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Social support mediates the effects of childhood unpredictability on anhedonia: A retrospective investigation in an online adult community sample

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ABSTRACT

Increasingly, research is highlighting the implications of exposure to unpredictable environments during childhood (i.e., "childhood unpredictability") on outcomes in adulthood. Converging evidence from preclinical and clinical studies has implicated childhood unpredictability in disrupted reward processing and anhedonia. From the stress generation literature, altered social support has emerged as a possible mechanism by which this effect may occur. In the current study, our goal was to understand whether the pathway from childhood unpredictability to anhedonia occurs through reduced perceptions of social support. Toward this end, we recruited an online community sample of adults in the US ($N = 242$) to complete surveys assessing childhood unpredictability, depressive symptoms, anhedonia, and social support, as well as a novel online version of the Probabilistic Reward Task. We found that childhood unpredictability was associated with increased depressive symptoms and anhedonia (but not objective measure of anhedonia), and reduced perceptions of social support in adulthood. Mediation analyses revealed a significant indirect effect of perceived social support on the association between childhood unpredictability and anhedonia, controlling for age, sex, and non-anhedonic depressive symptoms. Unexpectedly, measures of reward responsiveness from the behavioral task were not related to childhood unpredictability. The current findings replicate previous reports linking childhood unpredictability and self-reported anhedonia, and extend them to incorporate the potential mediating pathway of reduced social support. Implications for treatment for anhedonia are discussed.

1. Introduction

A growing body of literature exploring the long-term consequences of early experiences of unpredictable environments has emerged in recent years. Childhood unpredictability is theorized to be a dimension of childhood stress [1] which, though understudied compared to childhood traumatic events, may confer added risk for developing psychopathology and other negative outcomes in later life. While childhood trauma is typically thought to encompass experiences such as physical and emotional abuse and neglect, as well as sexual abuse, childhood unpredictability is characterized by experiences such as lack of parental monitoring, an unstable physical environment, precarious sense of safety and security, and low levels of parental predictability [2]. Preclinical experimental research in animals offers compelling evidence that fragmented care in early life alters neural development and reward circuitry [3–5], and human studies have linked early unpredictability with anhedonia [6,7]. The present study utilizes a recently developed self-report measure of childhood unpredictability to investigate the relationship between early life unpredictability and anhedonia in adults and, to the best of our knowledge, is the first to explore the putative role of reduced social support as a potential mediator in a community sample of adults.

While the sequelae of exposure to early unpredictability, measured as a broad, dimensional phenomenon, have only recently become a focus of clinical research [2,6,8,9], the relationship between childhood trauma and psychopathology is well-established. Childhood trauma has

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been linked to depression [10,11], anxiety [12], post-traumatic stress disorder [13], and borderline personality disorder [14,15]. Further, trauma in early life is associated with impairments in cognition in adults [16] and children [17]. Moreover, findings have linked childhood trauma with poorer health outcomes and altered physiological responses (e.g., elevated resting heart rate) in adulthood [18]. Recent work demonstrating differential impacts of different types of adversity has highlighted the importance of studying subtypes of early adversity, such as threat, deprivation, loss, and unpredictability [19–21].

Fewer studies have sought to understand the mechanisms through which early life unpredictability, specifically, may confer risk for developing psychopathology, but evidence can be drawn from preclinical research. Indeed, much of the current literature on stressful childhood experiences is retrospectively assessed and is correlational in nature, challenging efforts to establish the causal effects of early life experiences. Animal studies, however, are better equipped to employ controlled, experimental designs and to draw causal conclusions. In one preclinical study, rat pups exposed to early life unpredictability (induced by providing limited resources to mothers to support their pups, which leads to fragmented and unpredictable maternal behaviors) demonstrated impaired reward learning on a behavioral task (a rodent version of the Probabilistic Reward Task, PRT), as well as reduced reward consumption in the form of sucrose intake [5]. Similarly, rats with a predisposition for depressive traits who experienced early life unpredictability exhibited reduced sucrose preference, which is thought to reflect anhedonic behavior, compared to control rats with the same predisposition who did not experience unpredictable upbringings [22]. Taken together, these preclinical findings suggest that unpredictable childhood experiences lead to anhedonia. This pathway merits follow-up translational study in humans.

In humans, several studies support the association between childhood unpredictability and greater symptoms of depression and anxiety [2,6,19,23,24], as well as unpredictability and anhedonia [2,6]. After accounting for the effects of childhood trauma, childhood unpredictability was associated with increased grey matter volume in a number of brain regions, including the precuneus which has been associated with reward anticipation [25], which, in turn, mediated the associations between unpredictability and depression and anxiety [24]. Childhood unpredictability has additionally been shown to prospectively predict poorer relationship quality in adulthood, as well as greater levels of observer-rated emotional distress during disagreements with partners [26].

Overall, prior research suggests that a relationship exists between childhood unpredictability and increased anhedonia; however, the potential mechanisms of this pathway have not yet been thoroughly explored. In the context of stress and depression more broadly, the stress generation model suggests that while stress may contribute to the development of depression, depression may also lead to greater amounts of stress [27]. This may be more pertinent to dependent social stressors – individuals with depression may self-select into social environments or situations which have higher likelihood of adding to or prolonging their current levels of stress [28]. Thus, there may exist a cycle or bidirectional relationship between depression and dependent interpersonal stress specifically [29–31]. Deficits in reward processing have emerged as a potential mechanism of stress generation following early adversity, especially in interpersonal contexts. Reward processing deficits are associated with impairments with approach and avoidance tendencies, where individuals may be more likely to avoid potential negative outcomes or not approach, or even actively push away, potentially rewarding ones [32]. One study on peer social acceptance and rejection found that adolescents exhibited dampened subjective affective responsiveness to social acceptance from peers of lower interest, which may be evidence of interpersonal stress generation [32,33]. Moreover, anhedonia has been associated with decreased approach toward positive faces in a social decision-making task [34]. If rewarding social environments are not perceived as such, individuals may experience tangible consequences where they are less likely to seek out positive social rewards and therefore perceive decreases in social support [32]. Moreover, reductions in perceived social support predict future increases in symptoms of anhedonic depression for those with negative cognitive styles [35]. Cycles of dependent interpersonal stress and depression may prevent individuals from both accessing and subsequently experiencing the benefits associated with social reward.

