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Anhedonia Reduction and the Association Between Left Ventral Striatal Reward Response and 6-Month Improvement in Life Satisfaction Among Young Adults

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Key Points

Question

Which neural reward regions are associated with improved psychiatric symptoms and psychosocial function in young adults?

Findings

In this cohort neuroimaging study, reward activation in the left ventral striatum was associated with improvement in anhedonia symptoms during a 6-month period. The reduction in anhedonia mediated the association between left ventral striatal reward activation and improvement in psychosocial function.

Meaning

The left ventral striatum may be a plausible biomarker for novel treatments to improve psychiatric symptoms and psychosocial function.

Abstract

Importance

Anhedonia is a symptom of multiple psychiatric conditions in young adults that is associated with poorer mental health and psychosocial function and abnormal ventral striatum reward processing. Aberrant function of neural reward circuitry is well documented in anhedonia and other psychiatric disorders. Longitudinal studies to identify potential biomarkers associated with a reduction in anhedonia are necessary for the development of novel treatment targets.

Objective

To identify neural reward-processing factors associated with improved psychiatric symptoms and psychosocial function in a naturalistic, observational context.

Design, Setting, and Participants

A longitudinal cohort follow-up study was conducted from March 1, 2014, to June 5, 2018, at the University of Pittsburgh Medical Center after baseline functional magnetic resonance imaging in 52 participants between the ages of 18 and 25 years who were experiencing psychological distress.

Main Outcomes and Measures

Participants were evaluated at baseline and 6 months. At baseline, participants underwent functional magnetic resonance imaging during a card-guessing monetary reward task. Participants completed measures of affective symptoms and psychosocial function at each visit. Neural activation during reward prediction error (RPE), a measure of reward learning, was determined using Statistical Parametric Mapping software. Neural reward regions with significant RPE activation were entered as regions associated with future symptoms in multiple linear regression models.

Results

A total of 52 young adults (42 women and 10 men; mean [SD] age, 21.4 [2.2] years) completed the study. Greater RPE activation in the left ventral striatum was associated with a decrease in anhedonia symptoms during a 6-month period ($\beta = -6.152$; 95% CI, –11.870 to –0.433; $P = .04$). The decrease in anhedonia between baseline and 6 months mediated the association between left ventral striatum activation to RPE and improvement in life satisfaction between baseline and 6 months (total [c path] association: $\beta = 0.245$; $P = .01$; direct [c′ path] association: $\beta = 0.133$; $P = .16$; and indirect [ab path] association: 95% CI, 0.026-0.262). Results were not associated with psychotropic medication use.

Conclusions and Relevance

Greater left ventral striatum responsiveness to RPE may serve as a biomarker or potential target for novel treatments to improve the severity of anhedonia, overall mental health, and psychosocial function.

This cohort study uses neuroimaging to examine which neural reward regions are associated with improved psychiatric symptoms and psychosocial function in young adults.

Introduction

Young adulthood is a vulnerable developmental period in which psychiatric disorders, including mood and anxiety disorders, emerge.[1] Nearly one-fifth of young adults between ages 18 and 25 years seek mental health care for symptoms associated with depression, mood, and anxiety.[2] These symptoms have negative effects on psychosocial function, including life satisfaction, work performance, and interpersonal relationships.[3,4] Most people with clinical-level affective psychopathologic characteristics experience remission within 6 months.[5] However, there are few factors associated with outcomes and no objective neural biomarkers of future illness course and functional outcomes to guide prognosis or treatment.

Anhedonia is an early defining feature of the depression that characterizes several psychiatric disorders[6] including major depressive disorder and bipolar disorder. Anhedonia is an important symptom to monitor because it is associated with treatment response[7] and poorer psychosocial function.[3,8] Identifying biomarkers that are associated with future reduction in anhedonia may provide targets for novel treatments for numerous psychiatric disorders or markers of treatment response. This is particularly important in young adulthood, when interventions can take advantage of the neuroplasticity during this period[9] to reduce the severity of, or even prevent, psychiatric disorders.

