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Anhedonia in Trauma-Exposed Individuals: Functional Connectivity and Decision-Making Correlates

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ABSTRACT

BACKGROUND: Reward processing deficits have been increasingly associated with trauma exposure and are a core feature of posttraumatic stress disorder (PTSD). While altered resting-state functional connectivity (rsFC) of ventral striatal regions, including the nucleus accumbens (NAcc), has been associated with anhedonia in some stress-related disorders, relationships between NAcc rsFC and anhedonia have not previously been investigated in trauma-exposed individuals. Additionally, relationships between anhedonia and reward-related decision making remain unexplored in relation to trauma exposure. We hypothesized that elevated anhedonia would be associated with altered rsFC between NAcc and default mode network regions and with increased delay discounting.

METHODS: The sample included 51 participants exposed to a DSM-IV PTSD Criterion A event related to community trauma. Participants completed the Clinician Administered PTSD Scale, the Snaith-Hamilton Pleasure Scale, the Beck Depression Inventory, a computerized delay discounting paradigm, and resting-state functional magnetic resonance imaging. rsFC data were analyzed in SPM12 and CONN.

RESULTS: Higher levels of anhedonia were associated with increased rsFC between seed regions of bilateral NAcc and areas of right dorsomedial prefrontal cortex. This relationship remained significant after accounting for Clinician Administered PTSD Scale total scores, Beck Depression Inventory total scores, or diagnostic group in the regression. Additionally, anhedonia was associated with elevated (increased) delay discounting.

CONCLUSIONS: Greater anhedonia was related to higher positive connectivity between NAcc and right dorsomedial prefrontal cortex and to increased delay discounting, i.e., greater preference for smaller immediate versus larger delayed rewards. These findings contribute to a growing body of literature emphasizing the importance of anhedonia in trauma-exposed individuals.

Keywords: Anhedonia, Delay discounting, Functional connectivity, Posttraumatic stress disorder, Resting state, Reward

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Anhedonia and Trauma Exposure

While the role of anhedonia in major depressive disorder (MDD) has received extensive scrutiny (1–3), only recently have reward-processing deficits become implicated as a central component of the emotional and behavioral dysfunction caused by psychological trauma. Evidence from three major lines of research support this claim, including the literature on posttraumatic stress disorder (PTSD). Studies on the symptom structure of PTSD suggest that the DSM-5 cluster of negative alterations in cognitions and mood splits into separate factors reflecting anhedonia and negative affect (4,5), indicating that anhedonia is a core dimensional component of posttraumatic psychopathology. Moreover, patients with PTSD self-report reductions in positive emotionality and hedonic deficits (6). They also show performance deficits on reward-based tasks, including slower learning rates (7), less effort exertion to receive primary rewards (8), and lower satisfaction on receiving unexpected rewards (9). Functional neuroimaging studies also demonstrate abnormal reward-related brain circuitry in PTSD, including lower activation in the nucleus accumbens (NAcc) and medial prefrontal cortex (mPFC) in response to reward feedback (7); lower activation of the ventral striatum when viewing happy faces (10); and less engagement of temporal pole, superior temporal cortex, and left parahippocampal and fusiform gyrus in response to positive affect (11).

There is also a growing literature indicating that anhedonia symptoms and reward processing deficits are outcomes of traumatic stress among individuals who do not meet criteria for PTSD. Specifically, trauma exposure is associated with reduced reward responsiveness (12) and with blunted ventral striatal activity on reward-related tasks (13). Critically, while cross-sectional studies in humans cannot establish the causal

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relationships between high anhedonia and trauma exposure, preclinical studies in rodents suggest that anhedonia-like behaviors can arise as a consequence of exposure to severe stress via alteration of dopaminergic pathways (14,15). Thus, there is an association between trauma exposure and anhedonia and reward processing deficits that is not exclusive to PTSD samples. This motivates identification of neural mechanisms that may mediate relationships between trauma and anhedonia.

Critically, research has shown that anhedonia and reward processing deficits in trauma-exposed individuals are not merely attributable to depression. Although MDD occurs in approximately half of individuals with PTSD (16,17) and in a substantial percentage of trauma-exposed individuals (18,19), anhedonia also is seen at high rates in trauma-exposed individuals who do not have MDD. Of note, anhedonia is nearly as common in patients with PTSD and without MDD (63% anhedonic) as in patients with both PTSD and MDD (67%) (20). Additionally, abnormalities in learning rates on reward-based tasks and neural activity in reward-related regions are present in PTSD samples even when individuals with comorbid MDD are excluded (9,10). Collectively, these results support the claim that anhedonia is an outcome of trauma exposure, above and beyond putative associations with depression.