Extending this model to the context of early life unpredictability, it is possible that reduced social support is reciprocally related to experiences of unpredictability. Indeed, multiple studies demonstrate significant indirect effects of social support on the relationship between early adversity and various mental and physical health outcomes [36–38]. Unpredictability in early life has been related to disrupted social relationships [39]; however, the effects of perceived social support on the association between early unpredictability and mental health outcomes are unknown. Thus, in the current study our goal was to examine whether reduced levels of perceived social support might be the mediating variable by which unpredictability in early life may be associated with increased anhedonia in adulthood.

Conversely, an alternative model suggests the social support may modulate the relationship between stress and symptoms of depression. The stress buffering hypothesis proposes that social support may protect against the effects of stress [40,41]. In adolescents, social support buffered the effects of peer bullying on depressive symptoms in males, but not females [42]. Another study found that perceived social support from family interacted with childhood maltreatment (physical abuse, emotional abuse, and emotional neglect) to predict trauma symptoms, using a trauma symptom measure that included depressive symptoms, in a sample of adult females [43]. Buffering effects of social support were more prominent for low-to-moderate levels of childhood maltreatment [43]. Consequently, we also sought here to also examine whether the alternative stress buffering hypothesis of social support was associated with anhedonic symptoms in adulthood.

1.1. The present study

To expand upon this growing body of research, we evaluated the impacts of childhood unpredictability in a cross-sectional online study of a community sample of adults in the United States. Our study was led by the following aims. Using the recently developed Questionnaire of Unpredictability (QUIC), we assessed scale reliability in an online community sample and compare findings with previously collected in-person samples ([2]; Aim 1). We then sought to replicate associations between childhood unpredictability and internalizing symptoms in a community sample of adults, anticipating that increased levels of unpredictability in childhood would be related to increased depressive symptoms, anhedonia more specifically, and reduced social support in adulthood (Aim 2). In addition, we assessed associations between reward responsiveness measures from the PRT and the QUIC. Next, we implemented mediation and moderation analyses to clarify the role of social support in the relationship between childhood unpredictability and anhedonia. In particular, we aimed to investigate the potential indirect effects of social support on the relationship between early life unpredictability and anhedonia, in line with the stress generation model (Aim 3). To assess the alternative hypothesis, we sought to evaluate whether social support interacted with childhood unpredictability to predict differential levels of anhedonia, consistent with the stress buffering hypothesis (Aim 4).

2. Method

2.1. Participants

We recruited 300 participants using Amazon Mechanical Turk's (MTurk) CloudResearch platform. CloudResearch has been shown to be effective for recruiting samples with elevated psychopathology [44], as

well as for collecting high quality data from participants [45]. Findings have also demonstrated that CloudResearch outperforms other online recruitment platforms such as Prolific and MTurk alone [46]. Participants were required to be at least 18 years old, reside in the United States, have completed at least 100 prior jobs on MTurk, and have an online survey approval rating of at least 95%. In addition to these recruitment constraints, we excluded participants who did not complete surveys or pass all attention checks during the surveys. Studies applying similar screening criteria have shown reliability similar to laboratory samples [44].

In total, our survey was started by 344 participants through MTurk. Forty-four participants exited the study early and were subsequently replaced by CloudResearch to reach recruitment target of 300 participants. Of those 300, 52 failed to complete surveys and 6 failed attention checks in the questionnaires. Thus, in total, 102 participants were removed from the present analyses. To assess whether these 102 excluded participants differed from the included 242 participants on demographic variables, we performed a series of tests comparing means and frequencies, using all available data from excluded subjects in each test. Using independent samples *t*-tests, we found no significant differences between included and excluded participants on age ($t(335) = 0.49$, $p = 0.62$) and years of education ($t(293) = 0.70$, $p = 0.49$). Chi-square tests were utilized to assess differences in nominal variables between included and excluded participants. We found no significant differences ($ps > 0.11$) on sex, ethnicity, current or past endorsement of MDD, or endorsement of family history of mental illness. In cases where nominal variables contained frequencies of less than 5, Fisher's exact tests were applied. Using this method, we found no significant differences between included and excluded participants for income ($p = 0.45$), but we found a significant difference for race ($p < 0.001$). Visualization of race category frequencies for included and excluded subjects revealed result may be driven by the increased percentage of Asian participants in the included group ($N = 30$, 12.4%) compared to the excluded group ($N = 4$, 4.2%) or by the larger percentage of Black participants in the excluded group ($N = 13$, 13.5%) compared to the included group ($N = 12$, 5.0%).

The final sample consisted of 242 participants out of the planned 300 (80.67%) with complete data for the primary mediation analysis. This rate of usable, high quality data outperforms data quality and acceptance rates of many other studies utilizing CloudResearch [46,47]. Of the 242 participants included in primary analyses, participants were majority male (61.57%), white (80.17%), and non-Hispanic (88.84%). Regarding education, 48.8% of participants reported having a 4-year college degree. Additionally, they reported a variety of income levels, with most participants reporting a yearly income ranging from $25,000 to $75,000 (58.68%). The sample also reported a range of current psychopathology on a single checkbox response item assessing current MDD, past MDD, and other psychiatric diagnoses, respectively. The current sample reported a range of diagnoses, including current depression (12.40%), past depression (18.18%), and generalized anxiety disorder (21.90%). Other participant characteristics are summarized in Table 1. From this sample, an additional 24 failed quality checks for the PRT, leaving a final sample size of 218 for analyses involving PRT.