Given anhedonia's definition (the difficulty experiencing pleasure), neural circuits underlying reward learning—learning where mood and behaviors are modified in response to rewards—are especially relevant for studies identifying biomarkers associated with anhedonia.[6] This circuitry includes the ventral striatum (VS), ventrolateral prefrontal cortex (vlPFC), orbitofrontal cortex, anterior cingulate cortex (ACC), and amygdala. The VS supports aspects of reward processing[10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27] and encodes the discrepancy between expected reward and actual reward outcome[21] (reward prediction error [RPE]), a measure of reward learning and motivation to obtain future rewards.[28] The left vlPFC links stimuli to reward outcomes[29,30] and participates in decision making to obtain immediate rewards.[31,32] This laterality may be owing to the role of the left prefrontal cortex in approach-related behavior.[33] The orbitofrontal cortex encodes the incentive salience of expected rewards[16,17,18,19,20,25,27] and the rostral-dorsal ACC guides behavior in response to incentive salience of stimuli to obtain rewards.[11,16,18] The amygdala interacts with the VS during reward and punishment, playing a unique role in reward processing.[27,34] Studies of the neural circuitry of anhedonia implicate these regions, although they were performed primarily among individuals with major depressive disorder and show abnormal VS activation to reward anticipation and receipt.[21,35,36,37,38] Lower VS activation to reward is associated with lower positive affect and greater severity of anhedonia.[35] The association between greater anhedonia severity and lower VS activation to reward is consistent irrespective of depression severity,[39] as typically developing individuals exhibit an association between greater anhedonia severity and reduced VS activation to reward receipt.[40]

Despite evidence for altered activation in reward circuitry, particularly the VS, in individuals with psychiatric disorders associated with anhedonia, and the association of symptoms with psychosocial function, to date, no studies have focused on identifying neural biomarkers associated with future psychosocial function and anhedonia in young adults. Such biomarkers are critical for understanding symptom remission, treatment response, and developing novel treatments that may improve clinical and psychosocial function. One study demonstrated that adolescents with low VS activation to reward receipt were more likely to develop subthreshold depressive symptoms or meet full criteria for major depressive disorder over time.[41] It remains unclear, however, as to which psychiatric symptoms (including anhedonia) are specifically associated with alterations in neural reward response, at which phase of reward processing these abnormalities occur, and how links between neural reward circuitry response and psychiatric symptoms are associated with future psychosocial functioning in young adults.

In the present study, we recruited young adults (age, 18-25 years) seeking mental health care because of psychologic distress (ie, emotions negatively affecting level of functioning), irrespective of psychiatric diagnosis, to examine neural reward regions associated with future illness course and psychosocial functioning. Reward circuitry was examined using a monetary reward paradigm at baseline, with psychosocial functional and symptom trajectories examined over time. We hypothesized that response in neural regions underlying reward processing, including the VS, would be associated with trajectories of future affective and anxiety symptoms. We specifically hypothesized that greater VS activation to RPE would be associated with a reduction in anhedonia severity over time. We further hypothesized that the reduction in anhedonia severity would be associated with improved psychosocial function. Last, we hypothesized that anhedonia severity reduction would mediate the association between neural reward response and psychosocial functioning.

Methods

Participants and Study Design

A total of 52 individuals between the ages of 18 and 25 years who were seeking mental health care for psychological distress were included in this prospective, longitudinal study, conducted from March 1, 2014, to June 5, 2018. The goal was to recruit a young adult community sample during an age range when most psychiatric illnesses first manifest and, as part of observing the typical course of depression without specific treatment intervention, to increase the likelihood for observing significant changes in clinical and psychosocial functioning over time.[1] Participants were right handed and spoke fluent English. Of the 57 young adults originally recruited, 3 were excluded because of incomplete data, 1 because of excessive task performance errors (20 errors; other participants, <12 errors), and because of signal loss (>30%; see eAppendix 1 in the Supplement for full exclusion criteria). This study was approved by the University of Pittsburgh Institutional Review Board. Participants were recruited through community advertisement and student counseling centers in the Pittsburgh, Pennsylvania, area and provided written informed consent.

Participants completed 2 study visits: baseline (0 months; initial visit) and 6 months after the initial visit. Six months was selected as the follow-up visit as this is the conventional timeframe for determining recovery from a depressive episode[5] and is thus appropriate for evaluating clinical and psychosocial outcomes. At the initial visit, participants underwent functional magnetic resonance imaging (fMRI) and completed clinician-rated and self-report assessments of depression, anxiety, anhedonia, and mania. Symptom mea-

sures were administered again at the follow-up visit. Participants were allowed to pursue treatment; information on use of psychotropic medication was collected at each visit and quantified per individual by computing the psychotropic medication load[42] (eAppendix 1 in the Supplement).

