents exposed to different types of early trauma or adversity (eg, abuse, neglect, or witnessing parental violence[36]; neglect, maltreatment, or multiple foster placements before adoption[37]). In these studies, decreased behavioral inhibition and activation differences in the prefrontal cortex were observed in trauma-exposed subjects.

Studies that have examined the influence of child maltreatment using electroencephalography (EEG) have the advantage of temporal resolution on the order of milliseconds, a scale at which many relevant sensory, motor, and cognitive phenomena take place at the neural level.[38–41] Brain oscillations of different frequency bands are related to various cognitive functions,[42–44] and task-related event-related oscillations (EROs) provide time and frequency information for a specific sensory, motor, or cognitive event. Howells *et al*.[38] reported altered cortical arousal during GNG task performance in adults who retrospectively reported different types of childhood trauma exposures. Findings were dependent on the form of childhood trauma experienced; for example, child emotional abuse was correlated with increased theta activity during the GNG task. Other electrophysiologic studies conducted in children exposed to psychosocial deprivation[39] or other severe forms of neglect also found increased resting-state theta activity and decreased resting-state alpha and beta activity.[40,45] In one of the few longitudinal studies conducted in this area, McLaughlin *et al*.[40,41] reported lagged developmental trajectories of frontal resting-state EEG from 9 months to 8 years in children reared in Romanian institutions, many of whom were exposed to severe neglect. Importantly, this study also demonstrated that these changes predicted hyperactivity, impulsivity, and internalizing symptoms at approximately 4.5 years. Collectively, these findings have been interpreted as representing a maturational delay in cortical development associated with severe early life stress.[39–41,46–52]

Previous research has suggested that exposure to early childhood trauma is associated with a developmental lag in cortical arousal and relatedly behavioral inhibition, and that these neural responses might increase the risk for later onset of psychopathology, including mood, anxiety disorders, and behavioral disorders.[39–41,46–52] However, to our knowledge, no study has explicitly examined this prospectively through emerging adulthood, the period of highest risk for the onset of many of these disorders. The studies that have examined similar questions regarding the legacy of early trauma on neurodevelopment[21,40,41,49,50,53] have primarily relied on data from the Bucharest Early Intervention Study, which focuses on early

development (9 months through 8 years), but not thereafter. Whether early life stress influences adolescent and young adulthood neurodevelopment and/or increases risk for young adult mental health and substance use problems remains unknown. Further, this literature has been limited by several methodologic factors, including relatively small study sizes (N < 200), cross-sectional and/or retrospective nature of most of these data, and the robustness of these associations to other confounding factors, including participants' psychopathology, substance use, family history, and several key sociodemographic characteristics. In addition, no study to our knowledge has incorporated information on parents' psychopathology, which often co-occurs with adverse childhood experiences and has been shown to influence neurodevelopment and risk for mental health problems.[54,55] These factors pose serious challenges when attempting to disentangle which neurobiological effects are due specifically to early traumatic experiences, and whether those particular neurobiological changes influence risk for mental health and substance use problems.

The present study investigated the associations of non-assaultive, assaultive, and sexual assaultive trauma exposure before 10 years of age with developmental trajectories of frontal theta oscillations and posterior delta oscillations during no-go (response inhibition) and go conditions. Data are from a longitudinal, developmental sample of adolescents and young adults from the Collaborative Study of the Genetics of Alcoholism (COGA) prospective cohort. A second aim was to examine the role of parental history of alcohol use disorders (AUDs) and participants' substance use, impulsivity, gender, and race/ethnicity in these associations. A third aim was to assess whether trauma-associated neurophysiologic trajectories influence risk for AUDs and cannabis use disorders (CUDs) and/or related internalizing (INT) and externalizing (EXT) psychopathology.

METHOD

Sample

The COGA prospective study began data collection in 2004 and is ongoing. Details on data collection and procedures have been published previously.[56] Briefly, offspring from families densely affected by alcohol use problems and comparison community families who were 12 to 22 years old at intake and who had at least 1 parent interviewed in an earlier phase of the COGA study were enrolled, with new subjects added as they reached 12 years of age. Subjects were interviewed every 2 years with a comprehensive battery that included the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA[57]), covering substance use problems and other psychiatric disorders and related behavior, personality questionnaires, family history of alcohol use problems, and a neurophysiologic battery. An age-appropriate SSAGA (cSSAGA[58]) was used for subjects younger than 18 years. At the time of analysis, this study presents data on 2,625 offspring from 2,413 nuclear families who had at least 1 follow-up interview; 1,931 participants had a third assessment, 1,324 a fourth assessment, 842 had a fifth assessment, 428 had a sixth assessment, and thus far 8 participants have had a seventh assessment (data collection is ongoing). For the 2,625 offspring analyzed, the mean age at baseline was 17.1 years (standard deviation 3.6, range 12–26), 50.7% were female subjects, and self-reported race/ethnicity was 29.2% African

American, 62.0% Caucasian, and 9.0% Asian, Pacific Islander, or "other." Analytic sample details are presented in Table 1.

Experimental protocols were approved by each site's institutional review board, and informed consent was obtained from all participants. Participants were excluded from neurophysiologic assessment if they had positive breath-analyzer test and/or urine screen results; hepatic encephalopathy/cirrhosis of the liver; history of head injury, seizures, or neurosurgery; uncorrected sensory deficits; history/symptoms of psychoses; self-reported positive test result for human immunodeficiency virus; other acute/chronic medical illnesses that affect brain function; or psychotropic medications that affect electrophysiologic measurement.

