

Preliminary Evidence for Anhedonia as a Marker of Sexual Trauma in Female Adolescents

Ayse Irem Sonmez ^{1,2}Charles P Lewis¹Arjun P Athreya³Julia Shekunov²Paul E Croarkin ²

¹Department of Psychiatry and Behavioral Sciences, University of Minnesota Medical School, Minneapolis, MN, USA; ²Department of Psychiatry and Psychology, Mayo Clinic, Rochester, MN, USA; ³Department of Molecular Pharmacology & Experimental Therapeutics, Mayo Clinic, Rochester, MN, USA

Introduction: Major depressive disorder (MDD) is a common condition with heterogeneous presentations that often include predominant anhedonia. Previous studies have revealed that childhood trauma is a potent risk factor for the development of MDD; however, the clinical implications of this finding are not fully understood.

Methods: Participants were adolescents (age 13–21 years) with a diagnosis of moderate-to-severe major depressive disorder and healthy controls. We used generalized linear models to assess the relationship between anhedonia severity and trauma severity in a cross-sectional dataset.

Results: This cross-sectional analysis of an adolescent sample that underwent clinical evaluations and a trauma assessment, suggested that anhedonia was associated with historical trauma severity. The association between anhedonia and sexual abuse was greater in female participants compared to male participants.

Discussion: Our results were partially in line with the reported literature in adult samples. Future studies aiming to characterize the trauma–anhedonia relationship in adolescents should utilize scales designed specifically to measure these constructs in young populations, and scales that assess specific subtypes of anhedonia.

Keywords: adolescent, anhedonia, emotional abuse

Introduction

Anhedonia is defined as impaired interest and inability to experience pleasure in previously enjoyable activities.¹ Anhedonia is a long accepted core feature of major depressive disorder (MDD) that varies independently of other depressive symptomatology.² Anhedonia is also recognized as an important component of schizophrenia and post-traumatic stress disorder (PTSD),³ as well as a contributor to suicide risk.⁴ Increasingly, anhedonia is conceptualized as a transdiagnostic dimension⁵ with multiple risk pathways leading to its emergence.⁶

Previous studies have revealed that childhood trauma is a potent risk factor for the development of MDD; however, the impact of childhood trauma on specific depressive symptoms, is inadequately understood. MDD co-occurs in approximately half of individuals with PTSD⁷ and is common in other trauma-exposed individuals.⁸ Studies of patients with PTSD suggest that anhedonia may link traumatic experiences and development of depressive disorders.⁹

In previous studies with young adult participants, perceived stress has been found to increase negative affect and anhedonia.¹⁰ In another study with adults anhedonia was suggested to be the optimal target phenotype when examining the impact of childhood adversity on depression.¹¹ The aim of this study was to investigate the association

Correspondence: Ayse Irem Sonmez
Department of Psychiatry and Behavioral Sciences, University of Minnesota Medical School, 2312 S 6th St, Minneapolis, MN, 55454, USA
Tel +1 612-273-8383
Email sonme005@umn.edu

between anhedonia and past trauma in adolescents. We examined the trauma–anhedonia relationship in healthy adolescents, depressed adolescents, and the combined sample. We hypothesized that anhedonia would demonstrate positive correlations with the severity of various types of childhood traumas.

Methods

Overview

This study was a retrospective, secondary analysis of cross-sectional data from a study conducted by our research group that examined excitatory/inhibitory cortical physiology and glutamatergic neurochemistry in diverse groups of depressed adolescents and healthy youth. Written informed consent was obtained from parents or guardians of participants under 18 years of age, and directly from participants ≥ 18 years.¹² Written assents were obtained from participants < 18 years. All research procedures were approved by the Mayo Clinic institutional review board (Rochester, MN, USA). This study was conducted in accordance with the Declaration of Helsinki.