Affective and Psychosocial Function Measures

Participants' self-reported affective symptoms were measured using the Mood and Anxiety Symptom Questionnaire–Anhedonic Depression subscale (MASQ-AD),[43] MASQ–Anxious Arousal scale (MASQ-AA),[43] and the Snaith Hamilton Pleasure Scale (SHAPS).[44] Participants completed the following clinician rating scales: Hamilton Rating Scale for Depression,[45] Hamilton Anxiety Rating Scale,[46] and the Young Mania Rating Scale.[47] The Range of Impaired Functioning Tool[48] assessed psychosocial function across 4 domains (work, recreation, interpersonal relationships, and global satisfaction), with higher scores indicating greater functional impairment.

Monetary Reward fMRI Task

Neural activation during reward processing was evaluated using an adapted event-related card-guessing task[49,50] that included win, loss, mixed, and neutral trials (eFigure in the Supplement). The primary outcome, RPE, was determined as the difference in expected vs actual reward outcome. See eAppendix 1 in the Supplement for task description, fMRI acquisition parameters, and preprocessing.

Statistical Analysis

For each participant, Statistical Parametric Mapping software, version 12 (The MathWorks Inc) was used to build a fixed-effect general linear model, using RPE, reward expectancy, and outcome expectancy regressors for first-level imaging analyses (eAppendix 1 in the Supplement).

Functional connectivity maps were generated using generalized psychophysiological interaction using a priori reward regions previously shown to differentiate individuals with mood disorders from healthy individuals[51,52] as seed regions: left vlPFC (Brodmann area [BA] 47) and rostral-dorsal ACC (BA32) as defined by the Wake Forest University PickAtlas, and VS as defined by a prior meta-analysis of VS reward activation,[53] which were used as an a priori mask in earlier studies.[49,52]

Individual contrast images were entered into group-level Statistical Parametric Mapping analyses. Age, sex, parental educational level, IQ, MRI scanner model, and change in psychotropic load during the study period were included as covariates in activation and connectivity models. Regions for activation analyses were constrained to a single mask comprising all reward regions of interest, defined by Wake Forest University PickAtlas: amygdala, rostral-dorsal ACC (BA32), orbitofrontal cortex (BA11), and vlPFC (BA47); and VS as defined above.[52,53] Activation and connectivity maps were at a threshold of voxel $P < .05$ for familywise error. The blood oxygen level–dependent response for individual regions with significant activation and connectivity within the reward mask in second-level analyses was extracted using Marsbar (http://marsbar.sourceforge.net/).

Multiple linear regression models, implemented in SPSS, version 23 (SPSS Inc), tested whether baseline reward region activation and connectivity was associated with changes in affective symptoms during a 6-month period. Change in symptoms was calculated as the difference between scores at baseline and follow-up visits. Two separate multivariate linear regression models were performed: one for self-reported affective symptoms (MASQ-AD, MASQ-AA, and SHAPS) and another for clinician-rated affective symptoms (Hamilton Rating Scale for Depression, Hamilton Anxiety Rating Scale, and Young Mania Rating Scale). Models were performed separately, as the type of rating scales contributes uniquely to symptom severity.[54] For each model, affective symptom changes were entered as dependent variables and the 5 neural regions with significant reward activation and connectivity (see Results) were entered as independent variables. Pearson correlations were used to test the association between variables (eAppendix 2 in the Supplement).

Mediation analyses were performed using the Hayes[55] bootstrapped mediation model implemented using the PROCESS macro in SPSS to examine whether changes in affective symptoms linked with reward circuitry response were associated with domains of psychosocial function. Activation in and regions with connectivity to regions of interest were entered as independent variables, with 1 independent variable per model. Six-month changes in affective symptoms were entered as mediators and 6-month change in psychosocial function domains were entered as dependent variables. All models, including mediation models, were corrected for multiple comparisons using 2-sided tests at $P < .05$ using a Bonferroni correction.