Measures

Traumatic Exposures—Traumatic exposures were collected using the SSAGA[57] and have been described previously.[56,59] The SSAGA included 21 potentially traumatic events. Several events were excluded from the present study because they did not occur before 10 years of age (eg, combat-related trauma). All events used in the present analysis are presented in Table S1, available online. Based on evidence that interpersonal assaultive events have a stronger and more enduring effect on mental health/substance use than non-assaultive events,[60–62] that traumatic events cluster together,[63] and to remain consistent with prior studies,[59] 3 composite variables were examined, representing the report of at least 1 lifetime assaultive trauma (ie, stabbed, shot, mugged, threatened with a weapon, robbed, kidnapped, and held captive), non-assaultive trauma (ie, life-threatening accident, disaster, witnessing someone seriously injured or killed, and unexpectedly finding a dead body), or sexual assaultive trauma (ie, rape or molestation by relative or non-relative). Importantly, age at occurrence of each event was recorded, and this information was used in the present study. We focused on traumatic events occurring before 10 years of age, given the suggestion that trauma exposure at early stages of development might be more influential than later exposures for neurobiological development and onset of later psychopathology[23,64,65] and our desire to measure events that *preceded* measurement of neurophysiologic and behavioral outcomes. Any trauma experienced after 10 years was combined into a binary measure that was used as a covariate in all models, because trauma exposure is known to re-occur throughout the lifecourse.[66]

Parental AUD Status—Parental AUD was a lifetime measure based on available parent SSAGA interviews (60.8% of fathers and 89.8% of mothers) as described previously.[56,59] For parents who were not interviewed, reports about the parent's alcohol problems obtained in earlier COGA waves from other relatives or, less commonly, from their offspring during the prospective study assessment were used to code as affected parents with at least 2 positive family history reports based on the Family History Assessment Module.[67] Maternal and paternal variables were combined to represent lifetime AUDs in either or both parents.

Substance Use and Psychopathology—Data from all offspring SSAGA and cSSAGA interviews were used to obtain lifetime reports of alcohol and cannabis use as previously detailed.[56,59] Participants' AUD symptom count scores and CUD symptom count scores

were based on *DSM-5* lifetime symptom counts. INT psychopathology count scores included *DSM-IV* lifetime diagnoses for major depressive disorder, panic disorder, social phobia, and an additional item—suicidal ideation. EXT psychopathology count scores included conduct disorder and oppositional defiant disorder diagnoses. Data from each individual's most recent interview were used.

Barratt Impulsiveness Scale—The Barratt Impulsiveness Scale (BIS; version 11) is a 30-item scale that measures 3 aspects of impulsivity: attentional impulsiveness, motor impulsiveness, and non-planning.[68] All items are answered 1 (never), 2 (occasionally), 3 (often), or 4 (always). Separate scales were developed for adolescents and adults. Total scores were computed by summing subscale items. Data from each individual's baseline interview were used.

Sensation Seeking Scale—The Sensation Seeking Scale (SSS) measures individual differences in stimulation and arousal[69] and assesses boredom susceptibility, thrill and adventure seeking, experience seeking, and disinhibition. Total scores are computed by summing all 30 items. Data from each individual's baseline interview were used.

Theta ERO Power (GNG)—Using the protocol described by Pandey *et al.*,[70,71] each participant was presented with 4 types of visual stimuli consisting of white isosceles triangles pointing in the up, down, right, or left direction. The stimuli were presented for 100 ms at the center of a computer screen (17 inches diagonally, 75-Hz refresh rate, 1,024 × 768 resolution) against a dark background that subtended a visual angle of approximately 1°. In the practice session, participants were instructed to press a key whenever a white triangle pointed up or down (go stimulus) and refrain from pressing the key whenever the triangle pointed toward the right or left (no-go stimulus). A dollar sign ($) appeared on the screen for 200 ms at 1,200 ms after stimulus onset when participants responded correctly, whereas a cross sign (X) appeared on the screen for 200 ms at 1,200 ms after stimulus onset when participants responded incorrectly. Participants were instructed that speed and accuracy were equally important for making a correct response. In the next, experimental, phase, EEG was recorded. Participants were informed that each correct response would earn a reward. However, each subject received a predetermined fixed amount at the end of the experiment without deductions for errors, although they were not informed of this while performing the task. The probabilities of occurrence of go and no-go stimuli were equal (50/50), and the order of stimulus presentation was randomized. The intertrial interval was 2,400 ms. Go and no-go accuracy and go reaction time at each assessment also were recorded and used in statistical analysis.

Participants were comfortably seated in front of a computer monitor screen placed 1 m away in a dimly lit, sound-attenuated, radiofrequency-shielded room (IAC Acoustics, Bronx, NY). The EEG was recorded on a Neuroscan System (versions 4.1, 4.2, 4.3, 4.4 and 4.5; Neurosoft, Inc., El Paso, TX) using a 61-channel electrode cap (Electro-cap International, Inc., Eaton, OH) that had electrode placements based on the extended 10–20 International System (Electrode Position Nomenclature; American Clinical Neurophysiology Society, 1991) with the notch filter off. The electrodes were referenced to the tip of the nose, and participants were grounded using an electrode placed on the forehead (frontal midline, 2 cm

above nasion). Eye movements were recorded using a supraorbital vertical lead and a horizontal lead on the external canthus of the left eye. Electrode impedance was maintained below 5 kΩ throughout the recording. The continuous EEG signals were recorded and marked with all stimulus, response, and feedback event codes at sampling rates of 512 Hz (16-bit A/D) or 500 Hz (32-bit A/D) depending on the amplifier version, with a bandpass filter set at 0.02 to 100 Hz, and were amplified 10,000 times using a set of amplifiers (SynAmps^2, Neurosoft, Inc.).

