ORIGINAL ARTICLE

Disrupted Reinforcement Learning and Maladaptive Behavior in Women With a History of Childhood Sexual Abuse

A High-Density Event-Related Potential Study

Pia Pechtel, PhD; Diego A. Pizzagalli, PhD

Importance: Childhood sexual abuse (CSA) has been associated with psychopathology, particularly major depressive disorder (MDD), and high-risk behaviors. Despite the epidemiological data available, the mechanisms underlying these maladaptive outcomes remain poorly understood.

Objective: We examined whether a history of CSA, particularly in conjunction with a past episode of MDD, is associated with behavioral and neural dysfunction in reinforcement learning, and whether such dysfunction is linked to maladaptive behavior.

Design: Participants completed a clinical evaluation and a probabilistic reinforcement task while 128-channel event-related potentials were recorded.

Setting: Academic setting; participants recruited from the community.

Participants: Fifteen women with a history of CSA and remitted MDD (CSA + rMDD), 16 women with remitted MDD with no history of CSA (rMDD), and 18 healthy women (controls).

Exposure: Three or more episodes of coerced sexual contact (mean [SD] duration, 3.00 [2.20] years) between the ages of 7 and 12 years by at least 1 male perpetrator.

Main Outcomes and Measures: Participants' preference for choosing the most rewarded stimulus and avoiding the most punished stimulus was evaluated. The feedback-related negativity and error-related negativity—hypothesized to reflect activation in the anterior cingulate cortex—were used as electrophysiological indices of reinforcement learning.

Results: No group differences emerged in the acquisition of reinforcement contingencies. In trials requiring participants to rely partially or exclusively on previously rewarded information, the CSA + rMDD group showed (1) lower accuracy (relative to both controls and the rMDD group), (2) blunted electrophysiological differentiation between correct and incorrect responses (relative to controls), and (3) increased activation in the subgenual anterior cingulate cortex (relative to the rMDD group). A history of CSA was not associated with impairments in avoiding the most punished stimulus. Self-harm and suicidal behaviors correlated with poorer performance of previously rewarded, but not previously punished, trials.

Conclusions and Relevance: Irrespective of past MDD episodes, women with a history of CSA showed neural and behavioral deficits in utilizing previous reinforcement to optimize decision making in the absence of feedback (blunted "Go learning"). Although our study provides initial evidence for reward-specific deficits associated with CSA, future research is warranted to determine if disrupted positive reinforcement learning predicts high-risk behavior following CSA.

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Author Affiliations: Center for Depression, Anxiety and Stress Research, McLean Hospital, Harvard Medical School, Belmont, Massachusetts.

ACCORDING TO THE US Department of Health and Human Services,[1] in 2008 alone, more than 69 000 children experienced childhood sexual abuse (CSA) in the United States. The National Comorbidity Survey showed that severe childhood adversity accounts for nearly 32% of psychiatric disorders.[2] Although CSA sequelae are heterogeneous, affective disorders are the most common outcomes in adulthood.[3] For example, in a birth cohort of 1000 children, CSA involving sexual intercourse was associated with an increased odds ratio of 8.1 of developing major depressive disorder (MDD).[4,5] Similarly, in a sample of adults with a history of CSA, 62% met *DSM-IV* criteria for lifetime MDD compared with 28% with lifetime posttraumatic stress disorder.[6]

Childhood sexual abuse has also been linked to higher rates of maladaptive be-

haviors, including self-harm, unsafe sexual behavior, and substance abuse.[7,8] Although maladaptive behaviors can provide momentary relief from distress, they can have detrimental long-term implications, including increased risk of sexual revictimization.[9,10] Unfortunately, research examining the functional and neural mechanisms underlying maladaptive behaviors related to CSA is sparse.

Neurobiological studies have emphasized the effect of chronic stress on brain development. In particular, prolonged stress has been linked to dysregulation of the hypothalamic-pituitary-adrenal axis, leading to increased glucocorticoid release.[11] Excessive glucocorticoid release, in turn, has been hypothesized to impair neural plasticity in brain regions with prolonged postnatal development and/or a high concentration of glucocorticoid receptors.[12] The anterior cingulate cortex (ACC) reaches peak volume at 10.5 years,[13-15] and such protracted postnatal development[16] might leave it vulnerable to the neurotoxic effects of glucocorticoids.[11,17,18] In fact, adults reporting childhood adversities showed smaller ACC volumes than did adults without adversity.[19,20] Given the role of the ACC in reinforcement learning,[21] ACC abnormalities following CSA might disrupt the ability to learn from positive and negative outcomes, which might underlie maladaptive decision making. Our aim was to test these novel hypotheses.

Specifically, we investigated reinforcement learning and putative ACC abnormalities in women with a history of CSA that occurred between the ages of 7 and 12 years (see the eAppendix [jamapsych.com] for a rationale of sample selection). A reinforcement task was used in conjunction with 128-channel event-related potentials, which allowed the examination of electrophysiological indices of internal (error-related negativity [ERN]) and external (feedback-related negativity [FRN]) performance feedback. Both waveforms are thought to reflect dopamine-modulated ACC activity following negative feedback (FRN) and incorrect responses (ERN) critically implicated in reinforcement learning.[21] Blunted ERN/FRN may suggest decreased sensitivity to task-relevant outcomes, which might lead to deficits in reinforcement learning, including the acquisition of reinforced contingencies and the utilization of these contingencies in order to optimize decision making in a novel context (incentive-based decision making).