2.2. Procedure

Participants were recruited using CloudResearch, and were then directed to REDCap, which is a secure (HIPAA-compliant) electronic data collection and management system [48,49]. In addition to surveys, participants completed an online version of the PRT. All procedures were approved by the Mass General Brigham Institutional Review Board.

Table 1
Participant characteristics.

Total Sample	N = 242
Age in years, *M* ± *SD*	37.98 ± 10.50
Education in years, *M* ± *SD*	15.46 ± 2.19
Sex at birth, *N* (%)	
Male	149 (61.6.%)
Female	93 (38.4%)
Race, *N* (%)	
White	194 (80.2%)
Black	12 (5.0%)
Asian	30 (12.4%)
Other	6 (2.5%)
Ethnicity, *N* (%)	
Hispanic/Latinx	22 (9.1%)
Not Hispanic/Latinx	215 (88.8%)
Unreported	5 (2.1%)
Income, *N* (%)	
Less than $10,000	11 (4.5%)
$10,000 - $25,000	33 (13.6%)
$25,000 - $50,000	77 (31.8%)
$50,000 - $75,000	65 (26.9%)
$75,000 - $100,000	39 (16.1%)
More than $100,000	16 (6.6%)
Unreported	1 (0.4%)
Family History, *N* (%)#	
Major Depressive Disorder	33 (13.6%)
Anxiety Disorders	23 (9.5%)
Post-Traumatic Stress Disorder	5 (2.1%)
Bipolar Disorder	12 (5.0%)
Cyclothymic Disorder	1 (0.4%)
Alcohol Use Disorder	3 (1.2%)
Substance Use Disorder	2 (0.8%)
Schizophrenia	6 (2.5%)
Schizoaffective Disorder	1 (0.4%)
Borderline Personality Disorder	2 (0.8%)
Autism Spectrum Disorder	1 (0.4%)
Obsessive-Compulsive Disorder	3 (1.2%)
Attention-Deficit/Hyperactivity Disorder	2 (0.8%)
Trichotillomania	1 (0.4%)
Dementia	1 (0.4%)
None	184 (76.0%)
Psychiatric Medication, *N* (%)	
Selective Serotonin Reuptake Inhibitor	11 (4.5%)
Serotonin and Norepinephrine Reuptake Inhibitor	2 (0.8%)
Tricyclic Antidepressant	2 (0.8%)
Atypical Antidepressant	3 (1.2%)
Benzodiazepine	3 (1.2%)
Beta Blocker	3 (1.2%)
Antipsychotic	1 (0.4%)
Anticonvulsant	2 (0.8%)
Stimulant	7 (2.9%)
More than one	14 (5.8%)
None	194 (80.2%)
Self-Reported Psychiatric History, *N* (%)^	
Current Major Depressive Disorder	30 (12.4%)
Past Major Depressive Disorder	44 (18.2%)
Persistent Depressive Disorder	20 (8.3%)
Generalized Anxiety Disorder	53 (21.9%)
Panic Disorder	2 (0.8%)
Social Anxiety Disorder	29 (12.0%)
Specific Phobia	4 (1.7%)
Obsessive Compulsive Disorder	7 (2.9%)
Post-Traumatic Stress Disorder	9 (3.7%)
Attention-Deficit Hyperactivity Disorder	16 (6.6)
Borderline Personality Disorder	6 (2.5%)
Avoidant Personality Disorder	1 (0.4%)
Binge Eating Disorder	1 (0.4%)
Bipolar Disorder	5 (2.1%)
Schizoaffective Disorder	1 (0.4%)
Substance Use Disorder	4 (1.7%)
Alcohol Use Disorder	4 (1.7%)
None	156 (64.5%)
Unreported	6 (2.5%)

Note. All percentages are calculated based on the entire sample of $N = 242$. #27 participants reported a family history of more than one diagnosis. ^55 participants reported more than one psychiatric diagnosis.

2.3. Measures

2.3.1. Childhood unpredictability

The Questionnaire of Unpredictability in Childhood (QUIC) is a 38-item measure of childhood unpredictability rated on a binary scale of yes or no [2]. Total scores range from 0 to 38. In addition to a total score of unpredictability, scores can also be calculated for subscales of parental monitoring and involvement, parental predictability, parental environment, physical environment, and safety and security, where higher scores indicate increased unpredictability. In initial studies assessing psychometrics of the measure in multiple cohorts of participants, the QUIC has shown strong internal consistency (Cronbach's $\alpha = 0.84–0.92$) and test-retest reliability over an average of 13.6 weeks ($r = 0.92$; [2]). Additionally, evidence of construct validity was established by assessing associations with prospective, observational measures of unpredictability in maternal cues in adolescents, as well as by assessing associations between QUIC scores and other validated measures of childhood adversity across all cohorts. The authors determined that the QUIC demonstrated strong construct validity. In the current study, the QUIC also demonstrated high internal consistency (Cronbach's $\alpha = 0.92$), supporting Aim 1. Internal consistency of QUIC subscales were found to be similar to those presented in the initial validation samples by Glynn et al. (2019; see Supplementary Materials).

2.3.2. Social support

The Interpersonal Support Evaluation List-12 (ISEL-12) consists of 12 items from the original 40-item scale, rated on a scale of 1–4, where 1 indicates "definitely false" and 4 indicates "definitely true" [50]. From the ISEL-12, a total score of overall perceived social support was computed, as well as subscales of appraisal support, belonging support, and tangible support. Previous studies have demonstrated strong internal consistency for the ISEL-12 (Cronbach's $\alpha = 0.70–0.90$) across multiple samples [51,52]. In the current study, the total score of the ISEL-12 demonstrated strong internal consistency (Cronbach's $\alpha = 0.95$).