Because of prior evidence indicating the importance of frontal theta oscillations during the no-go condition and posterior delta oscillations during the go condition of the GNG task[38,70,71] and a preliminary analysis to determine time-frequency regions of interest, the present study used S-transformed frontal theta total power (4–7.5 Hz, 200–400 ms, Fz) during the no-go (response inhibition) and go conditions and, for comparison, posterior delta total power (1–3.5 Hz, 200–500 ms, Pz) during the go and no-go conditions at baseline and follow-up assessments 1 through 4. Further details about the ERO signal processing using S-transformed method can be found in a previous publication (that study was conducted in a different analytic sample).[72]

Statistical Methods

First, we estimated an unconditional growth model that predicted log-transformed ERO measures from baseline through the most recent assessment by age by incorporating individual participant's age at each follow-up (Mplus option: time scores; Muthén and Muthén; https://www.statmodel.com/company.shtml). This model specifies latent variables for the random intercept, the random slope for time (rate of change in ERO value by age), and a constant or individual deviation from these mean values. This approach allowed us to simultaneously estimate the variance in ERO within and between individuals across time. The slope and residual variances were fixed to be equal across all available time points. Separate models were run for delta and theta EROs (total power) during the go and no-go conditions.

Second, we examined time-invariant predictors of ERO trajectories. We simultaneously examined the association of 3 binary measures of trauma exposure before 10 years (nonassaultive, non-sexual assaultive, and sexual assaultive traumatic exposures) with ERO intercepts and slopes (linear change from baseline through follow-up 4). This is depicted in Figure 1. Initial results indicated no evidence of nonlinear (ie, quadratic) effects. Modeling was conducted in Mplus 7.4 (Muthén and Muthén, 1998–2015) using full maximum likelihood estimation with robust standard errors. Age, gender (0 = male, 1 = female), and self-reported race/ethnicity (0 = non-Hispanic white, 1 = non-Hispanic black/African American, 2 = other) were used as covariates in all analyses. In addition, we accounted for genetic relatedness among siblings. Subsequent models included participants' alcohol and cannabis use (0 = never used, 1 = ever used) at each interview, parental history of AUD, and participants' impulsivity as measured by baseline BIS and SSS scores. Third, we evaluated whether residualized change in ERO from baseline to most recent follow-up was related to AUD, CUD, and INT and EXT psychopathology at each participant's most recent interview.

RESULTS

Rates of traumatic exposure in the COGA prospective sample have been described previously.[56,59] When considering trauma experienced before 10 years (Table 1), 26.6% reported experiencing at least 1 type of trauma; 16.6% reported experiencing non-assaultive trauma, 4.5% reported experiencing assaultive trauma, and 6.6% reported experiencing sexual assault. Non-sexual assaultive trauma was more common for male subjects ($p < .05$), whereas sexual assaultive trauma was more common for female subjects ($p < .05$). Non-assaultive trauma exposure was higher for African-American than for white participants ($p < .05$).

Individuals exposed to early trauma differed with respect to measures of impulsivity as measured by the BIS and SSS, substance use behavior, and psychiatric symptoms (Table 2; associations were adjusted for gender, age at assessment, self-reported race, and parental history of AUD). Several associations withstood a Bonferroni multiple-test correction; sexual trauma before 10 years was associated with cognitive impulsivity (BIS), AUD symptom count, CUD symptom count, and INT and EXT psychopathology. Assaultive trauma exposure was associated with INT symptoms, and non-assaultive trauma was associated with EXT symptoms (Table 2). Correlations among all variables are presented in Table S2, available online. Go and no-go accuracy and go reaction time on the GNG task did not differ significantly among participants (Table S3, available online).

Results from ERO models, including parameter estimates and fit statistics, are presented in Tables 3 and S4, available online. The only statistically significant effect observed involved sexual assaultive trauma before 10 years and no-go frontal theta oscillation. That is, when all 3 trauma exposures were examined simultaneously (Table 3), no statistically significant effects were observed for non-assaultive trauma, non-sexual assaultive trauma, or oscillations in the go condition. In models including gender, race/ethnicity, non-assaultive trauma, and non-sexual assaultive trauma as covariates, sexual assaultive trauma before 10 years was associated with decreased no-go frontal theta oscillation at baseline (intercept, $p < .01$; Table 3) and a decreased rate of change in no-go frontal theta oscillation from baseline to follow-up 4 (slope, $p < .001$; Table 3). This is displayed in Figures 2 and 3. No significant effects were observed in the go condition. Further, no statistically significant effects were observed for posterior delta ERO in the go or no-go condition (Table S4, available online).

Associations remained statistically significant when participants' alcohol and cannabis use were included in the model (intercept, $p < .01$; slope, $p < .001$; Table 3). However, when parental AUD was included in the model, only a decreased rate of change in no-go frontal theta oscillation from baseline to follow-up 4 was observed (intercept, $p > .05$; slope, $p < .05$; Table 3). When cognitive impulsivity (BIS subscale, baseline assessment) was included in the model, associations were no longer statistically significant (intercept, $p > .05$; slope, $p > .05$). When additional pathways from the slope and intercept factors to INT pathology, EXT pathology, AUD symptoms, and CUD symptoms (≥18 years old) were included in the model, the rate of change in no-go frontal theta oscillation was positively associated with INT pathology and AUD symptoms at participants' most recent follow-ups ($p < .001$; Figure

2). In addition, models including intercepts as covariates were examined and results remained largely unchanged (results available upon request).