Given that CSA has been strongly linked to MDD,[4-6] women with a history of CSA and of MDD were compared with women with a history of MDD but no history of CSA and with healthy women (controls). We hypothesized that, relative to healthy controls and a psychiatric control group, women who experienced CSA would show behavioral and electrophysiological indices of disrupted reinforcement learning. Moreover, we hypothesized that such abnormalities would be associated with both ACC dysfunction and higher rates of maladaptive behaviors.

METHODS

PARTICIPANTS

Seventy-two participants were recruited through online and printed advertisements. Following the first screening, 56 women were eligible (eAppendix). Seven participants were excluded owing to artifacts (n=6) or task noncompliance (n=1). The final sample consisted of 3 groups: (1) 15 women with a history of CSA and remitted MDD (CSA + rMDD), (2) 16 women with remitted MDD but no trauma (rMDD), and (3) 18 women with no history of psychopathology or trauma (controls). Participants were right-handed, with no significant medical or neurological conditions, and were excluded if they reported current mood disorders or current or past psychotic symptoms, somatoform disorders, personality disorders, lifetime substance dependence, substance abuse within the past 6 months, seizures, or use of antidepressant medication in the past 2 months.

Inclusion criteria for the CSA + rMDD group included 3 or more episodes of coerced sexual contact (mean [SD] duration, 3.00 [2.20] years) between the ages of 7 and 12 years by at least 1 male perpetrator (eAppendix). The women in the CSA + rMDD group could not report concurrent physical or emotional abuse during childhood or adolescence on the Traumatic Antecedents Questionnaire.[22] Groups did not differ in frequency of being disciplined (χ^2_8=14.36, $P>.07$) or of exposure to family violence in childhood (χ^2_4=7.53, $P>.11$).

Both the CSA + rMDD and rMDD groups met criteria for a past episode of MDD, as assessed by the *Structured Clinical Interview for DSM-IV-R Disorders*.[23] The CSA + rMDD and rMDD groups were matched for the number of past MDD episodes, the time elapsed since the last episode, prior psychological or pharmacological treatment, and comorbidity (**Table 1**). Based on the *Structured Clinical Interview for DSM-IV-R Disorders* and the Traumatic Antecedents Questionnaire, controls did not have any current or past episodes of psychiatric disorder or lifetime trauma. Our study was approved by the Harvard University institutional review board. Participants provided written informed consent and were reimbursed $75.

CLINICAL ASSESSMENTS

In a first session, participants completed the Traumatic Antecedents Questionnaire, the *Structured Clinical Interview for DSM-IV-R Disorders*, the Beck Depression Inventory–II (BDI-II),[24] the Snaith-Hamilton Pleasure Scale,[25] and the Perceived Stress Scale (PSS).[26] The adult version of the Youth Risk Behavior Survey[27] was administered to assess frequency of self-harm, risk taking, violent behavior, unsafe sexual activity, and dysfunctional eating habits. The Coping Inventory for Stressful Situations[28] probed adaptive and maladaptive coping strategies.

On a separate day, electroencephalographic data were collected. The state versions of Spielberger's *Manual for the State-Trait Anxiety Inventory*[29] and the Positive and Negative Affect Schedule[30] were administered immediately before and after the electroencephalographic recording. The Digit Span Task[31] was administered to assess working memory capacity.

TASK

During electroencephalography, participants completed the Probabilistic Stimulus Selection Task[32] to probe reinforcement learning. This task consists of a learning phase with 2 to 6 training blocks (60 trials per block), to examine explicit learning from positive and negative feedback, and a test phase with a single block (120 trials), to assess decision making based on previously rewarded or punished contingencies.

In the learning phase, participants were randomly presented in each trial with 1 of 3 different stimuli pairs (A-B, C-D, or E-F) of Snodgrass images on a computer screen.[33] The images (at a duration of 1200 milliseconds) were preceded by a fixation cross (1000 milliseconds) and followed by a blank screen (jittered intertrial intervals: 350, 450, and 550 milliseconds).

Table 1. Demographics and Clinical Data for Women in the CSA + rMDD, rMDD, and Control Groups