Participants and Eligibility

Depressed participants were adolescents (age 13–21 years) with a diagnosis of a moderate-to-severe major depressive disorder for whom treatment with an antidepressant medication (SSRI) was indicated (but not administered). Healthy control adolescents (age 13–21 years) had no history of psychiatric disorder or treatment. The total number of participants was 56. The parent study was a cross-sectional biomarker study of MDD. No treatment was provided or administered in the form of antidepressant SSRI medications, repetitive transcranial magnetic stimulation (rTMS), or psychotherapy. Contraindications to MRI/MRS, as determined by the MRI safety screen and MRI safety codes were among exclusion criteria. Adolescents in the healthy control group had no current or historical psychiatric diagnosis and no current or previous psychopharmacologic or psychotherapeutic treatment. Participants in the depressed group had current diagnoses of unipolar depressive disorders on the K-SADS-PL diagnostic interview. Exclusion criteria consisted of lifetime history of mania or psychosis, the presence of an active substance use disorder (except nicotine), and any unstable medical condition.

Assessments

Participants were interviewed by a board-certified child and adolescent psychiatrist (PEC) using the Schedule for Affective Disorders and Schizophrenia for School Aged Children,

K-SADS-PL.¹³ Depressive symptom severity was rated with the Children's Depression Rating Scale, Revised (CDRS-R).¹⁴ A score that combined CDRS-R items 2 and 3 ("Difficulty having fun" and "Social Withdrawal") was used to measure anhedonia ("CDRS-R Anhedonia Subscale"). Participants also completed the Quick Inventory of Depressive Symptomatology (17-item) Adolescent and Parent Self Report (QIDS-A17-SR).¹⁵ Prior psychometric studies have demonstrated that CDRS-R and QIDS-A17-SR are reliable and valid instruments for assessing adolescents.^{15,16} A study from our group, suggested that QIDS-A17-SR has more clinical utility compared to CDRS-R when assessing depression severity.¹⁷ In a more recent review, the validity of CDRS-R as measurement of depression symptom severity in adolescents remained unclear.¹⁸ As a result of these related findings, depression symptoms severity was assessed with QIDS-A17-SR in the present study.

Participants' self-reported trauma histories were assessed with the Childhood Trauma Questionnaire (CTQ),¹⁹ which is comprised of 28 items, each rated on a five-point Likert scale. In addition to a total trauma score, five subscales are generated: emotional abuse (EAS), physical abuse (PAS), sexual abuse (SAS), physical neglect (PNS), and emotional neglect (ENS). Higher scores on the CTQ denote greater historical trauma severity. The CTQ was used as a continuous variable of trauma severity (total and subscale scores) to increase power and to evaluate trauma as a dimensional variable. CTQ has been used as a continuous variable in the literature recently.^{20,21}

Statistical Analysis

All analyses were conducted using SPSS version 25 (IBM Corp., Armonk, NY, USA). We assessed assumptions of normality with the Shapiro–Wilk test. Non-parametric tests were used to compare data that did not have a normal distribution. Demographics and clinical measures were compared between groups using Student's *t*-test, Mann–Whitney U or Chi square. Sex differences across groups were assessed with Chi-Square. Age and QIDS-A17-SR compared with two samples *t*-test. CDRS-R total score, Anhedonia subscale score and all CTQ scores were compared with Mann–Whitney U as these variables did not have a normal distribution.

Participants were categorized based on prior trauma with scoring cut-off from the CTQ scoring guidelines.¹⁹ The "No Trauma" group included participants who scored equal or less than 8 in emotional abuse score, equal or less than 7 in physical abuse score, equal or less than 5 in sexual abuse score, equal or

Table 1 Childhood Trauma Questionnaire Cutoff Scores

Level of Abuse	Emotional Abuse	Physical Abuse	Sexual Abuse	Emotional Neglect	Physical Neglect
None	8	7	5	9	7
Low	12	9	7	14	9
Moderate	15	12	12	17	12
Severe	16+	13+	13+	18+	13+

Notes: CTQ (Childhood Trauma Questionnaire) Manual cutoff scores and categories for each subscale. Example: Those who scored 8 or less in emotional abuse reported minimal or no trauma. Those who scored 9 or higher in emotional abuse reported some level of emotional abuse.

less than 9 emotional neglect score, equal or less than 7 in physical neglect score (Table 1). All other participants were categorized into the “Trauma Exposure” group which indicated that participants had low, moderate or high trauma in at least one subscale.

We used generalized linear models to assess the relationship between anhedonia severity and trauma severity. The dependent variables were CTQ scores (total and subscales). The CDRS-R Anhedonia Subscale was the independent variable. Model was built 1) without any covariates 2) controlling for QIDS-A17-SR (proxy for depression severity), age and sex. Akaike’s Information Criterion (AIC) was utilized to assess goodness of fit.