Anhedonia and NAcc Resting-State Connectivity

Given its central role in representing reward valuation (21,22), it is unsurprising that the intrinsic coordination of functional circuits involving the NAcc is associated with anhedonia. In a large transdiagnostic study of reward sensitivity, Sharma *et al.* (23) found that across diagnostic categories, lower reward sensitivity was associated with decreased NAcc connectivity, with default mode network (DMN) regions involved in self-generated thinking and introspection (24) and with increased NAcc connectivity with cingulo-opercular network regions (i.e., right insula and supplementary motor regions). Gabbay *et al.* (25) demonstrated in adolescents with MDD that greater anhedonia was associated with lower positive resting-state functional connectivity (rsFC) between the left NAcc and the subgenual anterior cingulate cortex and caudate. Wang *et al.* (26) contrasted striatal connectivity in undergraduates with high versus low social anhedonia. Elevated social anhedonia was associated with higher connectivity between the bilateral NAcc and the medial frontal gyrus and lower connectivity between the NAcc and the posterior cingulate cortex. Together, these prior investigations suggest that anhedonia may be associated with altered FC between the NAcc and DMN territories, including medial prefrontal regions such as dorsomedial frontal cortex (23) or medial frontal gyrus (26).

To our knowledge, there is no prior literature on the relationship between NAcc connectivity and anhedonia in trauma-exposed samples. In one study, Zhu *et al.* (27) identified lower NAcc-thalamus and NAcc-hippocampus connectivity in patients with comorbid PTSD and MDD compared with patients with PTSD only and trauma-exposed control subjects. Across all participants with PTSD, lower NAcc-thalamus connectivity was associated with depression symptom severity but not with PTSD symptom severity. Thus, this study identified NAcc rsFC abnormalities in PTSD that appeared to be particularly associated with depressive symptoms. However, it did not examine potential relationships with anhedonia, despite a parallel literature in healthy participants implicating increased NAcc-mPFC connectivity in relation to anhedonia. The present study is the first to examine relationships between NAcc rsFC and anhedonia in a trauma-exposed sample.

Reward-Related Decision Making and Anhedonia

Most studies of anhedonia in trauma-exposed populations rely solely on self-report measures of anhedonic symptoms. While both questionnaire-based measures of anhedonia and performance-based tasks assess underlying constructs related to reward processing, the relationship between self-reported hedonic deficits and decision making is still unclear (28). In contrast to self-report questionnaires, reward-related decision-making tasks do not require introspection (28,29), may be less subject to response biases and demand characteristics, and may have more direct translational potential in animal models. For all these reasons, extending research on anhedonia to include performance on reward-related tasks is an important direction.

Intertemporal choice paradigms can be used to evaluate changes in reward-related decision making associated with psychopathology. The process of assigning a lower subjective value to rewards available after a delay is known as delay discounting (DD). In humans, DD can be measured using paradigms that ask people to choose between small rewards available immediately or larger rewards available after specified delays (e.g., "Would you rather have $10 now or $17 in a week?"). Elevated preference for smaller sooner rewards versus larger delayed rewards (increased DD) has been reported in externalizing disorders (30,31), alcohol and substance use disorders (32–34), and suicidal behavior (35,36), all of which occur at elevated rates in trauma-exposed samples. One prior study compared DD between subjects with comorbid MDD and PTSD and subjects with MDD only; both groups showed increased DD of future gains relative to healthy participants (37). This study did not include a PTSD-only group, but given known reward processing deficits in trauma-exposed samples, increased DD in trauma-exposed individuals might be anticipated.

The extent to which alteration in the DD rate relates to anhedonia essentially remains an open question, although this has been investigated in a single study of healthy college students. Lempert and Pizzagalli (38) found that greater anhedonia was associated with decreased DD in a sample of healthy undergraduates with no history of MDD or current psychopathology. However, to our knowledge, there have been no prior reports of relationships between anhedonia symptoms and DD across broader ranges of anhedonia symptoms than are commonly seen in healthy undergraduates. While Lempert and Pizzagalli (38) found that decreased DD was associated with anhedonia in healthy individuals, increased DD has been more frequently associated with increased vulnerability to psychopathology (39). The literature on DD in internalizing disorders is mixed, with reports of increased, decreased, or unchanged DD in individuals with high trait anxiety (40–42) and social anxiety (43,44) but increased DD in MDD (45–47). It is possible that inconsistent findings of increased versus decreased DD in internalizing disorders may relate to the presence or absence of significant

anhedonia in the included samples, a feature that is not typically assessed or characterized.