DISCUSSION

Although previous studies have reported associations between childhood trauma exposure and neurobiological alterations,[9,10,21,41,73–75] it remains unclear to what extent childhood trauma influences adolescent and young adult neurodevelopment, and whether these effects influence risk for onset of psychopathology in young adulthood. Findings from the present study suggest that individuals exposed to sexual assaultive trauma before 10 years of age have atypical developmental trajectories of neurophysiologic functioning during response inhibition (no-go); the typical decrease in frontal theta oscillatory activity during response inhibition (no-go) observed throughout adolescence and young adulthood occurs at a slower rate in those who have been exposed to early sexual assault. Importantly, these effects remained significant after accounting for parental history of AUD and participants' substance use (intercept differences were no longer significant when parental AUD was included in the model; see Table 3, Model 3). However, effects were no longer significant when aspects of impulsivity were included in the model, suggesting that impulsivity could have an important role in the relation of early sexual trauma and frontal theta development during response inhibition. In addition, change in frontal no-go theta trajectories was associated with AUD symptom count and INT psychopathology (depression, anxiety, and suicidal ideation) in young adulthood.

Associations of Trauma and No-Go Theta ERO

Gradual decreases in frontal theta oscillations during response inhibition across adolescence and young adulthood were observed in all study subjects. Previous developmental ERO studies[76–78] have observed similar decreases in oscillatory power globally, likely reflecting synaptic pruning (ie, fewer, but more efficient, connections) that occurs rapidly during adolescence and continues through young adult- hood.[79–82] This also could correspond with gray matter development and progressive maturing of the prefrontal cortex as it assumes greater control over neural processing throughout adolescence and young adulthood.[83–85]

Findings from the present study suggest that individuals exposed to sexual assaultive trauma before 10 years have atypical developmental trajectories of frontal theta oscillations during response inhibition; the decrease in frontal theta power throughout adolescent and young adult development occurs at a slightly slower rate. This perhaps suggests that children exposed to early sexual assault might have atypical frontal cortical development that might be characterized by altered rates of synaptic pruning and gray matter production, which in turn could affect the development of top-down control over neural processing throughout adolescence and young adulthood. Research conducted in rodent models found that the enduring effects of early isolation and maternal separation on brain development could be a consequence of an arrested phase of synaptic overproduction.[80] This is in agreement with previous studies in humans, which found maturational delay in cortical development associated with severe early life stress.[39–41,46,48,50,52,75,86–90]

Further support comes from studies showing an association among childhood sexual abuse, cognitive deficits, and increased behavioral disinhibition.[20,35,91] In the present study, individuals exposed to early trauma also displayed higher rates of impulsivity as measured by the BIS and Zuckerman's SSS. Interestingly, statistically significant differences in impulsivity and sensation seeking were most pronounced in those who had experienced sexual assault. When these measures of impulsivity were considered in the association of early sexual trauma and trajectories of frontal no-go theta power, effects of early sexual trauma were no longer statistically significant. There are at least 2 possible explanations for this. Impulsivity could mediate the relation of early sexual trauma and frontal no-go theta development. Alternatively, impulsivity could be a shared risk factor for early trauma exposure and atypical neurodevelopment. Thus, participants in this study who had experienced sexual assault before 10 years showed atypical trajectories of frontal no-go theta power (possibly delayed frontal cortical maturation and synaptic pruning in neural circuits involved in response inhibition) and heightened levels of impulsivity and sensation seeking (ie, behavioral disinhibition). There also is the possibility that frontal no-go theta activity might mediate the relation between early sexual abuse and impulsivity; the timing of the assessment of trauma exposure, impulsivity (BIS and SSS), and no-go frontal theta oscillation preclude the testing of this hypothesized mediation model in the present study. Future studies are needed to disentangle the influence of behavioral aspects of impulsivity with frontal theta oscillatory activity during response inhibition in the context of trauma exposure.

Results from the present study also indicated that sexual trauma-related change in frontal no-go theta trajectories influenced risk for young adult AUD symptom count and INT psychopathology, but not CUD symptom count or EXT psychopathology. Taken together, these findings support the hypothesis that early sexual trauma exposure might influence the risk for psychopathology (ie, depression, anxiety, suicidal ideation, or AUDs), in part through neurodevelopmental mechanisms. However, future longitudinal studies are needed to further characterize the potential moderating and/or mediating effects of neurodevelopmental trajectories in the associations of early trauma and later psychopathology. More research is needed to examine other aspects of neural functioning during response inhibition and other aspects of stress-reactivity, including executive control and reward processing.