Results

Sample Characteristics

Data from 42 participants (17 healthy controls, 25 depressed; 59.5% female, age range 13–21) were analyzed. Demographics are summarized in Table 2. There were no differences in age or sex between healthy and depressed groups. CTQ scores ranged between 25 and 66. Depressed participants demonstrated significantly higher trauma.

Twenty-four participants reported some level of trauma in any of the five subscales of CTQ based on cut-off scores according to CTQ Manual (Table 1). Age and sex did not differ across two trauma levels. Anhedonia score was

Table 2 Demographics and Clinical Features

	Combined Sample n = 42	Healthy vs Depressed			No Trauma vs Trauma Exposure		
		Healthy Control n = 17	Depressed n = 25	p-value	No Trauma n = 18	Trauma Exposure n = 24	p-value
Age (years)	16.33 (2.01)	16.65 (2.21)	16.12 (1.88)	0.43	16.39 (1.94)	16.29 (2.1)	0.367
Female, n (%)	25 (59.5)	12 (70.6)	13 (52)	0.23	11 (61)	14 (58.3)	0.87
CDRS-R scores							
Total Score	36.69 (18.42)	19.12 (2.89)	48.64 (14.37)	<0.001	24.33 (11.89)	45.96 (17.06)	<0.001
Anhedonia subscale	4.79 (3.05)	2.12 (0.49)	6.6 (2.69)	<0.001	2.78 (1.96)	6.29 (2.87)	<0.001
QIDS-A17-SR score	8.43 (6.45)	2.71 (2.14)	12.32 (5.38)	<0.001	3.72 (2.22)	11.96 (6.19)	<0.001
CTQ scores							
Total Score	37.1 (11.04)	28.35 (3.28)	43.04 (10.49)	<0.001	27.67 (3.73)	44.17 (9.38)	<0.001
Emotional Abuse Scale	9.05 (4.23)	6.06 (1.39)	11.08 (4.31)	<0.001	5.83 (0.99)	11.46 (4.12)	<0.001
Emotional Neglect Scale	8.57 (3.85)	6.41 (1.91)	10.04 (4.17)	0.001	6.06 (1.66)	10.46 (3.97)	<0.001
Physical Abuse Scale	6.45 (2.28)	5.18 (0.53)	7.32 (2.59)	0.001	5.28 (0.67)	7.33 (2.65)	<0.001
Physical Neglect Scale	6.52 (2.2)	5.71 (1.36)	7.08 (2.5)	0.037	5.33 (0.59)	7.42 (2.54)	0.012
Sexual Abuse Scale	6.43 (3.98)	5 (0)	7.4 (4.96)	0.002	5 (0)	7.5 (5.04)	0.001

Notes: Means with standard deviations or % in parentheses. Trauma level is based on CTQ (Childhood Trauma Questionnaire) Manual. Participants who reported none or minimal trauma in all subscales were grouped as “No Trauma”; all others are grouped as “Trauma Exposure”. Anhedonia subscale is the total of CDRS-R items 2 and 3. Sex differences across groups were assessed with Chi-Square. Age and QIDS-A17-SR compared with two samples t-test. CDRS-R total score, Anhedonia subscale score and all CTQ scores were compared with Mann–Whitney U due to skewed distribution of the variable.