2.3.3. Anhedonia

The Snaith-Hamilton Pleasure Scale (SHAPS) is a 14-item measure of anhedonia, where individuals rate the level to which they believe they would or would not have enjoyed specific activities, such as watching television or spending time with friends or family, in the past few days [53]. The SHAPS is scored on a 1–4 scale of "strongly agree" to "strongly disagree" and subsequently scores are recoded into a binary scale of 0 for either for the "agree" scores or 1 for either of the "disagree" scores. The resulting total score ranges from 0–14, where higher scores indicate higher anhedonia. In psychometric studies in clinical and non-clinical samples, the SHAPS demonstrated excellent internal consistency (Cronbach's $\alpha = 0.91$) and acceptable test-retest reliability over a 3 week period ($r = 0.70$) [54]. In the current sample, the SHAPS demonstrated strong internal consistency (Cronbach's $\alpha = 0.85$).

2.3.4. Depression

The 21-item Beck Depression Inventory II [55] was administered without the question pertaining to suicidal ideation as the largely anonymous nature of data collection prevented us from monitoring subjects. The BDI-II measures depressive symptoms using a 4-point Likert scale from 0–3, where 0 indicates no symptom presence and 3 indicates the presence and increased severity of a symptom. Scores range from 0–63, where scores of 0–13 suggest minimal depression, 14–19 suggest mild depression, 20–28 suggest moderate depression, and 29–63 suggest severe depression [55]. To account for the removal of the suicidality question across all subjects, the average of BDI-II item ratings were used to impute the missing value, consistent with previous work (see [56]). We will refer to this score as the "modified BDI-II" score. The present sample had an average modified BDI-II score of 9.02 ($SD = 9.86$) without imputation, and 13.31 ($SD = 14.51$) with imputation. For the present study, the modified BDI-II demonstrated strong internal consistency (Cronbach's $\alpha = 0.96$).

To control for depressive symptoms in analyses without double-counting anhedonia, we calculated a partial score of depressive symptoms removing the anhedonia symptoms ("partial BDI-II"). To do this, we subtracted the sum of the 4 anhedonia items (loss of interest, loss of pleasure, loss of interest in sex, and loss of energy) from the BDI-II total score. Findings suggest that the anhedonia subscale of the BDI-II has adequate internal consistency (Cronbach's $\alpha = 0.66 – 0.74$) and sufficient reliability and validity [57]. In the present sample, we find strong internal consistency for the 4-item anhedonia subscale of the BDI-II (Cronbach's $\alpha = 0.87$). We computed internal reliability and descriptive statistics of the Partial BDI-II and the BDI-II Anhedonia Subscale, which are presented in Supplementary Materials.

2.3.5. Reward responsiveness

To measure reward responsiveness, we implemented a novel online version of the PRT (task code and stimuli available upon request), which was developed using jsPsych version 6 [58,59]. Utilizing a differential reinforcement schedule to assess responsiveness to reward, the PRT has been used in numerous studies with findings consistently demonstrating increased response bias (RB) toward the more often rewarded stimulus ('rich') in healthy participants compared to those with depression [58,60]. In our newly developed online version of the task, which was pilot tested to ensure psychometric properties consistent with the laboratory-based version of the task, participants were to make determinations about whether the stimulus contained more images of dogs or cats by pressing one of two keys on their keyboard ('S' or 'L'). Participants were informed that correct responses on some, but not all, trials would lead to a monetary reward of 5 cents, though all participants who completed the task received the maximum amount of $6.00. The stimuli were difficult to differentiate and contained images of dogs and cats in a ratio of 6:10. Across 3 blocks of 100 trials each, each trial began with a fixation cross (500 ms) followed by a stimulus (375 ms). The rich stimulus was rewarded more often than the other ('lean') stimulus pseudo-randomly in a 4:1 reward ratio. Thus, in each block, rich stimuli were rewarded in a maximum of 32 trials, while lean stimuli were rewarded in a maximum of 8 trials. Four versions of the task were administered, counterbalancing the rich stimulus (dog or cat) and key assignments ('S' or 'L'). Quality checks on PRT data were implemented to ensure that participants had at least 80 valid trials per block, 21 rich rewards presented per block, and 5 lean rewards presented per block.

The primary variable of interest in the present analyses is RB, which is a measure of preference for the rich stimulus. Response bias is a measure of accuracy for rich and lean stimuli and tends to increase when responses are more accurate for the rich stimulus and inaccurate for the lean stimulus. In current analyses, we utilize total response bias, which is a measure of response bias across all trials of the PRT, and change in response bias (ΔRB), which is calculated by subtracting block 1 RB from block 3 RB.

2.4. Analytic approach

We used R Studio version 4.3.0 [61] to conduct all analyses. First, we investigated putative associations between demographics, clinical variables, and childhood experiences with simple zero-order Pearson correlations (i.e., for continuous variables), Spearman correlations (i.e., for ordinal variables), and either a one-way ANOVAs or *t*-tests (i.e., for demographic group differences in QUIC scores; Aims 1 and 2). When homogeneity of variance was violated according to Levene's test, Welch's *t*-test was utilized. Analyses concerning psychometric validation of the online PRT are described in the Supplemental Methods. To assess for associations between the QUIC and reward responsiveness as measured by the PRT RB parameter, we calculated correlations between total RB and ΔRB with QUIC scores. We addressed Aim 3 using a regression-based mediation analysis. To this end, we conducted

diagnostic assessments of the *a*-path model and the direct effect, or *c'*-path, model, including assessment of unusual or influential cases, homoscedasticity, linearity, normality, and independence of observations. In the *a*-path, social support was regressed on childhood unpredictability, controlling for age, sex assigned at birth, and depressive symptom severity (minus anhedonia subscale). In the direct effect model, or *c'*-path, anhedonia was regressed on childhood unpredictability and social support, controlling for age, sex assigned at birth, and depressive symptom severity (minus anhedonia subscale). To conduct the mediation model, we implemented model 4 in the PROCESS function in R Studio [62] using heteroscedastic-consistent standard errors (HC3) and 10,000 bootstrap samples to calculate robust confidence intervals for all effects [63]. Finally, to test the moderating effects of social support on the association between unpredictability and anhedonia (Aim 4), we used model 1 of PROCESS in R Studio, and similarly applied HC3 standard errors and 10,000 bootstrapped samples to calculate 95% confidence intervals.