Results

Participants

A total of 52 participants completed baseline and 6-month visits (Table 1) and 39 participants met criteria for a *DSM-IV* diagnosis (18 participants met criteria for a single diagnosis and 21 participants met criteria for ≥2 diagnoses; eAppendix 2 in the Supplement). Affective symptoms improved between baseline and follow-up (eTable 1 in the Supplement). A total of 11 participants (21%) either started (n = 10) or had a dosage adjustment of (n = 1) psychotropic medication between baseline and follow-up (eAppendix 2 in the Supplement).

Table 1.

Demographic Characteristics of Participants at Baseline

Characteristic	Value[a]
Age, mean (SD), y	21.4 (2.3)
Sex	
Female	42
Male	10
IQ, mean (SD)	106.88 (7.84)
Race/ethnicity	
White	21
Black or African American	8
Asian	10
>1 Race	3
Parental educational level	
Some high school	1
High school or GED	10
Some college	27
Technical school	2
College degree	12
Current *DSM* diagnosis	
No current disorder	13
Depressive disorder	13
Anxiety disorder	26
Externalizing disorder	7
Trauma-related disorder	4
Sleep disorder	8
Somatoform disorder	3
Adjustment disorder	2
Baseline psychotropic load, mean (SD)	0.17 (0.37)
Clinician-rated affective symptoms, mean (SD)	
Anxiety (HAMA score)	12.71 (6.66)
Depression (HRSD score)	15.62 (6.77)

Abbreviations: GED, General Educational Development certificate; HAMA, Hamilton Anxiety Rating Scale; HRSD, Hamilton Rating Scale for Depression; MASQ-AA, Mood and Anxiety Symptom Questionnaire–Anxious Arousal subscale; MASQ-AD, Mood and Anxiety Symptom Questionnaire–Anhedonic Depression subscale; SHAPS, Snaith Hamilton

Pleasure Scale; YMRS, Young Mania Rating Scale.

[a]Data are presented as number of participants unless otherwise indicated.

Activation in Regions of Interest During RPE

The left and right VS, left and right rostral-dorsal ACC, and left amygdala were significantly activated to RPE within the reward mask (Table 2; Figure, A). Whole-brain activation mirrored mask activation, where the left and right VS and amygdala were activated as large clusters along with the ACC, the inferior parietal lobule, and middle cingulate cortex (eTable 2 in the Supplement). No regions of interest were activated significantly to reward expectancy and outcome expectancy (eTable 2 in the Supplement). No whole brain regions showed significant connectivity with seed regions.

Table 2.

Neural Activation to Reward Prediction Error

Region	Hemisphere	Voxel *P* Value for FWE[a]	Voxels, No.	T Score	Coordinates		
					x	y	z
Ventral striatum	Right	<.001	129	6.97	18	12	−10
	Left	<.001	42	6.27	−10	14	−4
Amygdala	Left	.04	24	4.22	−26	2	−18
Anterior cingulate cortex	Right	.02	158	4.39	4	46	2
	Left	.008	89	4.75	−4	48	−4

Abbreviation: FWE, familywise error.

[a]Threshold at $P < .05$ for FWE.

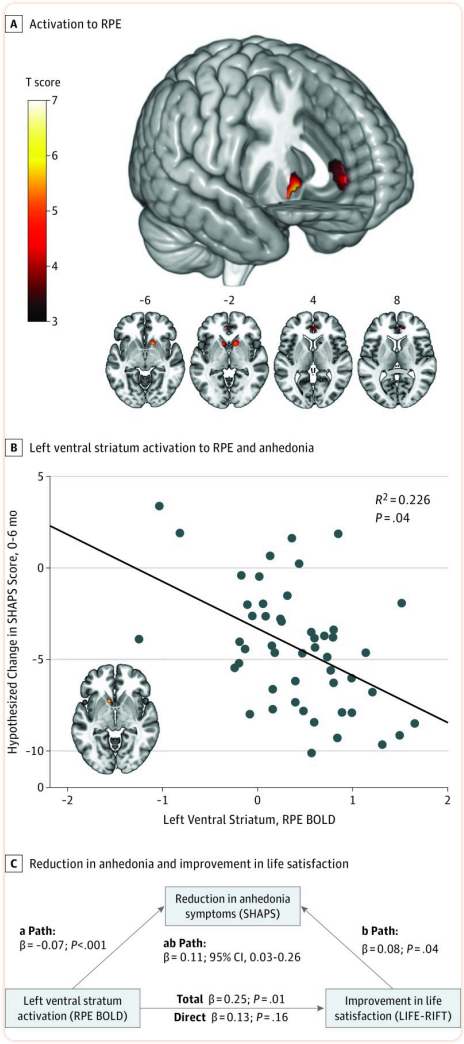

Figure.