Table 3 Sample Characteristics

Participant	Group	Trauma Exposure	Medication(s) and Total Daily Dose	Comorbidities	Sex
1	Dep/Med -	EAS, PAS, ENS	None	Cannabis use	M
2	Dep/Med +	No Trauma	Fluoxetine, methylphenidate hydrochloride ER	ADHD, stimulants were held on day of Scan	F
3	HC	No Trauma	None	None	F
4	HC	No Trauma	None	None	F
5	HC	EAS	None	None	F
6	HC	No Trauma	None	None	F
7	Dep/Med -	EAS, SAS, PNS	None	Panic disorder	M
8	HC	No Trauma	None	None	F
9	Dep/Med +	EAS, SAS, ENS	Sertraline, aripiprazole	None	M
10	Dep/Med +	SAS	Fluoxetine	Alcohol use disorder in remission 8 months, anxiety disorder NOS	F
11	HC	No Trauma	None	None	M
12	HC	No Trauma	None	None	F
13	HC	ENS	None	Subthreshold depressive symptoms	F
14	Dep/Med -	EAS, ENS	None	None	F
15	Dep/Med -	EAS, PAS, ENS, PNS	None	Cannabis use disorder	M
16	Dep/Med +	EAS, SAS	Sertraline	None	F
17	HC	No Trauma	None	None	M
18	Dep/Med -	EAS, PAS, SAS	None	None	F
19	Dep/Med -	EAS, SAS, ENS, PNS	None	Alcohol, cannabis, nicotine	F
20	Dep/Med -	EAS, ENS, PNS	None	None	F
21	Dep/Med -	EAS, SAS	None	ADHD, Osgood-Schlatter Disease	F
22	Dep/Med +	EAS, SAS, ENS	Fluoxetine, dextroamphetamine saccharate	ADHD, GAD, Motor Tic Disorder	M
23	Dep/Med +	EAS, ENS, PNS	Fluoxetine	Cannabis use disorder	M
24	Dep/Med -	EAS, ENS	None	Persistent dysthymic disorder	F
25	Dep/Med -	EAS, PAS, ENS, PNS	Methylphenidate hydrochloride	ADHD	M
26	Dep/Med +	No Trauma	Fluoxetine	Restless leg syndrome, migraines	F
27	Dep/Med -	EAS, PAS, ENS, PNS	None	Persistent dysthymic disorder, cannabis use disorder	F
28	HC	No Trauma	None	None	F

(Continued)

Table 3 (Continued).

Participant	Group	Trauma Exposure	Medication(s) and Total Daily Dose	Comorbidities	Sex
29	HC	PNS	None	None	F
30	Dep/Med +	No Trauma	Duloxetine	ADHD, minor depressive disorder	M
31	Dep/Med -	ENS	Methylphenidate, atomoxetine	ADHD	M
32	Dep/Med +	No Trauma	Bupropion hydrochloride xl	None	M
33	HC	PNS	None	Cannabis use disorder	M
34	HC	No Trauma	None	None	M
35	Dep/Med -	EAS, PAS, SAS, ENS	None	PTSD	F
36	HC	No Trauma	None	Mild concussion history	M
37	Dep/Med +	EAS, PAS, SAS	Fluoxetine	Cannabis use disorder	F
38	Dep/Med +	No Trauma	Amitriptyline	Learning disability, chronic headaches	M
39	Dep/Med +	EAS, PAS, SAS, ENS	Fluoxetine	None	M
40	HC	No Trauma	None	None	F
41	HC	No Trauma	None	None	F
42	HC	No Trauma	None	None	F

Notes: "No Trauma" group consisted of participants who scored in the "None or minimal" category on all subscales. This was defined according to Childhood Trauma Questionnaire Manual. The cut-off scores for each scale are shown in Table 1.

Abbreviations: EAS, Emotional Abuse Scale; PAS, Physical Abuse Scale; SAS, Sexual Abuse Scale; ENS, Emotional Neglect Scale; PNS, Physical Neglect Scale.

significantly higher in the Trauma Exposure group. Full list of medications, comorbidities and reported trauma levels in CTQ subscales were summarized in Table 3. Most frequent comorbidities were ADHD (n=6) and cannabis use disorder (n=7). One participant met criteria for PTSD.

Assessment of Trauma Severity and Anhedonia

There were significant positive relationships between the CDRS-R Anhedonia Subscale and CTQ total score, EAS, ENS, PAS and PNS (all $p < 0.05$), but not SAS, in the combined sample (Table 4). Among the subscales, the EAS showed the most robust association (highest coefficient) ($\beta = 0.93$, $p < 0.001$). Age did not have a significant relationship with the dependent variable therefore age was not controlled for in any of the models.

The correlation between CDRS-R Anhedonia Subscale and QIDS-A17-SR was $r = 0.801$ ($p < 0.001$). When QIDS-A17-SR score was added to the models to control for depression severity, the parameter estimates for anhedonia were non-significant in all models.

The main effect of diagnosis was factored in the models as a group along with the interaction of group by anhedonia score. Interaction terms were not significant in any of the models. Similarly, main effect of sex and interaction term sex by anhedonia scores were factored into the models. The interaction term was significant in the sexual abuse scale (Table 5). Figure 1 summarizes the graph of predicted values of sexual abuse scale by anhedonia scores.