Of note, power analyses for the present study were not conducted prior to data collection. While post hoc analyses of observed power are not meaningful [64], it can be useful to conduct post hoc sensitivity analyses to determine a minimal detectable effect size. A sensitivity analysis conducted in G*Power version 3.1 [65] revealed that with alpha set at 0.05 and power set at 0.80, the present sample size of 218 would allow us to detect a small effect size for bivariate correlational analyses for analyses involving PRT measures. Results suggest correlational analyses presented here are adequately powered.

3. Results

3.1. Descriptive statistics and correlations

Average QUIC scores in our sample ($M = 7.68$, $SD = 7.46$) were within the range of scores reported by Glynn et al. (2019) in samples of adult females ($M = 7.7$, $SD = 6.8$), veterans ($M = 10.8$, $SD = 8.4$), and adolescents ($M = 7.4$, $SD = 5.5$; Glynn et al., 2019), supporting Aim 1. Differences were found in QUIC scores by sex, Welch's $t(173.66) = 2.52$, $p = 0.013$, such that the female participants had higher QUIC scores ($M = 9.25$, $SD = 8.04$) on average compared to male participants ($M = 6.70$, $SD = 6.92$). Sex assigned at birth and reported gender identity were largely consistent in this sample, with the exception of one participant (assigned female at birth) who reported not identifying with a specific gender. Sex assigned at birth was used for all analyses due to the limited number ($N = 1$) of transgender or gender expansive individuals.

Spearman's rank correlation was calculated to assess the relationship between income (ordinal) and QUIC scores. The Spearman correlation coefficient was significant, $\rho = -0.18$, $p = 0.006$, and indicated that lower income levels were associated with increased QUIC scores. Further, QUIC scores were significantly greater for individuals who self-reported family histories of mental illness ($N = 58$, $M = 11.33$, $SD = 7.66$) than those without family histories of mental illness ($N = 184$, $M = 6.53$, $SD = 7.03$), $t(240) = -4.43$, $p < 0.001$ (see Table 1 for diagnoses indicated among family members). One-way ANOVA results indicated that QUIC scores did not vary based on race, $F(3,238) = 0.30$, $p = 0.83$. Pearson correlations indicated no relationship between QUIC scores and age ($r = -0.10$, $p = 0.13$) or years of education ($r = -0.08$, $p = 0.24$).

Lastly, QUIC scores were significantly correlated to other clinical self-report measures. Childhood unpredictability was positively correlated with depression ($r = 0.31$, $p < 0.001$) and anhedonia ($r = 0.22$, $p < 0.001$), and negatively correlated with perceived social support ($r = -0.38$, $p < 0.001$). Accordingly, higher levels of childhood unpredictability were associated with increased depressive symptoms, increased anhedonia, and reduced levels of perceived social support. Correlations and questionnaire descriptive statistics are reported in Tables 2 and 3. Fig. 1.

Table 2
Descriptive Statistics and Internal Reliability.

Questionnaires	*M*±*SD*	*Cronbach's α*
QUIC	7.68 ± 7.46	0.92
Modified BDI-II	9.02 ± 9.85	0.96
SHAPS	2.13 ± 2.90	0.85
ISEL	35.70 ± 9.87	0.95

Note. Descriptive statistics across entire sample ($N = 242$). QUIC = Questionnaire of Unpredictability in Childhood; Modified BDI-II = Modified Beck Depression Inventory-II; SHAPS = Snaith-Hamilton Pleasure Scale; ISEL-12 = Interpersonal Support Evaluation List-12.

3.2. Mediation

All regression diagnostics were visually assessed for the *a*-path and *c'*-path models. Slight departures from normality and homoscedasticity were identified in the c'-path model, indicating that use of the HC3 standard error and bootstrap confidence intervals would be appropriate. HC3 standard errors are robust to violations of homoscedasticity, whereas bootstrap confidence intervals are robust against violations of normality. Diagnostic testing is detailed in Supplementary Materials. The indirect effect of social support on anhedonia was statistically significant, indirect effect ($a*b$) = 0.02, *95% Bootstrap CI* = [0.004, 0.039]. Individuals reported reduced social support on average in relation to greater childhood unpredictability, which in turn was related to increased anhedonia, controlling for age, sex, and other depressive symptoms (see Fig. 2 and Table 4), in line with Aim 3. The sample model for the direct effect of childhood unpredictability on anhedonia, controlling for social support, age, sex, and other depressive symptoms, explained an estimated 21.35% of the variance in anhedonia. Further, the indirect effect of perceived social support remained when controlling for additional covariates of income and family history of mental health disorders (binarized to indicate presence or not of family history of mental health disorders), results of which are presented in Supplementary Materials.

3.3. Moderation

For Aim 4, moderation analyses revealed that perceived social support did not interact with childhood unpredictability in relation to anhedonia ($p = 0.49$, *95% CI* = [−0.003, 0.007]), holding constant age, sex, and other depressive symptoms. An additional model adding income and family history of mental illness as covariates also resulted in a non-significant interaction term.

3.4. Probabilistic reward task

Of the 242 subjects included in primary analyses, 218 provided PRT data which passed pre-determined quality control checks. The online version elicited the intended effects across key parameters (see Supplemental Results). Bivariate correlations among total RB and ΔRB with QUIC overall and subscale scores identified no significant correlations ($ps > 0.09$). Similarly, total RB and ΔRB were also not correlated with other clinical measures (BDI-II, ISEL-12, SHAPS; $ps > 0.40$).