Characteristic	CSA + rMDD Group (n = 15)	rMDD Group (n = 16)	Control Group (n = 18)	Statistical Value	*P* Value
Demographics					
Age, mean (SD), y	31.60 (10.98)[a]	24.81 (3.94)	30.44 (10.78)	$F = 2.48$	.10
Single, No (%)	12 (29.30)	16 (39.00)	13 (31.70)	$\chi^2 = 5.00$	.08
White, No (%)	4 (14.30)	13 (46.40)	11 (39.30)	$\chi^2 = 15.73$	.05
College degree, No (%)	4 (16.00)	10 (40.00)	11 (44.00)	$\chi^2 = 12.43$	.05
Annual income ≤$50 000, No (%)	15 (31.90)	15 (31.90)	17 (36.20)	$\chi^2 = 0.93$	.63
Clinical measures					
PSS score, mean (SD)	21.07 (7.83)[a,b]	15.81 (5.90)	12.67 (5.18)	$F = 7.29$	.002
BDI-II score, mean (SD)	8.00 (6.58)[a,b]	2.81 (2.99)	1.67 (1.78)	$F = 10.44$	<.001
Time elapsed since last MDD episode, mean (SD), y	3.80 (2.88)	4.06 (2.77)	NA	$t = -0.26$	.80
MDD episodes, mean (SD), No.	2.13 (1.23)	1.94 (0.85)	NA	$t = 0.55$	.59
Anxiety diagnosis, No. (%)	6 (66.70)	3 (33.30)	NA	$\chi^2 = 1.70$	.19
SHAPS score, mean (SD)	22.07 (6.09)	19.38 (4.00)	18.56 (4.59)	$F = 2.21$	.12
Digit Span Task score, mean (SD)	18.01 (5.16)	19.26 (3.15)	18.33 (3.74)	$F = 0.37$	.69
Coping scores, mean (SD)					
Task-oriented	48.27 (14.81)	51.69 (10.27)	55.06 (8.93)	$F = 1.45$	.25
Emotion-focused	49.53 (12.07)[b]	44.81 (5.97)	40.88 (6.94)	$F = 4.14$	.02
Avoidance	58.40 (11.27)	53.31 (7.26)	56.89 (10.78)	$F = 1.09$	.35
Maladaptive behavior, mean (SD)					
Self-harm/suicide	0.53 (0.83)[a,b]	0.13 (0.50)	0.00 (0.00)	$F = 4.22$	.02
Violence-related behavior	1.00 (0.53)[a,b]	0.00 (0.00)	0.00 (0.00)	$F = 59.85$	.001
Sexual behavior	9.47 (3.11)[a,b]	7.06 (2.93)	6.39 (2.97)	$F = 4.61$	.02
Body weight issues	3.20 (1.78)[a,b]	1.56 (1.67)	1.66 (1.71)	$F = 4.41$	.02

Abbreviations: BDI-II: Beck Depression Inventory–II; CSA, childhood sexual abuse; NA, not applicable; PSS, Perceived Stress Scale; rMDD, remitted major depressive disorder; SHAPS, Snaith-Hamilton Pleasure Scale.

[a] The CSA + rMDD group was significantly different from the rMDD group ($P = .05$, determined by use of the Fisher least significant difference test).

[b] The CSA + rMDD group was significant different from the control group ($P = .05$, determined by use of the Fisher least significant difference test).

Participants were instructed to press a key to the image that had the highest chance of being correct as quickly and accurately as possible. After each response, feedback (600 milliseconds) was given to indicate correct ("Correct! Well done!" in blue font) or incorrect responses ("Incorrect! Concentrate!" in red font), followed by a jittered intertrial interval (300-700 milliseconds, in 100-millisecond increments). Feedback was probabilistic; for the most reliably rewarded A-B trials, choosing A led to 80% positive and 20% negative feedback, whereas choosing B yielded 20% positive and 80% negative outcomes. For C-D trials, choosing C led to 70% positive and 30% negative feedback, and choosing D to 30% positive and 70% negative feedback. Contingencies for the least reliable stimulus type (E-F) were 60:40%. During this phase, participants learned to choose stimuli A, C, and E more frequently than B, D, and F. Favoring A over B can be achieved by learning that stimulus A usually leads to positive feedback ("Choose A" = learning from reward), stimulus B usually leads to negative feedback ("Avoid B" = learning from punishment), or both. The learning phase was completed when participants reached the performance criterion of 65% accuracy for A-B, 60% accuracy for C-D, and 50% accuracy for E-F. If performance criteria were not met, participants completed all 6 blocks before transitioning to the test phase. To ensure acquisition of learned contingencies, participants were excluded if they achieved less than 50% of correct A-B choices in half of the training blocks (eAppendix).

In the test phase, the 3 previously learned or "familiar" pairs (A-B, C-D, and E-F) were intermixed with 12 "novel" combinations of all possible stimuli pairs. No feedback was given because the test phase examined incentive-related decision making. "Go learning" is measured by the choice of the most rewarded stimulus A in A-C, A-D, A-E, and A-F trials. "NoGo learning" is measured by the avoidance of the most punished stimulus B in B-C, B-D, B-E, and B-F trials. The test phase (fixation: 1000 milliseconds; stimulus display: 3000 milliseconds; and jittered intertrial interval: 900-1300 milliseconds, in 100-millisecond increments) consisted of a single block with 120 trials.

APPARATUS

The Probabilistic Stimulus Selection Task was presented on a Dell personal computer using E-Prime 1.1 (Psychology Software Tools Inc). Electroencephalographic data were recorded using a 128-channel EGI (Electrical Geodesics Inc) system within an electrically and acoustically shielded room using a 250-Hz sampling rate (0.1-100 Hz bandpass filter) and referenced to Cz. Impedances were less than 100 kW.

DATA REDUCTION AND ANALYSES

Groups differed in BDI-II and PSS scores. Because both measures were highly correlated ($r = 0.79$, $P < .001$), main analyses entered BDI-II scores as covariates to avoid collinearity. Analyses entering PSS scores as a covariate yielded comparable results (available on request). The Greenhouse-Geisser correction was used when appropriate; significant findings from analysis of covariance were followed up with the Fisher least significant difference test.

Behavioral Task

For the training phase, mixed analyses of covariance (covariate: BDI-II scores) with group (CSA + rMDD, rMDD, and control groups) and condition (A-B, C-D, and E-F trials) as factors were run separately for accuracy and reaction time (RT). For RTs, a log transformation was applied to normalize the distribution, and analyses were performed on log-transformed data (untransformed data are presented for simplicity). In the test

phase, 2 sets of analysis evaluated whether participants relied on learned positive or negative reinforcement to optimize outcomes in the absence of explicit feedback. First, univariate analyses of covariance were used to evaluate group differences in accuracy and in RT among A-B trials, which represent the most distinctly reinforced stimuli. However, performance in A-B trials cannot be unambiguously linked to positive or negative reinforcement learning. Therefore, a second set of analyses of covariance with group × condition interaction were performed on the performance from trials including stimulus A or B paired with all other possible stimuli (hereafter referred to as "A novel" and "B novel," respectively) as condition.