Discussion

The present study sought to examine the association between anhedonia and past trauma in a sample of healthy

Table 4 Generalized Linear Model Results

	β	SE	95% CI for β	p-value
CTQ Total Score	2.485	0.41	1.689–3.281	<0.001
Emotional Abuse	0.93	0.16	0.619–1.241	<0.001
Emotional Neglect	0.67	0.17	0.346–0.994	<0.001
Physical Abuse	0.228	0.11	0.014–0.443	0.037
Physical Neglect	0.306	0.1	0.109–0.504	0.002
Sexual Abuse	0.364	0.19	–0.014–0.743	0.059

Notes: CTQ total scores and 5 subscale association with CDRS-R Anhedonia Subscale in combined sample (n=42, df=38, 1). Each β and p-value pair represents a separate generalized linear model. Independent variable: CDRS-R Anhedonia Subscale, dependent variable Childhood Trauma Questionnaire scores.

Table 5 Association of Sexual Abuse Score with Sex and Anhedonia Score

Parameter	β	SE	95% CI for β		p-value
			Upper	Lower	
CDRS-R Anhedonia Subscale	0.117	0.254	–0.38	0.21	0.64
Sex	–1.349	2.131	–5.53	2.83	0.53
Sex * CDRS-R Anhedonia Subscale	0.751	0.368	0.029	1.47	0.042

Notes: Dependent variable was Childhood Trauma Questionnaire Sexual Abuse Scale. Sample size and degrees of freedom were n=42, df=38, 1.

and depressed adolescents. In the combined sample, anhedonia was associated broadly with trauma measures (total CTQ score and all subscales, except SAS), although these relationships were nonsignificant when corrected for depression severity. This is likely due to covariance between anhedonia and depression severity. In the present study, the correlation between these variables were significant. Also trauma and depression are often collinear parameters, as demonstrated in population-level studies²² adding to the covariance of parameters.

In one prior study Fan and colleagues assessed a young adult sample (18–35 years) using the CTQ and three separate anhedonia-specific scales²³ and found that MDD patients with moderate-to-severe childhood trauma had elevated state anhedonia compared to MDD patients with no/low trauma. State anhedonia was measured by Beck Inventory of Depression. We believe this is in line with our

findings showing significant positive relationship of anhedonia and trauma. Fan and colleagues also reported that between depressed participants with trauma exposure had greater emotional abuse/neglect scales compared to healthy controls with trauma exposure. This was also noted in our sample despite small sample sizes of 4 healthy controls and 20 depressed participants who reported trauma. In our present study, the main effect of childhood trauma on anhedonia was not qualified further by a significant interaction of diagnosis. This was most likely due to the small sample sizes in our study.

A longitudinal study examining effects of maltreatment found that emotional abuse/neglect predicted depressed mood and anhedonia, with emotional neglect also predicting increased anhedonia over time.²⁴ This raises questions about the cumulative effects of trauma and differential impacts of maltreatment at different stages of social development. This also suggests that childhood adversity imparts later-onset anhedonia in adulthood.

In a prior study that investigated specific types of childhood adversity and social and cognitive capacity, verbal abuse and fear of abuse were found to be significantly associated with worse social motivation. Our findings are partially in line with this study. Physical neglect in our sample unlike the mentioned study results, had smaller parameter estimates compared to emotional abuse however both types of trauma were associated with state anhedonia which we believe covers the domain of social motivation.²⁵

Sexual abuse has been associated with various psychopathology.^{26,27} Our study was the first in the literature to report a differential effect of sex on the association between sexual abuse and anhedonia in adolescents. In this sample, the association between sexual abuse and anhedonia was stronger in female participants compared to male participants. These results could serve as a foundation for generating new hypothesis on this area.

Some other limitations apply to our findings. The CTQ is completed retrospectively, and the scores could be influenced by the inherent subjectivity and/or current mood state of the participants. Cross-sectional analyses also cannot causally link prior trauma and current depressive symptoms. Assessing anhedonia with two items from a depression scale may not be descriptive enough to appropriately measure all aspects of anhedonia and likely to be influenced by the participant's mood state at the time of assessment.