4. Discussion

In this study, we found evidence that reduced social support may be a mechanism linking early experiences of unpredictability and increased levels of anhedonia in adulthood. Specifically, results revealed an indirect effect of social support, wherein greater childhood unpredictability was associated with decreased perceived social support, which, in turn, was associated with increased anhedonia, controlling for age, sex, and other depressive symptoms. This finding is consistent with and expands upon theories of interpersonal stress generation. While the present cross-

Table 3
Zero Order Correlations.

	1	2	3	4	5	6
1. QUIC	-	-	-	-	-	-
2. Modified BDI-II	0.31 * **	-	-	-	-	-
3. SHAPS	0.22 * **	0.46 * **	-	-	-	-
4. ISEL12	-0.38 * **	-0.55 * **	-0.37 * **	-	-	-
5. Age in years	-0.10	-0.14 *	-0.16 *	0.14 *	-	-
6. Income^	-0.18 * *	-0.20 *	-0.11	0.25 * **	< 0.001	-
7. Education	-0.08	-0.05	-0.09	-0.03	0.12	0.26 * **

Note. QUIC = Questionnaire of Unpredictability in Childhood; Modified BDI-II = Modified Beck Depression Inventory-II; SHAPS = Snaith-Hamilton Pleasure Scale; ISEL-12 = Interpersonal Support Evaluation List-12. * $p < .05$, * * $p < .01$, * ** $p < .001$. ^Income was collected on an ordinal scale, so all correlations including income are Spearman's rank correlation coefficients.

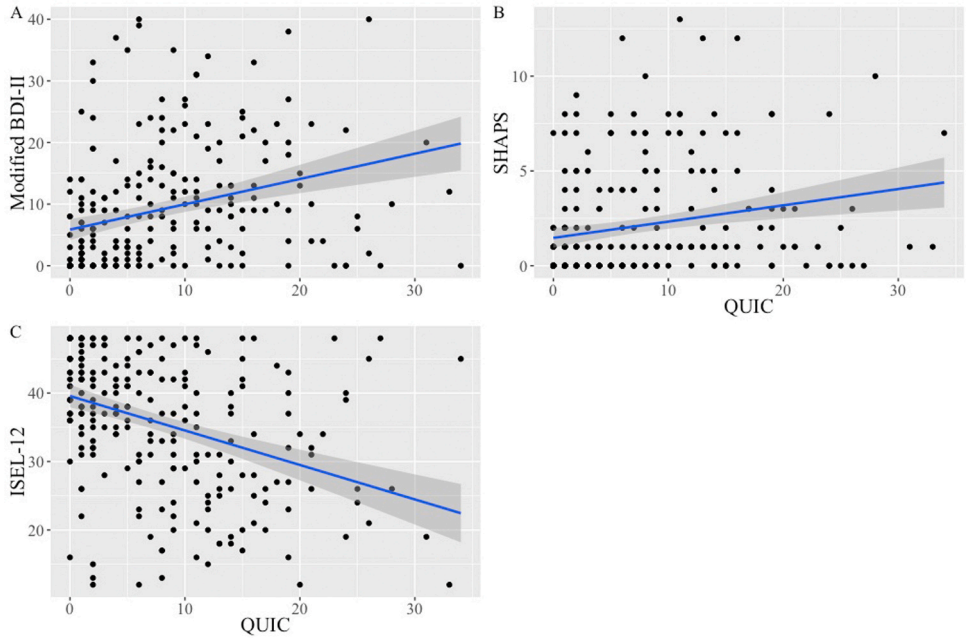

Fig. 1. Zero-order correlations. *Note.* Childhood unpredictability is significantly related to measures of depression, anhedonia, and perceived social support. Blue lines represent simple linear regression lines and shaded areas represent standard error. Modified BDI-II = Modified (i.e., suicidality not assessed) Beck Depression Inventory-II; QUIC = Questionnaire of Unpredictability in Childhood, SHAPS = Snaith Hamilton Pleasure Scale, ISEL-12 = Interpersonal Support Evaluation List-12. **(A)** Childhood unpredictability (QUIC) and depression severity (modified BDI-II) are significantly associated, $r = 0.31$, $p < 0.001$. **(B)** Childhood unpredictability and anhedonia (SHAPS) are significantly associated, $r = 0.22$, $p < 0.001$. **(C)** Childhood unpredictability and perceived social support (ISEL-12) are significantly associated, $r = -0.38$, $p < 0.001$.

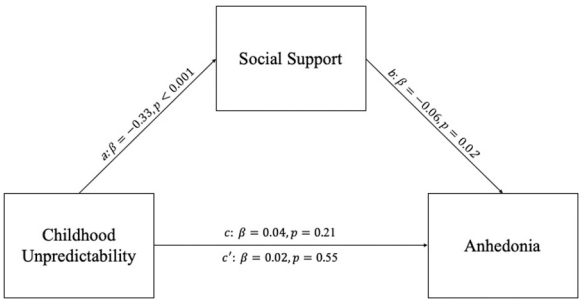

Fig. 2. Simple mediation model. *Note.* Childhood unpredictability was measured by the Questionnaire of Unpredictability in Childhood; Social support was measured by the Interpersonal Support Evaluation List-12; Anhedonia was measured by the Snaith-Hamilton Pleasure Scale. Covariates not shown include age, sex, and partial Beck Depression Inventory-II score (i.e., with anhedonia items removed).

sectional, retrospective study design prevents causal claims from being drawn, our findings provide preliminary evidence that childhood unpredictability may contribute to the initiation of the cycle of interpersonal stress and depressive symptoms, though longitudinal follow-up studies are necessary to make such claims. Indeed, previous work has demonstrated a mediation effect of social support on the effect of depressive symptoms and dependent interpersonal stress [29]. Our findings suggest that interpersonal stress generation may be relevant across diagnostic categories and that childhood unpredictability may be implicated in this positive feedback loop between interpersonal stress and depressive symptoms. We additionally found that elevated levels of childhood unpredictability were associated with increased symptoms of depression, lowered perceptions of social support, and increased anhedonia in an online community sample, consistent with past research [2,6,19,23,24]. Childhood unpredictability was not, however, related to a task-based measure of reward responsiveness.