Event-Related Potentials

Analyses of event-related potentials were conducted using established procedures[34,35] (eAppendix). Event-related potentials were computed time-locked to positive or negative feedback (FRN) for the learning phase and time-locked to responses (ERN) for the test phase.

For the learning phase, the FRN was evaluated at the frontocentral electrodes (Fz, FCz, and Cz) as the most negative peak between 200 and 400 milliseconds following feedback,[36,37] which was subtracted from the directly preceding positive peak (0-400 milliseconds). Accordingly, larger positive values indicate a larger (ie, more negative) FRN amplitude. Analyses of covariance with a mixed group × feedback (correct or incorrect) × electrode (Fz, FCz, or Cz) interaction were performed on FRN amplitude.

For the test phase, only the ERN (and its counterpart elicited by correct responses, the correct-response negativity [CRN]) was computed because no feedback was given. The ERN (and CRN) was defined as the most negative deflection 40 to 80 milliseconds after a response at the frontocentral electrodes (Fz, FCz, Cz, and Pz).[38-40] Peak-to-peak amplitudes were determined by subtracting the amplitude of the most negative peak 40 to 80 milliseconds after a response from the amplitude of the directly preceding positive peak (0-80 milliseconds). Larger positive values indicate larger (ie, more negative) ERN and CRN amplitudes. Similar to the behavioral analyses, ERN/CRN responses to A-B familiar trials were first evaluated in an analysis of covariance with group × response (ERN or CRN) × electrode (FCz, Fz, Cz, or Pz) interaction. Then, a mixed analysis of covariance with group × condition (A novel or B novel) × response × electrode interaction was conducted.

Source Localization

Low Resolution Electromagnetic Tomography (LORETA)[41] was used to estimate intracerebral sources. To test a priori hypotheses, current density was extracted for the training phase (average from 200 to 400 milliseconds) and the test phase (average from 40 to 80 milliseconds) from structurally defined regions of interest for cognitive and affective subdivisions of the ACC (eAppendix; eFigure). The current density was averaged within the respective time frame, intensity-normalized to unity, and log-transformed. Values were then entered in analyses of covariance with a group × response × ACC cognitive subdivision (Brodmann areas 24' and 32') interaction and a group × response × ACC affective subdivision (Brodmann areas 24, 25, and 32) interaction.

RESULTS

DESCRIPTIVE STATISTICS

Table 1 summarizes demographics and clinical measures. On average, participants were 29 years of age, single, completed high school or college, and reported an average annual income of $50 000 or less. Groups did not differ in age, marital status, or income, but the CSA + rMDD group included a smaller percentage of whites (assessed by self-report) and tended to have fewer participants who completed college (Table 1). The CSA + rMDD and rMDD groups were matched for past number of MDD episodes, time elapsed since last MDD episode, and comorbidity.

Relative to both the control group and the rMDD group, the CSA + rMDD group reported significantly higher levels of recent stress (based on PSS scores) and depressive symptoms (based on BDI-II scores) (all $P < .03$), whereas the rMDD and control groups did not differ ($P > .15$). No within-group or between-group differences were found in state anxiety or positive affect before and after the electroencephalographic recording. Overall, participants experienced a decrease in negative affect over time (eTable). Groups did not differ in working memory capacity (Table 1).

Coping and Maladaptive Behavior

Relative to the control group, the CSA + rMDD group reported significantly higher use of maladaptive behaviors and emotion-oriented coping strategies, including self-harm and suicidal ideation/suicide attempts, perpetrating violence, unsafe and high-risk sexual behaviors, and dysfunctional eating patterns associated with drastic changes in body weight (all $P < .02$) (Table 1). Importantly, these behaviors were also significantly more common in the CSA + rMDD group than in the rMDD group (self-harm/suicide, violence-related behavior, unsafe sexual behavior, and drastic changes in body weight; all $P < .04$). No differences between the control group and the rMDD groups emerged (all $P > .50$). Across the entire sample (N = 49), a higher level of emotion-oriented coping was related to violence-related behavior in the past 12 months ($r = 0.29$, $P = .04$) and dysfunctional eating ($r = 0.30$, $P = .04$).

BEHAVIORAL INDICES OF DISRUPTED REINFORCEMENT LEARNING

Learning Phase

Table 2 summarizes the average number of blocks completed and the accuracy and RT scores in the learning phase. On average, participants completed 3 training blocks with no differences between groups ($F_{2,46} = 0.13$, $P = .88$; eAppendix).

When considering accuracy, an analysis of covariance (covariate: BDI-II score) on percentage accuracy revealed condition ($F_{2,90} = 5.06$, $P = .008$) and group × condition interaction ($F_{4,90} = 2.45$, $P = .05$) effects. Consistent with the probabilistic reinforcement schedule, post hoc tests confirmed that E-F trials (0.62% [0.20%]) had a lower accuracy than did A-B (mean [SD] accuracy percentage, 0.76% [0.17%]) or C-D (0.70% [0.21%]) trials (all $P < .01$). A trend for higher A-B trial accuracy than C-D trial accuracy was also seen ($P = .06$). Follow-up tests for the group × condition interaction were not significant (all $P > .13$).