Summary

The present study examined relationships between anhedonia symptoms, NAcc rsFC, and DD in a community-based sample of adults exposed to a DSM-IV Criterion A event. We hypothesized that anhedonia would be associated with altered rsFC between the NAcc and DMN regions, including mPFC; our hypothesis was nondirectional, as previous work has demonstrated that anhedonia is associated with decreased NAcc-mPFC connectivity [e.g., with subgenual anterior cingulate cortex (25)] or increased NAcc-mPFC connectivity [e.g., with medial frontal gyrus (26)]. Based on the literature reviewed above, we hypothesized that greater anhedonia would be associated with increased DD in trauma-exposed individuals, even after accounting for severity of PTSD symptoms and depression symptoms.

METHODS AND MATERIALS

Participants

This sample included 51 right-handed participants exposed to a Criterion A event, 20 to 50 years of age, recruited via advertisements or by recontacting participants of prior research studies. All participants provided written informed consent. The Institutional Review Board of McLean Hospital and the Partners Human Research Committee approved the study procedures. The study complied with the ethical standards of the relevant national and institutional committees on human experimentation. Participants were paid up to $200 for their participation in a 2-day protocol. Inclusion and exclusion criteria are described in the Supplement.

Clinical Interviews and Measures

PTSD symptom ratings were made with the Clinician Administered PTSD Scale (CAPS), current and lifetime diagnostic version (48). The DSM-IV CAPS yields total symptom severity scores as well as subscale scores for re-experiencing, avoidance and numbing, and hyperarousal symptoms. Current and lifetime histories of other psychiatric diagnoses were obtained using the Structured Clinical Interview for DSM-IV Axis I Disorders (49). Both interviews were administered by doctoral-level clinical psychologists.

To assess anhedonia, participants completed the Snaith-Hamilton Pleasure Scale (SHPS) (50), a 14-item self-report scale assessing recent hedonic experiences. Each item has four response options indicating how strongly a person agrees that they would enjoy engaging in particular activities. Responses were scored from 0 (strongly agree) to 3 (strongly disagree) and summed; high scores reflect low capacity for hedonic experience (anhedonia), while low scores reflect high capacity for hedonic experience. The SHPS demonstrates adequate test-retest reliability, internal consistency, and convergent and discriminant validity in nonclinical and psychiatric samples (51–53).

Additional questionnaire measures included the Beck Depression Inventory (BDI) version IA (54), a 21-item self-report measure of depressive symptoms, with each item rated on a scale of 0 to 3 points; the Adverse Childhood Experiences questionnaire, a 10-item self-report measure of childhood abuse, neglect, and stressful life experiences (55); and the Life Events Checklist (56), a measure of lifetime exposure to potentially traumatic Criterion A events.

Magnetic Resonance Imaging Acquisition, Processing, and Analysis

Magnetic resonance imaging scans were performed using a 32-channel head coil on a 3.0T Siemens MAGNETOM Tim Trio scanner (Siemens, Erlangen, Germany) (acquisition parameters are provided in the Supplement). Data preprocessing was conducted in SPM12 (Wellcome Trust Centre for Neuroimaging, London, United Kingdom), using standard preprocessing steps (slice time correction, realignment and unwarping, normalization in Montreal Neurological Institute space, and smoothing with a 6-mm kernel). Volumes of excessive motion or signal spiking were calculated for subsequent censoring in the noise correction step using the Artifact Detection Toolbox (Supplement).

After preprocessing, physiological noise correction was performed using the CONN FC toolbox version 15.h (https://www.nitrc.org/projects/conn/) (57). CompCor (58) was employed to estimate and remove physiological noise from white matter and cerebrospinal fluid using principal components analysis. For each subject, noise correction consisted of linear regression of 1) white matter and cerebrospinal fluid components yielded by the above principal components analysis, 2) regressors for motion and for outlier volumes (output from Artifact Detection Toolbox), 3) a regressor to exclude the first volume of the time series, and 4) the main effect of rest as well as its first temporal derivative (to eliminate ramping effects). After the denoising regression, a bandpass filter (0.008–0.09 Hz) was applied to the residual time series. These corrections resulted in a residual blood oxygen level–dependent time course at each voxel, which was used in subsequent analyses.

For the first level whole-brain connectivity analysis, bilateral NAcc seeds were derived from the FSL Harvard-Oxford Atlas maximum likelihood subcortical atlas implemented in CONN. Pearson correlations between the time course of each NAcc seed and the time course of all other voxels in the brain were computed, and Fisher's z transformation was applied. At the second level, first-level maps were entered into a whole-brain regression analysis and were regressed against SHPS scores, controlling for age and sex. Results across the combined NAcc seeds were obtained at a height threshold of $p_{uncorrected} < .001$, cluster threshold $p < .05$ cluster-size $p_{false\ discovery\ rate\ corrected}$, two-tailed. These thresholds were conservatively selected to protect against type I errors; at this cluster-defining threshold, the familywise error rate is accurately controlled (59).