While social support is often found to have positive effects on mental health outcomes, the literature is currently mixed as to whether that role is buffering or interposing. There is a large body of research exploring the stress-buffering hypothesis [40,66]. This theory states that perceptions of social support buffer, or moderate, the effects of stress on aspects

Table 4
PROCESS Mediation Results.

		***α*-path**							
Outcome	Predictor	*β*	*SE*	*t*	*df*	*p*	*LLCI*	*ULCI*	R^2
ISEL-12	Constant	42.52	2.57	16.53	237.00	< 0.001	37.45	47.59	0.34
	QUIC	-0.33	0.09	-3.81	237.00	< 0.001	-0.50	-0.16	
	Age	0.03	0.06	0.44	237.00	0.66	-0.09	0.14	
	Sex	-2.08	1.08	-1.92	237.00	0.06	-4.21	0.05	
	Partial BDI-II	-0.62	0.09	-6.96	237.00	< 0.001	-0.80	-0.44	
		Total Effect							
Outcome	Predictor	*β*	*SE*	*t*	*df*	*p*	*LLCI*	*ULCI*	R^2
SHAPS	Constant	2.06	0.77	2.68	237.00	0.01	0.55	3.58	0.19
	QUIC	0.04	0.03	1.27	237.00	0.21	-0.02	0.09	
	Age	-0.03	0.01	-1.90	237.00	0.06	-0.06	0.00	
	Sex	-0.16	0.38	-0.43	237.00	0.67	-0.90	0.58	
	Partial BDI-II	0.14	0.03	4.21	237.00	< 0.001	0.08	0.21	
		Direct Effect							
Outcome	Predictor	*β*	*SE*	*t*	*df*	*p*	*LLCI*	*ULCI*	R^2
SHAPS	Constant	4.43	1.28	3.47	236.00	< 0.001	1.91	6.95	0.21
	QUIC	0.02	0.03	0.59	236.00	0.55	-0.04	0.08	
	ISEL-12	-0.06	0.02	-2.43	236.00	0.02	-0.10	-0.01	
	Age	-0.03	0.01	-1.78	236.00	0.08	-0.05	0.00	
	Sex	-0.28	0.39	-0.72	236.00	0.47	-1.04	0.48	
	Partial BDI-II	0.11	0.04	2.99	236.00	0.003	0.04	0.18	
		Indirect Effect							
Outcome	Predictor	*β*	*SE*	*t*	*df*	*p*	*LLCI*□	*ULCI*□	R^2
SHAPS	ISEL-12	0.02	0.01	-	-	-	0.004	0.039	-

Note. QUIC = Questionnaire of Unpredictability in Childhood; Partial BDI-II = Partial Beck Depression Inventory-II; SHAPS = Snaith-Hamilton Pleasure Scale; ISEL-12 = Interpersonal Support Evaluation List-12; LLCI = Lower Limit Confidence Interval; ULCI = Upper Limit Confidence Interval; SE = Standard Error (HC3); □Bootstrapped Confidence Interval.

of health, including mental health. Some findings have supported this hypothesis, highlighting a moderation effect of perceived social support [42,43,67,68]. Contradictory findings have also been described, however, suggesting a mediating effect of perceived social support among stress and outcomes related to wellbeing [37,38,69]. In the present study, a cross-sectional moderation analysis demonstrated no interaction effect between childhood unpredictability and perceived social support on anhedonia. Accordingly, the present research adds support for a mediating role of social support, rather than a moderating effect. This contradicts the stress buffering hypothesis and is instead consistent with the interpersonal stress generation theory.

In addition to finding support for a mediating role of reduced social support, rather than a moderating effect, on early life stress and anhedonia, our results revealed that reported childhood unpredictability was higher in female participants. This finding is inconsistent with previous work, which showed elevated reporting of childhood unpredictability in adult male veterans compared to adult female and adolescent samples [2]. This discrepancy suggests that sex and gender differences in retrospective recall of childhood unpredictability, as well as sex and gender differences concerning the impact of childhood unpredictability, should continue to be explored in future research. However, our sample consisted of a greater number of male participants (61.57%) compared to female participants (38.43%). This bias in our sample may have prevented us from identifying sex differences in childhood unpredictability consistent with previous findings.

Furthermore, we found an association between unpredictability and lower incomes in adulthood. Glynn et al. (2019) also found that socioeconomic status was linked to childhood unpredictability in a sample of adolescents, and the current results replicate this association in adult participants. This finding is consistent with recent work demonstrating a negative association between childhood adversity and adult socioeconomic status [70]. This study found additional evidence supporting childhood adversity as a mediator between childhood socioeconomic status and adult socioeconomic status [70]. In light of an emerging body of literature exploring the complex effects of socioeconomic status on individuals neural activation in a range of contexts, further study of the effects of current and past socioeconomic status and potential interactions with interpersonal stress generation is warranted [71–74]. Finally, a history of familial psychopathology (e.g., 13.6% endorsed family history of depression, 9.5% indicated family history of anxiety disorders) was also associated with childhood unpredictability. Parental history of depression is associated with increased risk of depression in children [75]. Extending beyond family risk for depression, other work has shown that family history of depression and emotional abuse were associated with reduced volumes of regions of the hippocampus, dorsolateral prefrontal cortex, medial prefrontal cortex, and anterior cingulate cortex [76]. Moreover, adolescents with familial history of depression have shown reduced reward responsiveness in a behavioral task, and performance on this gambling task was prospectively associated with depression and reward-seeking behaviors at follow-up [77]. While we did not distinguish type of family history of mental illness here, it is possible that early forms of adversity and familial risk factors interact to produce alterations to the reward system, which warrants further investigation.