An analogous analysis of covariance with group × condition interaction on log-transformed RT data revealed

Table 2. Summary of Performance in the Learning Phase

	Mean (SD)			
	CSA + rMDD Group (n = 15)	rMDD Group (n = 16)	Control Group (n = 18)	ANCOVA *P* Value
Training blocks, No.	3.27 (1.75)	3.50 (1.51)	3.56 (1.85)	.88
Accuracy, %				
Total	0.67 (0.13)	0.70 (0.16)	0.71 (0.14)	.67
A-B trials	0.75 (0.15)	0.83 (0.13)	0.71 (0.20)	.12
C-D trials	0.70 (0.19)	0.64 (0.25)	0.76 (0.18)	.27
E-F trials	0.56 (0.17)	0.64 (0.22)	0.65 (0.21)	.73
Reaction time, ms				
Total	783.67 (117.59)	659.81 (115.05)	705.56 (105.16)	.04[a]
A-B trials	781.33 (163.07)	634.06 (122.44)	700.94 (117.69)	.06
C-D trials	765.80 (106.87)	667.44 (134.19)	691.67 (121.55)	.18
E-F trials	804.27 (122.13)	678.38 (112.85)	724.83 (127.15)	.03[a]

Abbreviations: ANCOVA, analysis of covariance; CSA, childhood sexual abuse; rMDD, remitted major depressive disorder.
[a]Statistical significance set at $P < .05$.

a main effect of condition ($F_{2,90} = 3.72$, $P = .03$), owing to slower responses on E-F trials relative to both A-B and C-D trials (all $P = .02$), and a main effect of group ($F_{2,45} = 3.27$, $P = .05$). Post hoc tests revealed a slower RT in the CSA + rMDD group than in the rMDD group ($P = .02$) but no other differences (all $P > .16$). In sum, all groups reached a similar learning accuracy, although the participants in the CSA + rMDD group were generally slower than the participants in the rMDD group.

TEST PHASE

Familiar Trials

An analysis of covariance for accuracy on A-B trials revealed a significant group effect ($F_{2,45} = 3.51$, $P = .04$), with the CSA + rMDD group showing lower accuracy on these familiar, most distinctly reinforced trials relative to both the rMDD group ($P < .02$) and the control group ($P < .05$). Similarly, an analysis of covariance for RT on A-B trials showed a significant group effect ($F_{2,45} = 6.12$, $P = .004$), with the CSA + rMDD group responding slower than the rMDD group ($P < .003$). No other differences emerged ($P > .12$).

Novel Trials

An analysis of covariance for accuracy with group × condition (A novel or B novel) interaction revealed no significant effects (all $P > .11$). When examining reward and punishment trials separately, however, we found group differences in trials that required participants to rely on previously rewarded information (A novel: $F_{2,45} = 4.02$, $P = .03$) but not previously punished information (B novel: $F_{2,45} = 0.17$, $P > .85$; **Figure 1**). Post hoc tests revealed that the CSA + rMDD group showed significantly lower accuracy in A novel trials than did the control group ($P = .05$) or the rMDD group ($P = .007$), with no differences between the latter ($P > .37$). When considering RT, we found that an analogous analysis of covariance with group × condition (A novel or B novel) interaction showed only a main effect of condition ($F_{1,45} = 19.88$, $P < .001$), owing to a shorter RT for A novel than B novel stimuli ($P < .001$).

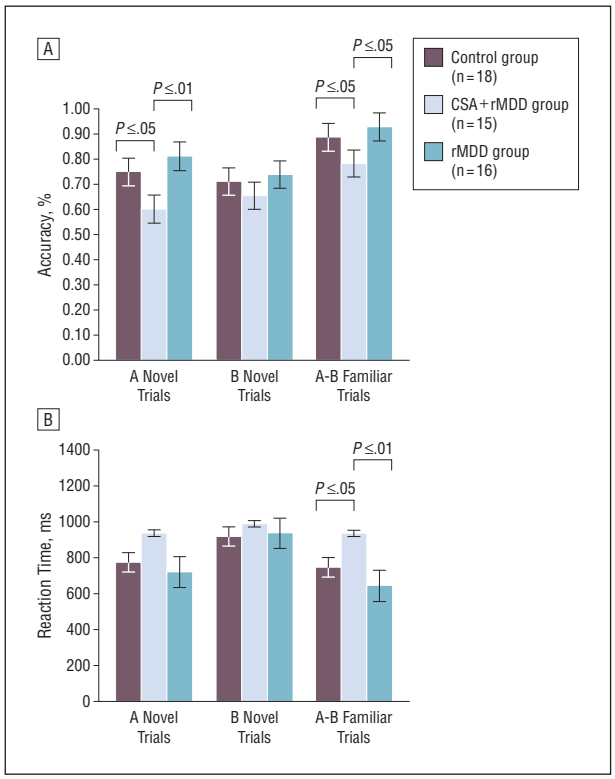

Figure 1. Mean percentage accuracy (A) and reaction time (B) for healthy women (controls), women with a history of childhood sexual abuse and remitted major depressive disorder (CSA + MDD), and women with remitted MDD with no history of abuse (rMDD) in reward (A novel), punishment (B novel), and familiar (A-B) trials. Error bars indicate standard error.