DD Analyses

DD data were collected using a computerized adjusting amount paradigm (60). For each trial, participants chose between a small amount available immediately or $10 available after a delay. Rewards were hypothetical; participants were asked to choose as if one random trial would be selected for a

real payout. Discounting was assessed at six delays (1, 2, 10, 30, 180, and 365 days). Indifference points reflect the subjective value of $10 at the given delay point. We implemented nonlinear multilevel modeling in R (R Foundation for Statistical Computing, Vienna, Austria) to analyze DD data (60) (Supplement). This approach involves simultaneous estimation of k, the hyperbolic DD parameter, at the individual subject level and at the group level, with down-weighting of cases with incomplete data or poor consistency in choice behavior. This approach allows inclusion of inconsistent discounters in the model, a considerable advantage over other methods of handling DD data, such as applying consistency criteria to hold-out cases with inconsistent discounting.

RESULTS

Usable resting-state functional magnetic resonance imaging data were available for 51 participants, and 40 of those participants also completed the DD paradigm. Fifty participants had complete BDI scores; 1 participant's BDI score could not be used owing to selection of multiple response options on several items (Table 1). SHPS scores (n = 51) were normally distributed, and there were no outliers. Two participants had past alcohol abuse, 3 had past cannabis abuse, and 2 had past alcohol dependence. Three participants were currently taking stable doses of antidepressant medications (bupropion, duloxetine, sertraline). Eleven participants had current MDD, and an additional 12 participants had past MDD.

Demographic Correlates of Anhedonia

Consistent with previous reports (61,62), men (mean 13.76, SD 7.674) endorsed greater anhedonia than women (mean 9.43, SD 7.468) (t_{49} = 2.01, p = .049). SHPS scores were not associated with age (r_{49} = .19, p = .176). However, given known effects of age and sex on FC (63–65), these variables were included as nuisance covariates in all subsequent analyses.

Clinical Correlates of Anhedonia

Higher SHPS scores were associated with greater current CAPS total scores (r_{47} = .70, $p < .001$) and with higher scores on each CAPS subscale (re-experiencing: r_{47} = .60, $p < .001$; avoidance: r_{47} = .71, $p < .001$; hyperarousal: r_{47} = .62, $p < .001$) (Table 2). Eleven participants met Structured Clinical Interview for DSM-IV Axis I Disorders criteria for current MDD. Greater anhedonia (higher SHPS) was strongly associated with depression severity (higher BDI total score) (r_{46} = .71, $p < .001$). Importantly, the correlation between SHPS scores and CAPS total scores remained statistically significant after controlling for BDI scores (r_{45} = .38, p = .009); the correlations between SHPS and re-experiencing and avoidance CAPS subscales also remained significant, whereas the association with hyperarousal decreased to a nonsignificant trend (r = .28, p = .056).

Table 1. Demographic and Clinical Characteristics of Participants

	Mean (SD)	Minimum	Maximum
Sex, Male/Female, n	30/21		
Age, Years	32.27 (7.61)	20.36	49.73
SHPS	11.22 (7.78)	0	31
BDI (n = 50)	12.00 (11.19)	0	40
LEC	7.43 (3.50)	1	18
ACE Scale	3.69 (2.45)	0	9
CAPS, Current	29.37 (29.20)	0	101
CAPS, Re-experiencing	7.47 (8.06)	0	26
CAPS, Avoidance	13.33 (13.87)	0	44
CAPS, Hyperarousal	8.57 (8.97)	0	33
CAPS, Lifetime	49.92 (33.55)	0	114

ACE, Adverse Childhood Experiences; BDI, Beck Depression Inventory; CAPS, Clinician-Administered PTSD Scale; LEC, Life Events Checklist; SHPS, Snaith-Hamilton Pleasure Scale.

rsFC Correlates of Anhedonia

Higher levels of anhedonia (higher SHPS scores) were associated with significantly increased rsFC between seed regions of bilateral NAcc and areas of right dorsomedial PFC (DMPFC) (Figures 1 and 2). Importantly, the correlation between SHPS scores and NAcc-to-DMPFC connectivity remained significant after adding CAPS total scores, BDI total scores, trauma load (Life Events Checklist), childhood trauma exposure (Adverse Childhood Experiences questionnaire), or group (PTSD participants, trauma-exposed non-PTSD participants) to the regression model (Table 3). Thus, connectivity between NAcc and DMPFC was robustly associated with anhedonia, even after accounting for the effects of total symptom severity or diagnostic status.