Reduction in Anhedonia Severity and Mediation of the Association Between Left Ventral Striatum Activation to Reward Prediction Error (RPE) and Improvement in Life Satisfaction

A, Activation to RPE in the ventral striatum, amygdala, and anterior cingulate cortex. B, Left ventral striatum activation to RPE is associated with a decrease in anhedonia (Snaith Hamilton Pleasure Scale [SHAPS] score) severity during a 6-month period. C, Reduction in anhedonia severity at 6 months mediates the association between left ventral striatal activation during RPE and 6-month improvement in life satisfaction. a Path indicates the association between left ventral striatum blood oxygen level–dependent (BOLD) response and change in anhedonia symptoms over 6 months; ab path, the indirect association of the mediation model; b path, the association between the reduction in anhedonia symptoms over 6 months and the improvement in life satisfaction over 6 months; and LIFE-RIFT, Range of Impaired Functioning Tool.

Association of Neural Activation to RPE With Improvement in Affective Symptoms

In a multiple linear regression model with multiple comparisons correction, left VS activation to RPE was negatively associated with change in self-reported anhedonia symptoms during a 6-month period (β = −6.152; 95% CI, –11.870 to –0.433; $P = .04$), where individuals with greater left VS activation demon-

strated greater improvement in SHAPS (Figure, B; Table 3). This association remained significant even after controlling for baseline SHAPS (β = −5.338; 95% CI, –10.523 to –0.153; *P* = .04). The right VS, left amygdala, and left and right rostral-dorsal ACC activation to RPE were not associated with self-reported affective symptoms. The multiple linear regression model hypothesizing the 6-month change in clinician-reported affective symptoms based on neural activation to RPE was not significant (eTable 3 in the Supplement). Psychotropic medication use did not moderate these results and including diagnosis in analyses did not change their significance (eAppendix 2 in the Supplement).

Table 3.

Association of Neural Activation to RPE With Change in Self-reported Affective Symptoms Between Baseline and 6 Months

Affective Symptom	β (95% CI)	*P* Value
Anhedonic depression (MASQ-AD)		
Left ventral striatum	−0.079 (−0.792 to 0.545)	.80
Left amygdala	−0.360 (−0.782 to 0.062)	.09
Left ACC	−0.231 (−0.795 to 0.333)	.41
Right ventral striatum	0.225 (−0.332 to 0.783)	.42
Right ACC	0.398 (−0.257 to 1.054)	.23
Anxious arousal (MASQ-AA)		
Left ventral striatum	−0.029 (−0.466 to 0.409)	.89
Left amygdala	−0.058 (−0.361 to 0.238)	.69
Left ACC	−0.120 (−0.521 to 0.275)	.54
Right ventral striatum	0.025 (−0.365 to 0.416)	.90
Right ACC	0.018 (−0.456 to 0.478)	.94
Anhedonia (SHAPS)		
Left ventral striatum	−6.152 (−11.870 to −0.433)	.04
Left amygdala	−1.451 (−5.318 to 2.416)	.45
Left ACC	−3.485 (−8.649 to 1.679)	.18
Right ventral striatum	4.790 (−0.319 to 9.899)	.07
Right ACC	4.129 (−1.876 to 10.134)	.17

Abbreviations: ACC, anterior cingulate cortex; MASQ-AA, Mood and Anxiety Symptom Questionnaire–Anxious Arousal subscale; MASQ-AD, Mood and Anxiety Symptom Questionnaire–Anhedonic Depression subscale; RPE, reward prediction error; SHAPS, Snaith Hamilton Pleasure Scale.