Using a behavioral measure of reward learning, we identified no significant relationships between RB and self-report measures, including childhood unpredictability. This finding conflicts with preclinical research demonstrating a negative relationship between childhood unpredictability and RB [5]. Multiple factors may help to explain our finding that behavioral measures of reward were not related to childhood unpredictability, nor to other self-reported measures. Our sample demonstrated relatively low levels of depression and anhedonia. This limited variability may have prevented us from detecting a relationship between RB and childhood unpredictability. Additionally, it may be that other aspects of reward processing not measured by the PRT, such as reward anticipation or motivation, may be more relevant to the study of early life unpredictability. Previous research has found dissociable effects of acute stress [78] and early life stress [79] on neural activation during anticipation and consumption of rewards. A review of preclinical and human research on the effects of early life stress and reward processes suggested that the timing of early adverse experiences may result in differential effects on reward processes of motivation and responsiveness at the neural level [80]. Therefore, it remains possible that effects of childhood unpredictability may be observed on other behavioral measures of reward processing, such as those directly targeting reward motivation, anticipation, or consumption. The authors of the review

additionally emphasized that commonly utilized behavioral reward paradigms (e.g., monetary incentive delay and reward guessing task) occasionally do not align with neural findings. Across multiple studies, they noted that alterations in ventral striatum activation have been observed without corresponding alterations in reaction time [80–83]. Thus, effects of unpredictability on aspects of reward processing may be more effectively studied at other levels of analysis (e.g., neural). In sum, future work would benefit from recruiting samples with increased depressive symptoms, assessing other aspects of reward processing, and incorporating multiple levels of analysis of reward processing (e.g., behavioral, neural, self-report).

Considering multiple limiting factors, our results must be interpreted cautiously. The present work was retrospective and cross-sectional in nature. Thus, we are unable to draw causal conclusions. The retrospective design may be impacted by mood-congruent reporting or memory biases [84–86], although the non-affective nature of many of the items' wording (e.g., asking about structural factors) may reduce these biases. Longitudinal studies should be conducted to further address these limitations and substantiate the present findings. Experimental research employing social inclusion paradigms or in animal studies is also warranted to determine causal associations among childhood experiences of unpredictability, social support, and depressive phenotypes. Additionally, it should be noted that we did not perform a priori power analyses. Therefore, it is possible that our sample size of 242 may have been underpowered to test mediation effects. Previous work has suggested that for percentile bootstrap mediation analyses, a sample size of over 400 is ideal to obtain 80% power to detect small effects [87]. Future work would benefit from conducting a priori power analyses and recruiting a larger number of participants. Aspects of the current sample also deserve consideration here. The current sample, which was recruited online using CloudResearch via MTurk, contained individuals experienced in completing online surveys, and so the present results may not generalize to other populations. Further, our sample endorsed low levels of depressive symptomatology, which may in part explain the non-significant findings regarding the PRT. It is possible that in a sample with increased depressive symptoms, including heightened anhedonic features, a relationship between childhood unpredictability and reward responsiveness may emerge.

In spite of these limitations, the current study is the first to our knowledge to employ the QUIC to study childhood unpredictability and the role of perceived social support in a community sample of adults. Determining whether perceived social support is a moderator or mediator of stress and mental health outcomes is crucial to developing effective interventions following stress—our work provides initial evidence of a *mediating* role of reduced social stress and adds further contradictory evidence of a stress buffering effect of social support. Future research should aim to continue this line of research to explore the causal mechanisms underlying interpersonal stress generation following early environmental unpredictability. Further, in line with theories of interpersonal stress generation, results point to dependent interpersonal stress as a possible point of intervention. While we are unable to draw causal conclusions here, our findings provide added support for the importance of raising early life experiences of unpredictability in treatment and suggest that perceptions of social support may be a key point of intervention in such contexts.

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Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Diego Pizzagalli reports a relationship with Boehringer Ingelheim that includes: consulting or advisory. Diego Pizzagalli reports a relationship with Compass Pathways that includes: consulting or advisory and equity or stocks. Diego Pizzagalli reports a relationship with Engrail Therapeutics that includes: consulting or advisory and equity or stocks. Diego Pizzagalli reports a relationship with Neumora Therapeutics that includes: consulting or advisory and equity or stocks. Diego Pizzagalli reports a relationship with Neuroscience Software that includes: consulting or advisory and equity or stocks. Diego Pizzagalli reports a relationship with Otsuka Pharmaceuticals that includes: consulting or advisory. Diego Pizzagalli reports a relationship with Sage Therapeutics that includes: consulting or advisory. Diego Pizzagalli reports a relationship with Sunovion Pharmaceuticals that includes: consulting or advisory. Diego Pizzagalli reports a relationship with Takeda Pharmaceuticals that includes: consulting or advisory. Diego Pizzagalli reports a relationship with American Psychological Association and Springer that includes: honoraria for editorial work. Diego Pizzagalli reports a relationship with Alkermes that includes: honoraria. Diego Pizzagalli reports a relationship with Bird Foundation that includes: funding grants. Diego Pizzagalli reports a relationship with Brain and Behavior Research Foundation that includes: funding grants. Diego Pizzagalli reports a relationship with Dana Foundation that includes: funding grants. Diego Pizzagalli reports a relationship with Defense Advanced Research Projects Agency that includes: funding grants. Diego Pizzagalli reports a relationship with Millennium Pharmaceuticals that includes: funding grants. Diego Pizzagalli reports a relationship with National Institute of Mental Health that includes: funding grants. Diego Pizzagalli reports a relationship with Wellcome Leap Fund that includes: funding grants. Kaylee Null and Jessica Duda report no biomedical financial interests or potential conflicts of interest.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.xjmad.2024.100057.

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