Interestingly, non-sexual assaultive trauma and non-assaultive trauma exposure before 10 years were not associated with developmental trajectories of theta ERO. This could indicate that although exposure to these traumas clearly has adverse mental and physical health consequences, exposure to early sexual abuse might be a particularly potent risk factor for neurocognitive development, behavioral disinhibition, and subsequent INT and alcohol use pathology. This is in agreement with prior evidence that interpersonal assaultive events have a stronger and more enduring effect on substance use and psychopathology than non-assaultive events.[60,62] In addition, GNG behavioral data (ie, go and no-go accuracy and go reaction time on the GNG task) did not differ among participants exposed to trauma (Table S4, available online). This is in agreement with previous work[71,92,93] that reported that differences in neural oscillations during task performance (eg, no-go frontal ERO) can be observed even when behavioral differences are not (eg, no performance errors), suggesting

that one major strength of ERO data is detection of extremely subtle effects occurring at the neural level, which have important implications for neurocognitive functioning and risk for psychopathology. However, it should be noted that no-go frontal ERO and performance on the GNG task are significantly correlated—suggesting that frontal theta ERO is relevant to task performance, although this is not reflected in a statistically significant behavioral difference among the trauma exposure groups. In the context of the present study, the atypical frontal ERO during the no-go task observed in individuals who were exposed to trauma could be a subtle index of risk for psychopathology and suggests less efficient neural processing during response inhibition, necessitating the use of alternate neural strategies to effectively inhibit their responses in the GNG task. Also of note is the effect of parental history of AUD on the associations of trauma exposure and no-go frontal theta ERO. Given previous evidence that decreased no-go frontal theta ERO is observed in individuals with a family history of AUD, this suggests that the association of sexual assaultive trauma exposure before 10 years with a slower rate of change in developmental trajectories of frontal oscillations during response inhibition (no-go frontal theta power) across adolescence and young adulthood remains after accounting for mean level differences in no-go frontal theta power due to familial risk for AUD. Future studies should investigate the extent of these findings in individuals with a family history of AUD and in community control families.

These findings should be considered in light of several caveats. First, the sample consists of offspring primarily from high-risk, densely AUD-affected families, and as such findings might not be generalizable to other populations. Second, although data across multiple waves of assessment were included in the analyses, some individuals who might have eventually developed AUD, CUD, or INT or EXT problems are treated in this study as unaffected. Third, effects of maternal AUD present in 45.3% of the analytic sample could reflect in part in utero exposure to alcohol (which is unknown for most offspring), which can affect neurodevelopment. Fourth, the present study did not have information on the frequency or duration of specific traumatic exposures. Fifth, given the relatively small number of participants meeting criteria for posttraumatic stress disorder in this sample, posttraumatic stress disorder was not incorporated into the present study. Sixth, attrition of the sample owing to participants who did not return for follow-up assessments could have affected the present study's findings. A nonresponse analysis indicated that individuals who did not return for follow-up were younger ($p < .001$) and were more likely to have had a diagnosis of alcohol dependence ($p < .001$), and that fewer non-responders were exposed to assaultive ($p < .001$) and non-assaultive ($p < .001$) trauma and had a diagnosis of cannabis dependence ($p < .001$); no differences regarding gender, race/ethnicity, impulsivity, sexual trauma exposure, or ERO values were observed. In light of the absence of attrition effects for the primary findings for sexual trauma exposure and ERO power, we believe that inferences made in this report are likely to be sound. Relatedly, decreased sample sizes available in follow-ups 4 and 5 might limit the statistical power of some complex models examined in this study, leading to the possibility of type I and II errors. Despite these limitations, this is the first study to our knowledge to examine associations of early trauma exposure, neurophysiologic developmental trajectories in adolescence and young adulthood, and risk for later psychopathology. This is particularly important because this is the peak age range

for the onset of substance use and mental health-related problems and has been previously understudied. Further, information provided on clinical, behavioral, and familial influences enables characterization of neurobehavioral functioning in a relatively large and racially/ethnically diverse sample.

In conclusion, findings from the present study suggest sexual assaultive trauma exposure before 10 years of age is associated with a slower rate of change in developmental trajectories of frontal oscillations during response inhibition (no-go frontal theta power) across adolescence and young adulthood and increased levels of behavioral disinhibition. In addition, this atypical neurophysiologic development, which might reflect delays in frontal cortical maturation and synaptic pruning, was associated with young adult INT and alcohol use problems. Taken together, these findings support the hypothesis that changes in neural development related to early sexual trauma exposure could increase later risk for mental health problems. These findings highlight the importance of developing effective prevention strategies to decrease exposure to childhood sexual assault and to increase treatment after trauma exposure, because this early experience significantly increases the risk for a cascade of mental and physical health problems throughout the individual's life course. Researchers, clinicians, and policy makers should build on ongoing work aimed at identifying interventions and therapeutic strategies to mitigate the risk associated with early sexual assaultive trauma exposure.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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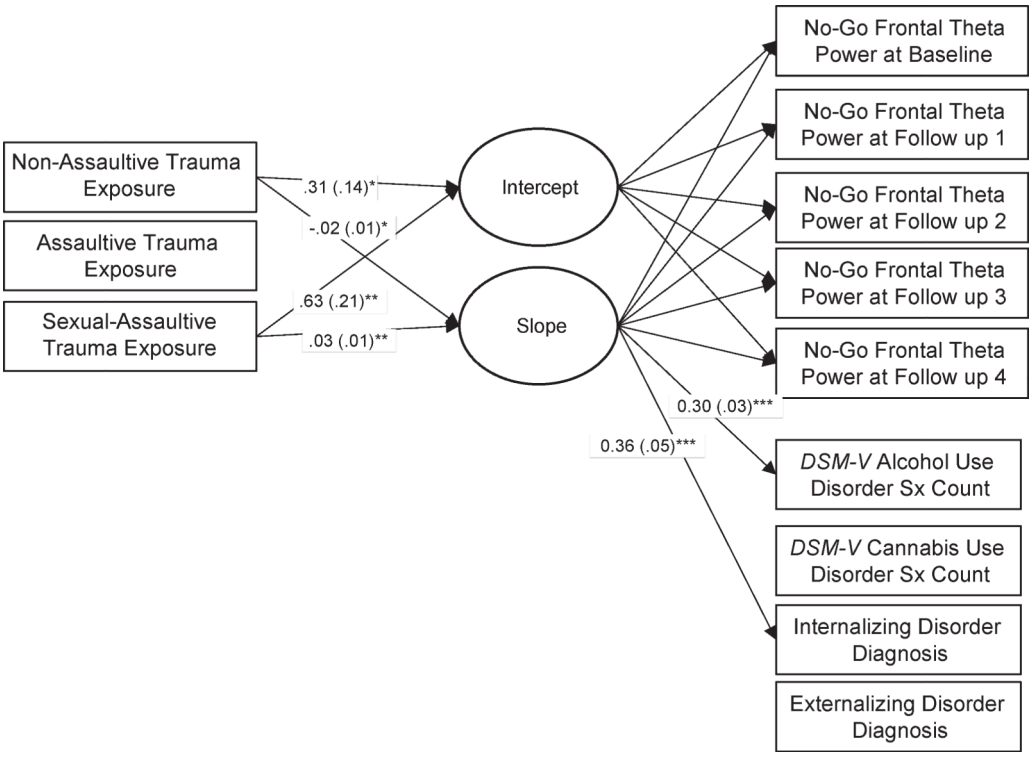