Reward-Related Decision-Making Correlates of Anhedonia

Multilevel modeling in R was used to examine relationships between anhedonia and DD in the subset of participants (n = 40) who completed the computerized DD paradigm. After controlling for sex and age, higher SHPS scores were significantly associated with higher log k (i.e., increased DD) (t_{197} = 2.78, p = .0060). Thus, increasing anhedonic symptoms were associated with greater preference for smaller sooner rewards versus larger delayed rewards.

A model also including bilateral NAcc-to-DMPFC connectivity values did not provide a better fit to the DD data (Akaike information criterion = 939.9 for this model; Akaike information criterion = 937.7 for the model including sex, age, and SHPS only), indicating that FC values were not significant predictors of discounting. SHPS remained the only significant predictor of discounting in the model.

Anhedonia Mediates the Relationship Between CAPS Scores and NAcc-DMPFC Connectivity

As evident in Table 2, CAPS scores also were associated with right NAcc–DMPFC connectivity. Therefore, the indirect effect of SHPS score in mediating the relationship between total CAPS scores and NAcc-DMPFC connectivity was computed. There was a significant indirect effect of SHPS scores (95% bootstrapped confidence interval [CI] = 0.0016 to 0.0049 [right] and 95% bootstrapped CI = 0.0011 to 0.0042 [left]), indicating that SHPS scores mediate the relationship between CAPS total scores and NAcc-DMPFC connectivity. In a reversed model in which CAPS was proposed as a mediator of the relationship between SHPS and NAcc-DMPFC connectivity,

Table 2. Partial Correlations Between All Study Variables, Controlling for Age and Sex

	SHPS	BDI	CAPS Current	CAPS Reexp.	CAPS Avoid.	CAPS Hyper.	DD (log *k*)	rNAcc-DMPFC	lNAcc-DMPFC
SHPS									
BDI	.708[a]								
CAPS Current	.697[a]	.732[a]							
CAPS Reexp.	.604[a]	.633[a]	.902[a]						
CAPS Avoid.	.708[a]	.749[a]	.957[a]	.768[a]					
CAPS Hyper.	.618[a]	.667[a]	.952[a]	.839[a]	.863[a]				
DD (log *k*)	.423[a]	.478[a]	.325[a]	.144	.384[a]	.310			
rNAcc-DMPFC	.610[a]	.241	.347[a]	.329[a]	.343[a]	.298[a]	.086		
lNAcc-DMPFC	.451[a]	.104	.225	.226	.206	.208	.064	.869[a]	

Avoid., avoidance; BDI, Beck Depression Inventory; CAPS, Clinician Administered PTSD Scale; DD, delay discounting; DMPFC, dorsomedial prefrontal cortex; Hyper., hyperarousal; lNAcc, left nucleus accumbens; Reexp., re-experiencing; rNAcc, right nucleus accumbens; SHPS, Snaith-Hamilton Pleasure Scale.

[a]$p < .05$.

there was no significant indirect effect (95% bootstrapped CI = −0.0094 to 0.0035 [right] and 95% bootstrapped CI = −0.0090 to 0.0038 [left]), indicating that the relationship between anhedonia and NAcc-DMPFC rsFC is not mediated by PTSD symptom severity.

DISCUSSION

In this study of trauma-exposed adults, greater anhedonia was associated with higher positive connectivity between the NAcc and the right DMPFC. Of note, this association persisted after controlling for PTSD severity, depression severity, trauma load, early adverse experiences, or group status. From a behavioral perspective, greater self-reported anhedonia was associated with increased DD performance (greater preference for immediate vs. delayed rewards). Although overall PTSD symptom severity also was associated with higher NAcc-DMPFC connectivity, this effect was mediated by anhedonia. As anticipated, NAcc rsFC was related to anhedonia in this trauma-exposed sample. Specifically, increased rsFC from the NAcc to a medial prefrontal region, the DMPFC, was associated with greater anhedonia. Broadly speaking, the current result in trauma-exposed samples is consistent with an existing literature implicating higher striatal-DMPFC connectivity in internalizing samples, including individuals with MDD (66) and obsessive-compulsive disorder (67).