Task Performance and Maladaptive Behavior

Across the CSA + rMDD and rMDD groups (n = 31), more frequent engagement in self-harm and suicidal behavior correlated with slower responses in trials that required participants to rely on familiar (A-B trial: $r = 0.38$, $P = .03$) and previously rewarded trials (A novel trial: $r = 0.40$, $P = .03$). Both correlations were confirmed when using nonparametric (Spearman) correlations (A-B trial: Spearman $r = 0.48$, $P = .006$; A novel trial: Spearman $r = 0.44$, $P = .02$). The findings did not survive a Bonferroni cor-

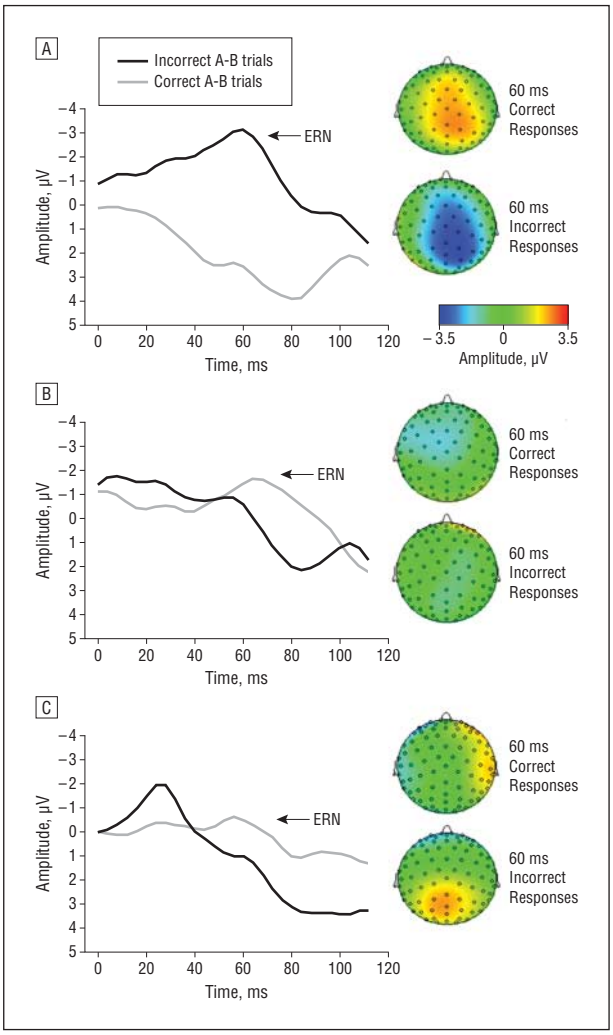

Figure 2. Response-locked waveforms (testing phase) for healthy women (A), women with a history of childhood sexual abuse and remitted major depressive disorder (B), and women with remitted major depressive disorder with no history of abuse (C) averaged for all A-B familiar trials following correct responses (grey curve) and incorrect responses (black curve) at electrode position Cz. Negative values are plotted upward. ERN indicates error-related negativity.

rection (set at $P = .05$; for 16 correlations, $P = .003$; eAppendix) and thus should be considered preliminary.

ELECTROPHYSIOLOGICAL INDICES OF DISRUPTED REINFORCEMENT LEARNING

Learning Phase: FRN to Outcome Feedback (A-B, C-D, and E-F Trials)

An analysis of covariance with group × feedback × electrode interaction yielded a main effect of feedback ($F_{1,42} = 7.09$, $P = .01$), with the expected larger (ie, more negative) FRN amplitude following incorrect rather than correct responses ($P = .004$). No other effects emerged (all $P > .12$).

Test Phase: ERN and CRN (AB, A Novel, and B Novel Trials)

Familiar Trials. An analysis of covariance with group × response × electrode interaction showed a significant group × response effect ($F_{2,26} = 4.05$, $P = .03$). Similar to previous research,[42] and because no effect of electrode emerged, follow-up analyses focused on Cz. Significant group differences emerged on correct ($F_{2,26} = 9.74$, $P = .001$) but not incorrect ($F_{2,26} = 2.48$, $P = .10$) A-B trials. On correct A-B trials, the control group showed smaller (ie, less negative) CRN amplitudes than did the CSA + rMDD group ($P = .004$) and the rMDD group ($P < .001$); the CSA + rMDD and rMDD groups did not differ ($P = .54$) (**Figure 2**).

Novel Trials. An analogous analysis of covariance with group × condition (A novel or B novel) × response × electrode interaction showed no significant effects. (It should be noted that ERN and CRN are indices of error monitoring and thus are expected to be more pronounced in response to familiar rather than novel pairings.)

SOURCE LOCALIZATION

Learning Phase

Similar to the behavioral and scalp data, no group differences emerged in ACC activity during the learning phase.

Test Phase

Familiar Trials. Analyses of covariance for A-B trials did not yield group differences.

Novel Trials. A group × response × ACC affective subdivision interaction for A novel trials revealed a main effect of the ACC affective subdivision ($F_{2,66} = 46.45$, $P < .001$), a group × response interaction ($F_{2,33} = 6.73$, $P = .004$), and a group × response × subdivision interaction ($F_{4,66} = 4.54$, $P = .014$). Follow-up analyses of the triple interaction revealed a group × response interaction for the subgenual ACC (Brodmann area 25; $F_{2,33} = 7.87$, $P = .002$) and the rostral ACC (Brodmann area 24; $F_{2,33} = 5.88$, $P = .007$). Groups differed in subgenual activation on correct A novel trials ($F_{2,33} = 3.93$, $P = .03$) but not on incorrect A novel trials ($F_{2,33} = 1.79$, $P = .18$). Relative to the rMDD group, the CSA + rMDD group had significantly higher activation in the subgenual ACC ($P = .01$); they also tended to show higher activation than did the control group ($P = .07$; **Figure 3**). No differences were found between the control group and the rMDD group ($P = .33$). Further analyses of the rostral ACC did not yield between-group differences.