FIGURE 1.

Effects of Early Trauma Exposure on No-Go Frontal Theta Power From Baseline Through Follow-Up 4 and Associations With Substance Use Disorder and Psychopathology

Note: *Parameter estimates (and standard errors) are displayed only for statistically significant pathways. Not pictured, but also included in this model, are the following covariates: gender, race/ethnicity, age, alcohol use and cannabis use, and parental alcohol use disorder. Internalizing psychopathology count scores included* DSM-IV *lifetime symptoms for major depressive disorder, panic disorder, social phobia, and an additional item—suicidal ideation. Externalizing psychopathology count scores included conduct disorder and oppositional defiant disorder symptoms. Data from each individual's most recent interview were used. Sx = symptom.*

*p < *.05;* **p < *.01;* ***p < *.001.*

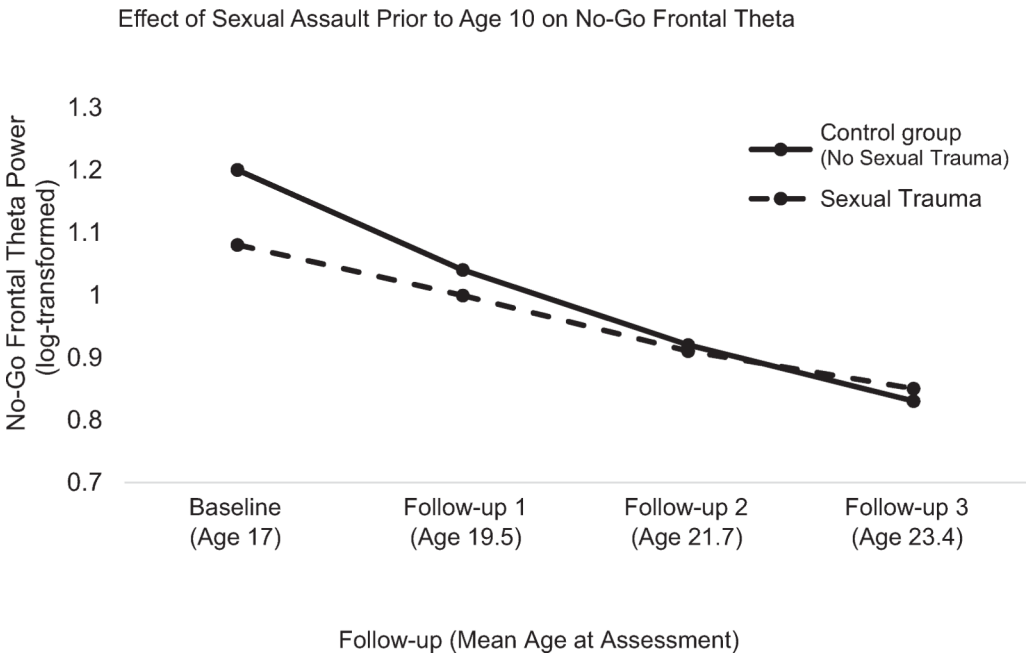

FIGURE 2.

Adjusted Mean Trajectories of No-Go Frontal Theta by Sexual Assaultive Trauma Exposure

Note: Models are adjusted for gender, self-reported race/ethnicity, age at assessment, and parental history of alcohol dependence. The comparison group includes participants who were not exposed to sexual trauma before 10 years of age (93.4% of analytic sample).