These results are consistent with results of a prior study in healthy participants demonstrating that anhedonia is associated with increased NAcc–medial frontal gyrus connectivity (26); the current study extends this finding to a sample of trauma-exposed participants. The DMPFC region in this study falls within the dorsal DMN (Figure 3A) (68), suggesting that anhedonia may occur in the setting of amplified coordination of a functional circuit linking the NAcc with a specific region of DMN involved in self-focused appraisal. One possibility is that in some trauma-exposed individuals, amplified monitoring of self-focused thinking may hijack striatal reward systems, perhaps interfering with the responsiveness of those reward systems to other routine sources of reward. This is consistent with findings of amplified DMPFC activity in response to reward outcomes in this region in MDD (69). Alternatively, amplified rsFC in anhedonia could reflect compensatory efforts by medial prefrontal self-monitoring systems to recruit striatal reward regions. Additionally, it is possible that anhedonia in trauma-exposed individuals occurs in the setting of increased interaction between striatal reward systems and DMN regions, perhaps at the expense of coordination between the NAcc and regions involved in external attention. While prior studies of healthy participants have implicated broader sets of brain regions, including salience network regions, the present study points to central relevance of the DMPFC as a neural correlate of anhedonia in trauma-exposed individuals.

The interpretation of the finding that higher NAcc-DMPFC rsFC is associated with anhedonia is somewhat complicated by functional heterogeneity within the DMPFC. Amodio and Frith

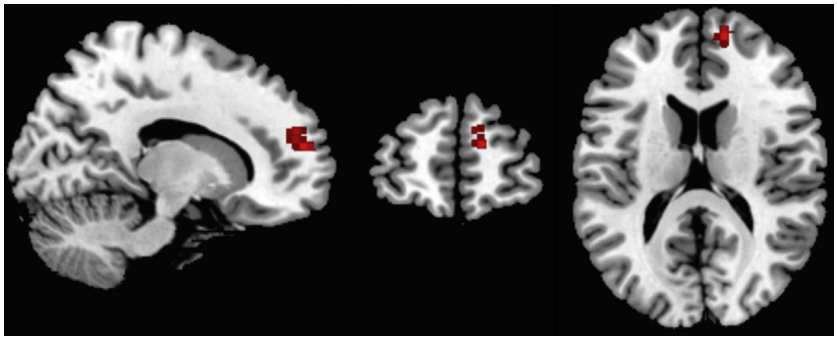

Figure 1. Cluster characterized by a relationship between increased anhedonia (higher Snaith-Hamilton Pleasure Scale score) and increased connectivity with bilateral nucleus accumbens, after controlling for age and sex. Cluster size = 95 voxels; peak = [14, 56, 16]; cluster $p_{false\ discovery\ rate}$ = .021.