A group × response × ACC cognitive subdivision interaction showed a main effect of the ACC cognitive subdivision ($F_{1,33} = 13.00$, $P = .001$) and a group × ACC cognitive subdivision interaction ($F_{2,33} = 3.84$, $P = .03$). Follow-up analysis did not yield group differences. No group differences in ACC affective or cognitive subdivisions emerged for B novel trials.

COMMENT

The goal of our study was to investigate the putative disruption in positive and negative reinforcement learning in women with a history of CSA, and whether such dysfunctions are related to maladaptive behavior. Several novel findings emerged. First, the groups did not differ in their ability to acquire the probabilistic reinforcement schedule.

Results from the test phase revealed, however, that women in the CSA + rMDD group had lower accuracy percentages and slower RTs on familiar A-B trials than did women in the rMDD group or the control group. Although familiar A-B trials do not allow us to disentangle whether participants made choices guided primarily by their positive or negative history of reinforcement, these distinctly reinforced trials provide a critical test of the utilization of reinforced information in the absence of explicit feedback. Importantly, additional analyses clarified that women with a history of CSA choose less reliably the most positive stimulus A in the test phase, indicating impaired performance in trials requiring reliance on previously rewarded information (A novel trials). Notably, groups did not differ in their avoidance of the most negative stimulus B, suggesting that the CSA + rMDD group was not affected in trials requiring reliance on previously punished information (B novel trials). Highlighting the clinical relevance of these findings, we found that slower RTs in A novel (and A-B) trials correlated with self-harm and suicidal behavior. Because correlations did not survive a Bonferroni correction, these latter findings should be considered preliminary. Collectively, these findings confirm our first hypothesis that women with a history of CSA demonstrate disrupted reinforcement learning, and they highlight that these impairments are specific to trials that require reward-based reinforcement learning. Of note, lack of group differences (at both the behavioral level and the neural level) in (1) B novel trials, (2) the acquisition of the reinforcement contingencies, and (3) working memory performance indicate that blunted Go learning in the CSA + rMDD group was not due to global cognitive impairments. Finally, the CSA + rMDD and rMDD groups were matched for the number of prior depressive episodes and for time elapsed since last depressive episode, and analyses included BDI-II (and PSS) scores as covariates, which suggested that current depressive symptoms or past MDD episodes did not influence outcomes.

Our second hypothesis focused on neural indices of reinforcement learning. Because ERN and CRN index correct and incorrect responses, respectively, to known stimuli, the largest (ie, most negative) amplitudes were expected on incorrect familiar trials. Compared with controls, women with a history of CSA showed more negative amplitudes in response to correct A-B trials, which suggests a more error-like response following correct answers. Although intriguing, it is important to note that the rMDD group showed a similar pattern, which suggests that this electrophysiological marker of disrupted reinforcement learning might not be specific to CSA.

More specificity with respect to CSA emerged from the source-localization analyses, in which the CSA + rMDD group showed increased activation in the affective but not cognitive subdivision of the ACC during the "Go learning" trial relative to the rMDD group and, to a lesser extent, the control group. Specifically, women with a history of CSA demonstrated increased subgenual ACC activation during correct responses in trials that required reward-based decision making (A novel trials). The affective ACC subdivision has extensive connections to limbic and paralimbic structures (eg, the amygdala, the nucleus accumbens, and the orbitofrontal cortex) and is thought to play a key role in stress responsivity, emotional responding, and evaluation of feedback salience.[43,44] Thus, we speculate that the CSA + rMDD group may experience a higher level of emotional arousal in trials requiring reliance on previously rewarded information, which, in turn, may interfere with adaptive decision making. Notably, the onset of CSA in this sample (7-12 years of age) coincides with a time period in which the ACC undergoes significant change.[14,15] Prolonged postnatal development might thus leave the ACC vulnerable to the effects of glucocorticoids.[18,19] Consistent with these arguments, maltreated adults with MDD exhibited reduced volume in the affective ACC subdivision, and such volume reduction correlated with maltreatment severity and high cortisol levels.[20] Thus, the present findings add to emerging evidence indicating that the affective ACC subdivision may be affected by early-life stress.

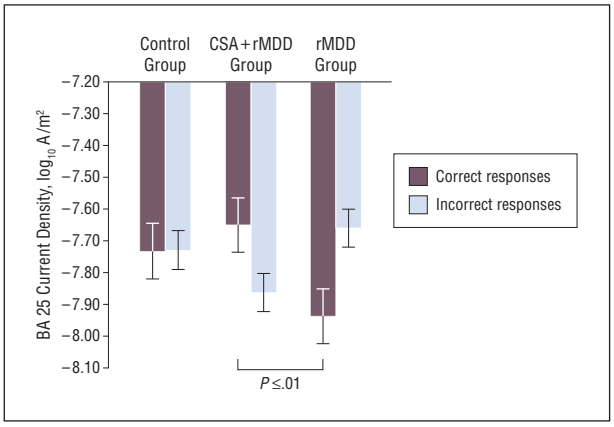

Figure 3. Subgenual (Brodmann area [BA] 25) activation in A novel trials for healthy women (controls), women with a history of childhood sexual abuse and remitted major depressive disorder (CSA + rMDD), and women with remitted major depressive disorder with no history of abuse (rMDD). Less negative values denote a higher current density (ie, activation). Error bars indicate standard error.