Improvement in Anhedonia at 6 Months and the Association Between VS Activation to RPE and Improvement in Psychosocial Function at 6 Months

After Bonferroni correction for multiple comparisons, change in SHAPS between baseline and follow-up mediated the association between left VS activation to RPE and baseline 6-month change in the satisfaction domain of the Range of Impaired Functioning Tool (Figure, C; Table 4). Specifically, the total extent of the association between left VS activation to RPE and improvement in the satisfaction domain of the Range of Impaired Functioning Tool during a 6-month period (total [c path] association: $\beta = 0.245$; $P = .01$) was accounted for by the change in anhedonia severity during those 6 months (indirect [ab path] association: 95% CI, 0.026-0.262); after accounting for the reduction in anhedonia, this association was no longer significant (direct [c′ path] association: $\beta = 0.133$; $P = .16$). Including psychotropic medication as a covariate did not change the significance of the results (eTable 4 in the Supplement), and psychotropic medication use did not moderate these results (eAppendix 2 in the Supplement). Including diagnosis in analyses similarly did not change the significance of the results (eAppendix 2 in the Supplement).

Table 4.

Six-Month Change in Anhedonia Symptoms and Association Between Left Ventral Striatum Activation to Reward Prediction Error and Improved Life Satisfaction

LIFE-RIFT Domain	Mediation Model, β (*P* Value)		Mediation Effect Size	SE (Bootstrapping Bias-Corrected 95% CI)
	Direct (c′ Path) Association	Total (c Path) Association		
Total	−0.013 (.66)	0.017 (.60)	1.779	0.019 (0.003 to 0.081)
Work	−0.018 (.81)	0.020 (.81)	1.900	0.040 (−0.029 to 0.136)
Interpersonal relationships	−0.032 (.73)	0.080 (.41)	1.401	0.060 (0.023 to 0.264)
Satisfaction[a]	0.133 (.16)	0.245 (.01)	0.456	0.060 (0.026 to 0.262)
Recreation	−0.095 (.14)	−0.113 (.12)	0.156	0.034 (−0.103 to 0.041)

Abbreviation: LIFE-RIFT, Range of Impaired Functioning Tool.

[a]Significant at $P < .05$ with Bonferroni correction.

Discussion

To our knowledge, this is the first prospective, longitudinal study to identify a transdiagnostic neural biomarker for improvement in psychiatric symptoms from a dimensional perspective and psychosocial function in a community sample of young adults. Neural reward regions including the VS, rostral-dorsal ACC, and amygdala were significantly activated during RPE. Of these neural regions, greater left VS activation

to RPE was associated with improvement in self-reported anhedonia severity during a 6-month period, and this improvement mediated the association between left VS activation to RPE and improved life satisfaction. Activation to RPE in other reward regions was not associated with 6-month change in self-reported affective and anxiety severity, and change in clinician-rated psychiatric symptom severity was not associated with activation in any reward circuitry regions.

Studies have identified potential neural biomarkers associated with progression of psychiatric illness. Two independent studies examined the development of depression in healthy individuals. In one, lower bilateral VS activation to anticipated monetary reward in adolescents was associated with prospective development of major depressive disorder during a 2-year period.[41] The other study reported that left VS resting state functional connectivity was associated with the onset of depressive symptoms after 3 years.[56] In our sample of young adults who had already started experiencing psychologic distress, left VS activation to RPE was associated with progression of anhedonia severity, but not with overall depressive or anxiety severity. This difference may be due to the role of VS in encoding motivational aspects of reward. Phasic firing of dopaminergic neurons in the ventral tegmental area encode and transmit RPE signals to the VS to facilitate goal-directed behavior.[57] The association between greater VS activation to RPE and improvement in anhedonia suggests that individuals with greater VS activation to RPE may retain the capacity for reward learning and motivation to obtain rewards. This capacity may facilitate recovery from anhedonia symptoms over time. In contrast, lower VS activation to RPE suggests an impaired ability to learn from, and be motivated by, rewards, which may perpetuate anhedonia. Recovery from other symptoms, such as anxiety and depression, may involve a more distributed reward network beyond the VS or may be dependent on neural regions beyond reward circuitry; however, to our knowledge, this is the first longitudinal study to identify a psychiatric neural biomarker of a dimensional construct (ie, anhedonia) that may play a critical role in the development of numerous psychiatric disorders

One important question in determining potential biomarkers is whether a single measurement of VS activation is reliable. Animal models suggest that RPE-associated activation may be stable over time,[58,59] and 1 study in healthy children found that negative RPE encoding (eg, the omission of an assumed reward) was stable across 3 years in the insula, while positive RPE encoding (eg, the presence of an unassumed reward, as measured in our study) was stable only across a period of months.[60] The authors of this study hypothesized this duration of stability may be due to several factors, including premature responses to trials and the signal to noise ratio. Our finding that left VS activation to positive RPE is associated with improvement in anhedonia symptoms over a period of months parallels these results and suggests that left VS activation to positive RPE may be a potential biomarker for short-term progression of anhedonia severity.