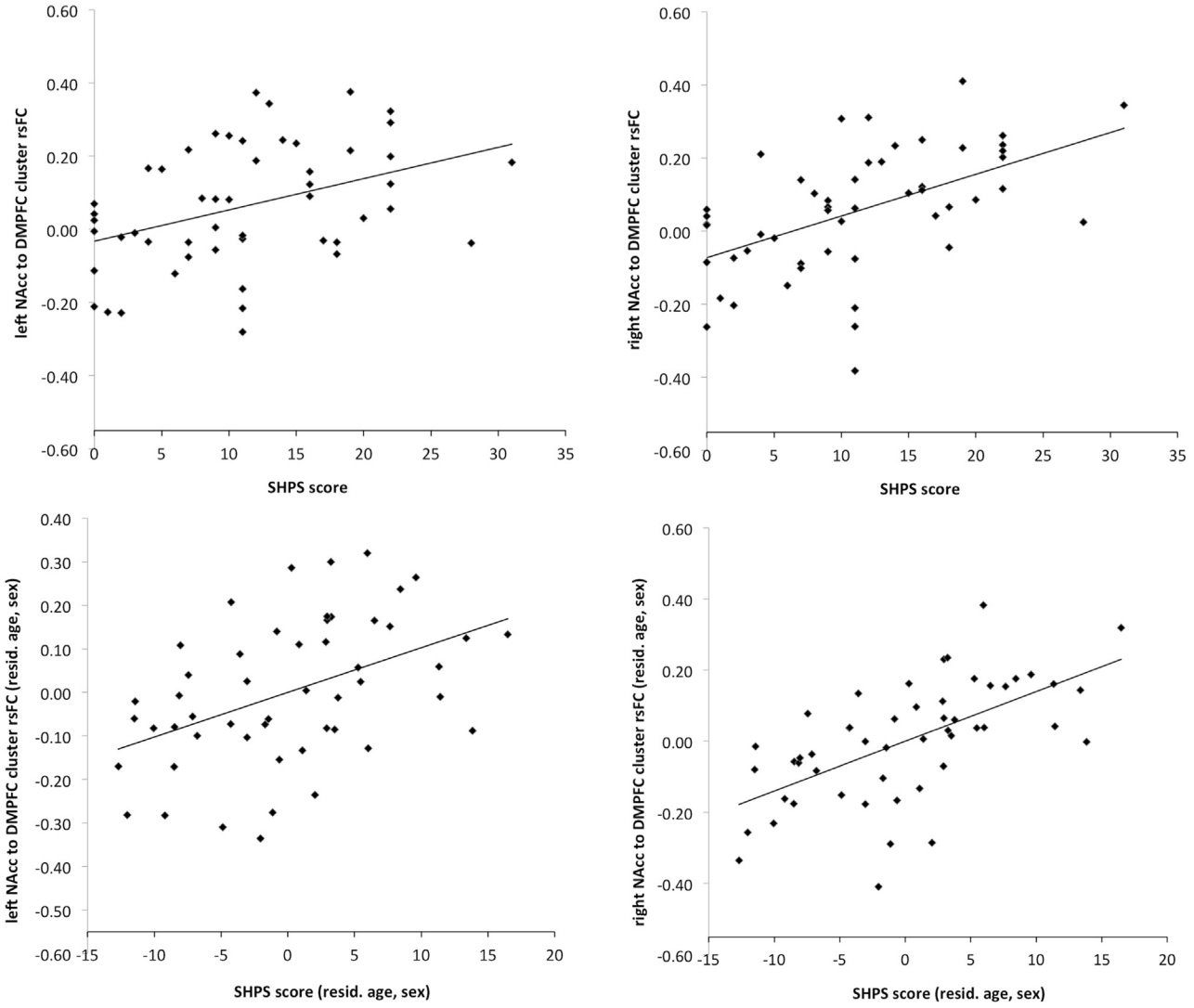

Figure 2. Scatterplots showing the association between Snaith-Hamilton Pleasure Scale (SHPS) scores and right and left nucleus accumbens (NAcc) to dorsomedial prefrontal cortex (DMPFC) cluster connectivity values. Raw scores (not partialled out for age and sex) are displayed at the top for visualization purposes. Partial plots are displayed at the bottom, residualized for age and sex.

(70) identified the particular region of the right DMPFC emerging from the present analysis as part of the anterior rostral mPFC ($|x| < 20$, $y > 20$, $z > 0$), an area implicated in social cognition, including self-knowledge, person perception, and mentalizing. Activation in this region is reduced in individuals with high levels of social anhedonia during an emotional face discrimination task (71). A recent functional parcellation study of the DMPFC identified four subregions with separable connectivity patterns, including right caudal, left caudal, rostroventral, and rostrodorsal subregions (72). The cluster in the present study partially overlaps with the rostrodorsal subregion (Figure 3B), which has strong connections to DMN regions (including posterior cingulate and inferior parietal cortex) as well as to the amygdala and hippocampus. One possibility that could be explored in future work is that the association between anhedonia and increased NAcc-DMPFC connectivity following trauma exposure could arise in the context of elevated input to the DMPFC from hippocampal and amygdalar regions. Finally, there is evidence that the DMPFC works in parallel with the dorsolateral PFC to support cognitive control, particularly via self-monitoring of cognitive performance (72). It is possible that anhedonia may be associated with excessive self-monitoring, leading to excessive downregulation of reward responsivity. The present study's identification of this relationship contributes to the increasing recognition of the centrality of anhedonia in trauma-related and stress-related disorders and identifies a possible neural circuit for future investigation and potentially ultimately treatment targeting.

In this sample, greater anhedonia was associated with altered choice behavior, i.e., increased DD. This contrasts with a prior study of healthy undergraduates, in whom greater anhedonia was associated with decreased DD (38). One potential interpretation of the association between increased DD and anhedonia in the present sample is that this merely

Table 3. Partial Correlations Between Anhedonia Scores and Resting-State Functional Connectivity, Controlling for Possible Demographic and Clinical Confounds

	Right NAcc-DMPFC Connectivity	Left NAcc-DMPFC Connectivity
SHPS (Age, Sex)	.610	.451
SHPS (Age, Sex, CAPS Total)	.548	.421
SHPS (Age, Sex, BDI Total)	.641	.538
SHPS (Age, Sex, Diagnostic Group)	.515	.335
SHPS (Age, Sex, LEC)	.584	.485
SHPS (Age, Sex, ACE)	.599	.446

Possible demographic and clinical confounds are in parentheses. All variance inflation factor values are under 2.5, indicating no problematic multicollinearity in each model. All correlations are statistically significant at $p < .05$.