ACQUISITION OF REINFORCEMENT CONTINGENCIES

Although group differences emerged in the utilization of previously reinforced contingencies, groups did not differ with regard to behavioral, scalp, or brain data in their ability to initially acquire the probabilistic reinforcement schedule. During training, participants showed similar accuracy levels and required an equal number of trials before transitioning to the test phase. As expected, FRN amplitude was increased (ie, more negative) following incorrect rather than correct feedback, which indicates that participants displayed similar reward and punishment responsivity. This was also reflected in a similar ACC activation in response to explicit feedback across groups. No association was found between maladaptive behaviors and any of the behavioral or neural measures during training. It can be concluded that participants successfully acquired reinforcement contingencies and that a history of CSA does not affect the ability to learn from explicit positive and negative feedback.

DISRUPTED REINFORCEMENT LEARNING

Across levels of analyses, the present findings suggest that CSA is related to deficits in incentive-based decision mak-

ing and, in particular, reduced "Go learning." The results fit prior evidence suggesting disrupted reward processing following maltreatment. For example, Guyer and colleagues[45] found that children with a history of maltreatment did not modulate RT as a function of the likelihood of receiving reward. In a longitudinal sample, adults with a history of childhood maltreatment rated reward-predicting cues less positively and showed reduced anticipatory reward activity in the left pallidus, a brain region implicated in goal-directed behavior.[46]

In our study, a history of trauma did not affect the use of previously learned punishment information in a novel context (B novel trials). In addition, although a reduced level of sensitivity to punishment (as indexed by a smaller ERN amplitude) emerged in individuals with high levels of impulsivity,[47] risk taking,[48] and externalizing behavior,[49] such outcomes were not associated with maladaptive CSA sequelae. Instead, frequent self-harm and suicidal behavior was related to slower RT in trials requiring incentive-based decision making, including integrating information from previously rewarded trials.

MALADAPTIVE BEHAVIOR AND DISRUPTED REINFORCEMENT LEARNING

Consistent with clinical evidence suggesting that adults with CSA frequently engage in maladaptive behaviors despite negative outcomes,[7,9] the present sample of participants from the CSA + rMDD group reported elevated levels of self-harm, violence-related behavior, unsafe sexual behavior, and dysfunctional eating. Moreover, violent behavior and dysfunctional eating were more frequently engaged in when the individual adopted an emotion-oriented maladaptive coping style. Although maladaptive behaviors can provide initial relief from CSA-related distress, they also form a primary predictor of future sexual victimization.[9,10] The pathways linking CSA to later revictimization are a growing concern because 30% to 50% of individuals who experienced CSA are likely to experience sexual violence later in life.[50,51] Our aim was to examine whether the high-risk behaviors commonly seen in adults with a history of CSA are associated with disrupted reinforcement learning. The frequency of self-harm/suicidal behaviors was significantly related to slower responses in trials that required incentive-based decision making (A-B trials) and Go learning (A novel trials). Because maladaptive behaviors were assessed retrospectively, future studies are needed to examine whether disrupted positive reinforcement learning predicts future high-risk behaviors and revictimization.

LIMITATIONS

Some limitations should be acknowledged. First, the experiences of CSA were based on retrospective reports and were not externally validated by police or court reports. However, careful assessments of adverse childhood events were conducted as part of the initial clinical assessment. All participants were able to recall central details of the abuse (eg, age at onset and frequency). Second, although our study excluded participants with other childhood adversities, no causal inference between CSA and disrupted reinforcement learning can be made. The ACC develops over an extended period of time and may therefore be vulnerable to other environmental insults. Third, although follow-up analyses guided by our a priori hypotheses revealed that the participants in the CSA + rMDD group had a lower mean accuracy percentage in A novel trials (but not in B novel trials) than did the participants in the control group or the rMDD group, it is important to emphasize that the group × condition interaction was not significant. Thus, the specificity of this behavioral finding is limited. Finally, although MDD is a common outcome of CSA, our findings cannot be generalized to women with a history of CSA in general; in addition, in the present study, lifetime somatoform or personality disorders represented exclusion criteria. Future studies should include a CSA group without psychopathology to further investigate CSA-specific effects in reinforcement learning.

In conclusion, behavioral and source-localization results provide preliminary evidence for deficits in relying on previously reinforced information to optimize decision making following CSA. Performance in trials involving incentive-based decision making, including learned reward contingencies, was associated with more frequent engagement in self-harm/suicidal behavior. No group differences emerged when participants needed to rely on negatively reinforced information, which suggests that maladaptive behavior may not be related to difficulties in using punishments to guide decision making. Future studies will need to confirm the role of disrupted positive reinforcement learning and further explore neurobiological dysfunctions as potential mechanisms implicated in high-risk behavior.

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Correspondence: Pia Pechtel, PhD, Center For Depression, Anxiety and Stress Research, McLean Hospital, 115 Mill St, Room 233B, Belmont, MA 02478 (ppechtel@mclean.harvard.edu).
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