In our sample, left and right VS were not differentially activated to RPE, although only left VS activation to RPE was associated with the trajectory of anhedonia severity. This finding is consistent with previous reports supporting a role for the left VS in integrating information from emotion processing and reward regions.[56,61,62] Although no reward regions showed significant connectivity with the VS to RPE in our sample, the activation results nonetheless might have been influenced by the integration of signals from nonreward regions. Resting state connectivity analyses reveal lateralized patterns of connectivity between the left and right VS, with the left VS exhibiting greater connectivity with the dorsomedial prefrontal cortex and the posterior cingulate gyrus.[63] Heightened connectivity of the left VS with these default mode regions suggests a lateralization of internally directed and self-regulatory processes that are known to be disrupted in depressive disorders.[6,56] These findings support the importance of examining the laterality of potential biomarkers associated with future clinical and psychosocial outcome measures.

Limited research has examined associations between neural and psychosocial function, and to our knowledge, no studies have examined neural biomarkers associated with future psychosocial function. One study found that self-reported anxiety mediated the association between amygdala and vlPFC activation and overall psychosocial function.[64] Although it is not surprising that the reduction in anhedonia was associated with improved life satisfaction, given the association between anhedonia and decreased experience of pleasure, this is the first prospective study, to our knowledge, to identify a neural region associated with improved psychosocial function. This finding suggests that the left VS may be a particularly salient neural target for improving anhedonia severity and life satisfaction.

Strengths and Limitations

There was no significant activation to the other 2 main regressors, reward expectancy and outcome expectancy, in our study. Although previous findings indicated robust patterns of activation to reward expectancy,[52] this earlier study focused on individual differences in behavioral traits and links with reward expectancy–associated activation among healthy individuals and those with psychological distress. By contrast, our study examined patterns of neural reward activation that were common to young adults with psychological distress and examined how this pattern of neural activation was associated with future symptom changes. Although we did not find specific effects of medication, only 11 participants were taking psychotropic medication at follow-up, with variability in medication type, dosing, and duration. Our findings replicate the natural course of depression in which symptoms partially remit over time even without treatment[65,66]; however, additional research is needed to determine how neural biomarkers may also be associated with recurrence and future severity of depression. One limitation is the absence of a 6-month fMRI scan, which could examine the specificity of the association between observed symptoms and left VS activation; however, this study's purpose was to identify neural biomarkers at the time of presentation in psychological distress that are associated with future symptoms and psychosocial function.

Conclusions

Our findings identify a reward circuitry biomarker associated with anhedonia reduction, and a specific directional association between reduction in anhedonia severity and improved psychosocial function, in young adults experiencing psychological distress. To our knowledge, this is the first longitudinal, prospective study to identify neural biomarkers associated with psychiatric symptom reduction and improved psychosocial function in young adulthood, a critical period of development when psychiatric symptoms typically emerge. Left VS activation to RPE is associated with a reduction in anhedonia severity, and this reduction mediates the association between greater left VS activation and improvement in life satisfaction. Our findings suggest that left VS activation to RPE can, in future studies, be used to monitor response to treatments for anhedonia, and that the left VS can ultimately be used as a target for novel interventions to facilitate anhedonia reduction and psychosocial function improvement in young adults.

Notes

Supplement.

eAppendix 1. Methods

eAppendix 2. Results

eFigure. Standardized Monetary Reward Task

eTable 1. Improvement in Baseline Affective Symptoms Between Baseline and 6-Month Follow-up

eTable 2. Whole Brain Neural Activation

eTable 3. Association of Neural Activation to RPE With Change in Clinician-Rated Affective Symptoms Between Baseline and 6 Months

eTable 4. Six-Month Change in Anhedonia Symptoms Mediates the Association Between Left VS Activation and Improved Life Satisfaction Including Psychotropic Medication Use as a Covariate

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