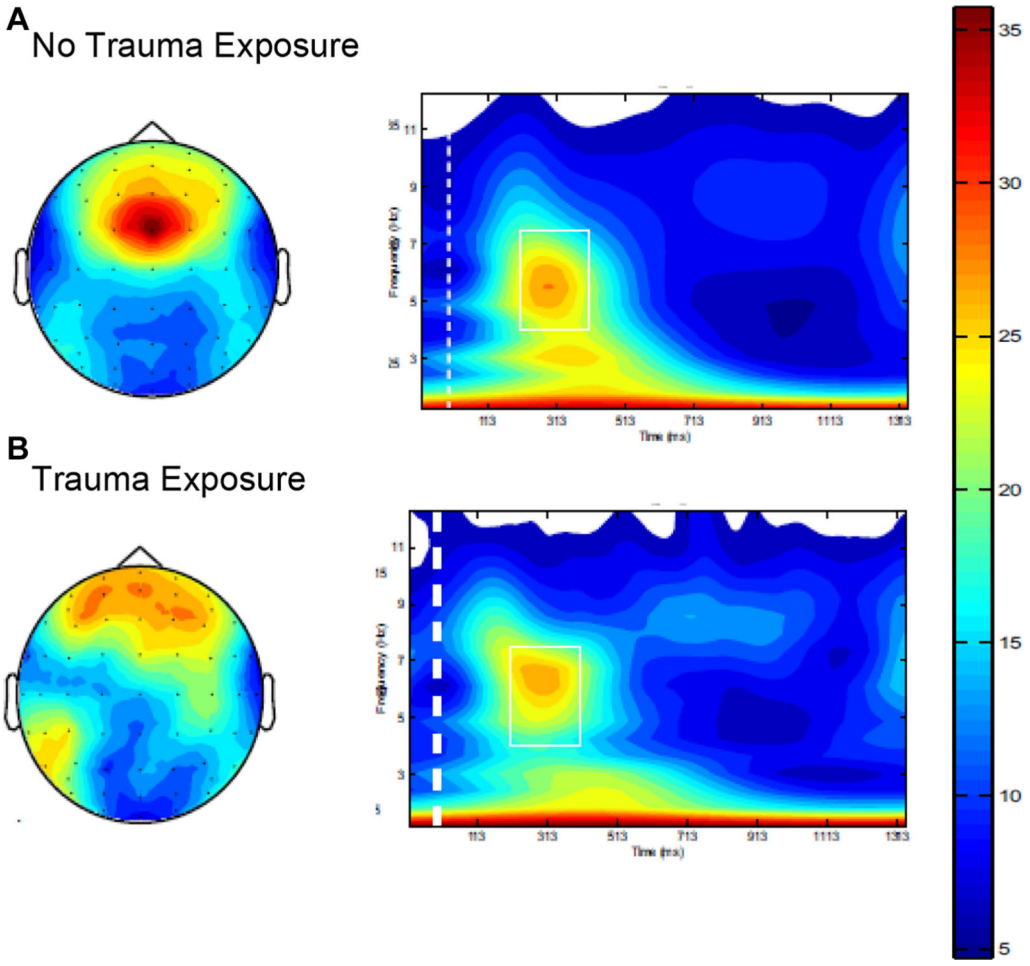

FIGURE 3.

No-Go Frontal Theta by Early Sexual Assaultive Trauma Exposure

Note: This figure depicts differences in frontal theta no-go power values at baseline observed in participants who (A) were not exposed and (B) were exposed to sexual trauma before 10 years of age. Note the more focused frontal topography and more efficient neural synchronization (ie, higher theta event-related oscillation power values) during response inhibition (no-go condition of go/no-go task) in participants who were not exposed to trauma. In contrast, the frontal topography indicates a less efficient neural synchronization (ie, lower event-related oscillation power values) during response inhibition (no-go condition of go/no-go task) in participants who were exposed to trauma. Please note color figures are available online.

Table 1

Analytic Sample Descriptive Statistics

	All Participants (N = 2,625)	Male Participants (n = 1,286)	Female Participants (n = 1,339)
Mean Age At:			
Baseline interview	17.1 (12.0–26.2)	17.2 (12.0–29.2)	17.2 (12.0–28.7)
Follow-up 1 (n = 1,931)	19.5 (13.3–32.2)	19.2 (13.3–32.2)	19.7 (13.8–31.6)
Follow-up 2 (n = 1,324)	21.7 (15.3–32.2)	21.7 (15.3–31.8)	21.8 (15.8–32.2)
Follow-up 3 (n = 842)	23.4 (17.4–32.3)	23.5 (17.4–32.3)	23.3 (17.7–31.7)
Follow-up 4 (n = 428)	25.1 (19.6–32.2)	25.0 (19.6–32.2)	25.2 (19.8–31.9)
Follow-up 5 (n = 8)	27.9 (22.1–31.9)	27.4 (22.3–31.8)	28.4 (22.1–31.9)
Most recent interview	22.4 (12–32.0)	22.1 (12.0–32.0)	22.7 (12.0–32.0)
Self-reported race/ethnicity (%)			
White/Caucasian	62.0	61.9	62.0
Black/African American	29.2	29.6	28.7
Other	9.0	8.6	9.3
Non-assaultive < 10 y, %	16.6	18.0	15.3
Assaultive < 10 y, %	4.6	5.6	3.5
Sexual assaultive < 10 y, %	6.6	4.0	8.9
Parental history of AUD, %	41.1	41.6	40.7
Alcohol ever use, %	94.7	95.8	93.7
Cannabis ever use, %	77.4	82.4	72.5
DSM-5 Symptoms			
AUD (any), %	64.6	65.4	64.0
Mean (SD)	3.0 (3.6)	2.1 (2.4)	1.6 (2.3)
CUD (any), %	72.2	53.0	75.2
Mean (SD)	1.5 (2.7)	2.5 (3.0)	1.3 (2.4)
INT (any), %	38.7	32.5	44.6
Mean (SD)	0.4 (0.5)	0.3 (0.5)	0.5 (0.5)
EXT (any), %	16.8	19.4	12.0
Mean (SD)	0.2 (0.4)	0.2 (0.4)	0.1 (0.3)

Note*: Assaultive traumas (ie, stabbed, shot, mugged, threatened with a weapon, robbed, kidnapped, and held captive), non-assaultive traumas (ie, life-threatening accident, disaster, witnessing someone seriously injured or killed, and unexpectedly finding a dead body), and sexual assaultive traumas (ie, rape or molestation) before 10 years of age. Internalizing (INT) psychopathology count scores included*

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DSM-IV lifetime symptoms for major depressive disorder, panic disorder, social phobia, and an additional item—suicidal ideation. Externalizing (EXT) psychopathology count scores included conduct disorder and oppositional defiant disorder symptoms. Data from each individual's most recent interview were used. AUD = alcohol use disorder; CUD = cannabis use disorder; SD = standard deviation.