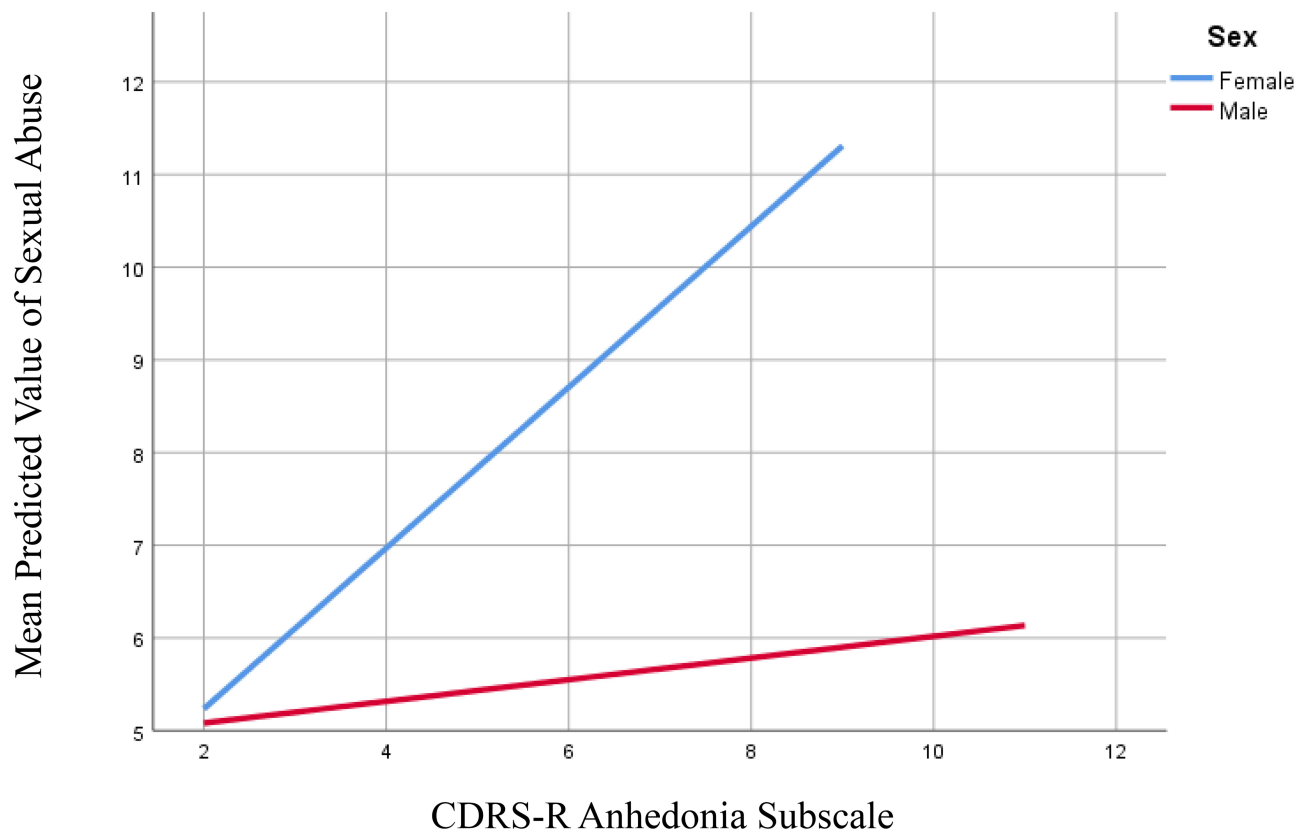


Figure 1 CTQ Sexual Abuse Scale by Anhedonia in Males and Females.

Future studies aiming to characterize the trauma–anhedonia relationship in adolescents should utilize scales designed specifically to measure these constructs in young populations, and scales that assess specific subtypes of anhedonia. Similarly, newer conceptualizations of childhood adversity, such as fragmented or chaotic early environmental stimuli, are currently under study as contributors to development of anhedonia via effects on developing reward circuits.²⁸ Novel instruments measuring early life unpredictability have correlated with anhedonia in various cohorts, including adolescents,²⁹ and may enhance our understanding of adversity-related antecedents to development of anhedonia in future clinical studies.

Longitudinal observational studies in larger cohorts are also necessary to eliminate recall bias and establish temporal relationships when measuring outcomes of childhood trauma. If replicated, measures of anhedonia could be considered for future efforts focused on trauma screening.

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