ACE, Adverse Childhood Experiences; BDI, Beck Depression Inventory; CAPS, Clinician Administered PTSD Scale; DMPFC, dorsomedial prefrontal cortex; LEC, Life Events Checklist; NAcc, nucleus accumbens; SHPS, Snaith-Hamilton Pleasure Scale.

reflects the general relationship between increased DD and psychological distress (39). Another possibility, not testable in the present dataset, is that anhedonia may be associated with pessimism about the future, or reduced certainty about the delivery of delayed rewards. Notably, DD rates are also lower when individuals engage in episodic future thinking (73), and positive (but not negative) episodic future thinking is reduced in PTSD (74). The extent to which the effects of anhedonia on DD may be attributable to reductions in positive episodic future thinking is currently unknown. Future studies should include measures assessing beliefs about the certainty of reward delivery and episodic future thinking to evaluate these possibilities. In the present study, DMPFC-NAcc connectivity did not contribute to the prediction of DD rates over and above the contribution of SHPS and demographic predictors, which may occur if the relationship between anhedonia and DD arises because both relate to a third mechanism (e.g., episodic future thinking). From a clinical perspective, one implication of the present finding is that trauma-exposed individuals with elevated anhedonia may be particularly prone to comorbidities characterized by impulsive choice (increased DD), such as substance use, aggression, and suicidal behavior. Future studies identifying longitudinal relationships between these constructs in relation to the time of trauma exposure will be needed to clarify whether, for instance, increased baseline DD is a vulnerability factor for developing anhedonia following trauma exposure or whether anhedonia following trauma exposure leads to acceleration in the DD rate.

This study has several limitations. First, because this study developed from a broader project examining trauma-related neurochemistry, individuals with current or recent substance use disorders were excluded. While this provides greater precision about the role of trauma exposure for neuroimaging analyses, it likely truncates the distribution of impulsive decision making present in this sample. Second, although this project collected data from non–trauma-exposed control subjects in the context of broader aims, these data were not included in the present analysis because of a lack of sufficient variability in anhedonia. Intentionally recruiting non–trauma-exposed control subjects across a broad range of anhedonia would allow for analyses that differentiate whether anhedonia itself is related to NAcc-DMPFC connectivity or whether the relationship occurs in the context of trauma exposure. Third, collection of DD data was added after the study was underway, and DD data were not available for all participants who had rsFC data. Finally, the sample size prevents us from conducting more fine-grained trauma-related analyses, such as exploring whether the observed effects are specific to particular types of trauma exposure.

Despite these limitations, in this trauma-exposed cohort, greater anhedonia was associated with higher NAcc-DMPFC rsFC and with increased DD (i.e., increased preference for smaller immediate rewards vs. larger future rewards). These findings contribute to a growing body of literature emphasizing the importance of anhedonia as a clinical construct in trauma-related and stress-related disorders.

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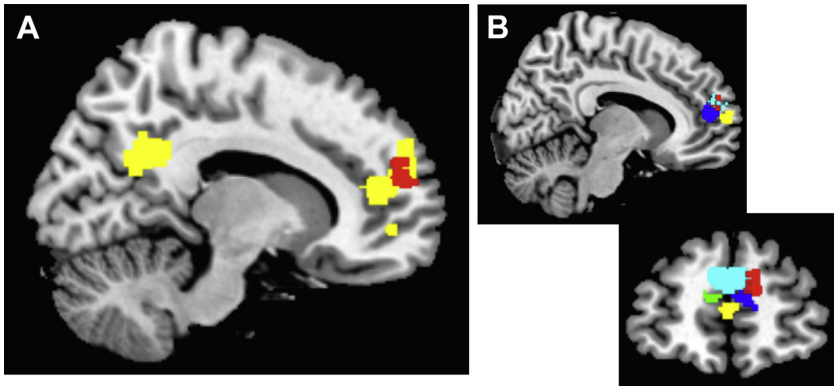

Figure 3. **(A)** Dorsomedial prefrontal cortex cluster (red) overlaid on dorsal default mode network mask (yellow) (68). **(B)** Dorsomedial prefrontal cortex cluster (red) overlaid on dorsomedial prefrontal cortex subregions: light blue, rostrodorsal; yellow, rostroventral; green, caudal left; dark blue, caudal right (72). [Panel **B** retrieved from ANIMA (75), http://anima.fz-juelich.de.]

Over the past 2 years, DAP has received consulting fees from Akili Interactive Labs, BlackThorn Therapeutics, Boehringer Ingelheim, and Posit Science for activities unrelated to the present work. SLR is employed by McLean Hospital/Partners Healthcare; serves on a Department of Veterans Affairs Research Advisory Committee on Gulf War Illness; provides unpaid Board service for nonprofit organizations Society of Biological Psychiatry, Anxiety and Depression Association of America, and Project 375; receives royalty payments from Oxford University Press; and has received honoraria for lectures and/or consultations from Harvard University, Brown University, Columbia University, University of Miami, University of Cincinnati, and Centre for Addiction and Mental Health in Toronto. The authors report no biomedical financial interests or potential conflicts of interest related to the present work.

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