Table 2

Associations of Early Trauma Exposure With Impulsivity, Substance Use, and Psychiatric Disorder Symptoms

	Non-Assaultive Trauma < 10 y (n = 418)			Assaultive Trauma < 10 y (n = 111)			Sexual Assaultive Trauma < 10 y (n = 121)		
	B	**SE**	***p***	**B**	**SE**	***p***	**B**	**SE**	***p***
BIS total score	0.69	0.95	.47	1.04	1.67	.53	**3.03**	**1.40**	**.03**
Non-planning	−0.25	0.41	.54	0.73	0.73	.32	**1.12**	**0.56**	**.05**
Motor impulsive	0.32	0.35	.35	0.31	0.62	.66	0.82	0.48	.09
Cognitive impulsive[a]	**0.82**	**0.32**	**.01**	**1.31**	**0.57**	**.02**	**1.21**	**0.45**	**<.001**[a]
Zuckerman score	0.19	0.64	.77	0.79	1.15	.49	**1.71**	**0.82**	**.04**
Disinhibition	−0.07	0.24	.79	−0.57	0.44	.19	0.44	0.31	.15
Boredom susceptibility	−0.16	0.19	.41	−0.08	0.34	.81	0.43	0.24	.07
Thrill seeking	0.04	0.29	.19	0.98	0.52	.06	0.26	0.37	.48
Experience seeking	0.02	0.21	.92	0.46	0.37	.22	**0.57**	**0.27**	**.03**
Ever drinking	−0.01	0.01	.39	0.01	0.03	.73	**0.05**	**0.02**	**.04**
Ever used cannabis	−0.04	0.03	.15	0.03	0.05	.63	0.07	0.05	.15
DSM-5 AUD sx[a]	0.13	0.15	.40	**0.55**	**0.29**	**.05**	**0.91**	**0.25**	**<.001**[a]
DSM-5 CUD sx[a]	0.24	0.16	.14	**0.75**	**0.31**	**.02**	**1.00**	**0.27**	**<.001**[a]
DSM-5 INT sx[a]	**0.06**	**0.02**	**.01**	**0.33**	**0.05**	**<.001**[a]	**0.20**	**0.06**	**<.001**[a]
DSM-5 EXT sx[a]	**0.09**	**0.03**	**<.001**[a]	**0.13**	**0.06**	**.02**	**0.19**	**0.05**	**<.001**[a]

Note*: All associations are adjusted for gender, self-reported race/ethnicity, age at assessment, and parental history of alcohol dependence. Comparison groups are participants who were not exposed to any trauma type before 10 years of age. Boldface type denotes significance* ($p < .05$). *AUD = alcohol use disorder; BIS = Barratt Impulsiveness Scale; CUD = cannabis use disorder; EXT = externalizing; INT = internalizing; SE = standard error; sx = symptom.*

[a] *Associations that withstood Bonferroni multiple test correction* (*0.05/45 tests conducted for* $p < .001$).

Table 3

Effects of Early Trauma Exposure on the Developmental Trajectory of No-Go Frontal Theta Power From Baseline Through Follow-Up 4

Trauma Exposure < 10 y	Model 1	Model 2	Model 3	Model 4
Non-assaultive				
Intercept	−0.29 (1.50)	−0.29 (1.50)	1.22 (1.98)	0.59 (2.37)
Slope	−0.01 (0.07)	−0.01 (0.07)	−0.08 (0.09)	−0.01 (0.09)
Assaultive				
Intercept	−2.58 (1.56)	−2.58 (1.56)	2.36 (1.99)	3.05 (2.09)
Slope	0.09 (0.07)	0.09 (0.07)	−0.08 (0.08)	−0.09 (0.09)
Sexually assaultive				
Intercept	−4.41 (1.59)**	−4.41 (1.59)**	−3.11 (1.99)	0.13 (1.89)
Slope	0.22 (0.07)***	0.22 (0.07)***	0.17 (0.08)*	0.03 (0.07)

Note*: All models Include age modeled by time scores. Model 1 (free parameters = 20; Akaike Information criterion [AIC] = 39,270.74; Bayesian Information criterion [BIC] = 39,387.91) includes gender, race/ethnicity, and age. Model 2 (free parameters = 24; AIC = 21,607.93; BIC = 21,713.31) adds to covariates in model 1 alcohol use and cannabis use. Model 3 (free parameters = 26; AIC = 21,601.10; BIC = 21,725.64) adds to covariates in model 2 parental alcohol use disorder. Model 4 (free parameters = 28; AIC = 12,627.05; BIC = 12,748.28) adds to covariates in model 3 participants' impulsivity as measured using the Barratt Impulsiveness Scale and Sensation Seeking Scale.*

* p < *.05*

** p < *.01*

*** p < *.001.*

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