Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Association Between Behavioral Activation System, White Matter Microstructure, and Depressive Symptoms in Major Depressive Disorder

Weixiong Li
Guizhou Normal University
Ping Yang
yangp@gznu.edu.cn
Guizhou Normal University
Ming Wang
Guiyang Medical University
Weihua Guo
Guizhou Normal University
Ruidie Shen
Guizhou Normal University
Renxia Tian
Guizhou Normal University

Research Article

Keywords: Major depressive disorder, Anhedonia, White matter microstructure, Fractional anisotropy, Behavioral activation system, Beck Depression Inventory

Posted Date: November 11th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11231730/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Association Between Behavioral Activation System, White Matter Microstructure, and Depressive Symptoms in Major Depressive Disorder

Weixiong Li, Ping Yang, Ming Wang, Weihua Guo, Ruidie Shen, Renxia Tian

Authors and Affiliations

Weixiong Li[1], Ping Yang[1]*, Ming Wang[2], Weihua Guo[1], Ruidie Shen[1], Renxia Tian[1]

[1] School of Psychology, Guizhou Normal University, Guiyang, Guizhou, China

[2] Guiyang Medical University, Guiyang, Guizhou, China

*** Corresponding Author:**

Ping Yang, School of Psychology, Guizhou Normal University, Guiyang, Guizhou, China. Email: yangp@gznu.edu.cn

Author Information

Weixiong Li, School of Psychology, Guizhou Normal University, Guiyang, Guizhou, China. Email: 853797185@qq.com

Ping Yang (Corresponding Author), School of Psychology, Guizhou Normal University, Guiyang, Guizhou, China. Email: yangp@gznu.edu.cn

Ming Wang, Guiyang Medical University, Guiyang, Guizhou, China. Email: 1240584562@qq.com

Weihua Guo, School of Psychology, Guizhou Normal University, Guiyang, Guizhou, China. Email: 2544606240@qq.com

Ruidie Shen, School of Psychology, Guizhou Normal University, Guiyang, Guizhou, China. Email: 3181895614@qq.com

Renxia Tian, School of Psychology, Guizhou Normal University, Guiyang, Guizhou, China. Email: 1029484915@qq.com

Abstract

Reduced behavioral activation system (BAS) sensitivity is a core behavioral phenotype of anhedonia, a key symptom of major depressive disorder (MDD) that involves multifaceted dysfunctions in the reward processing system. However, the white matter microstructural basis of this phenotype remains unclear. We examined fractional anisotropy (FA) in 54 MDD patients and 72 healthy controls (HC) and explored relationships among FA, BAS Total scores, and depressive symptom severity (Beck Depression Inventory, BDI) in MDD patients. All participants underwent diffusion-weighted imaging (DWI) and completed the BDI, BAS, and Behavioral Inhibition System (BIS) scales. Tract-based spatial statistics (TBSS) was used to extract FA values from seven a priori white matter tracts. Compared with HC, the MDD group showed significantly lower FA values in six tracts (right superior corona radiata, superior longitudinal fasciculus, posterior thalamic radiation, genu of corpus callosum, sagittal stratum, and fornix), as well as significantly lower BAS Total scores and higher BDI scores. Partial correlation analyses within the MDD group showed that FA values in four tracts (right superior corona radiata, superior longitudinal fasciculus, posterior thalamic radiation, and sagittal stratum) were significantly positively correlated with BAS Total scores. Mediation analyses controlling for age, sex, and BIS score revealed that BAS Total scores significantly mediated the relationship between FA values in these four tracts and BDI scores, with an indirect-only mediation pattern. When BIS was tested as an alternative mediator, none of the indirect effects were significant, supporting the specificity of the BAS-mediated

pathway. These findings provide new imaging evidence for a "white matter microstructure–behavior–symptom" pathway, suggesting that targeting white matter microstructure and BAS function may help alleviate anhedonia in MDD.

Keywords: Major depressive disorder; Anhedonia; White matter microstructure; Fractional anisotropy; Behavioral activation system; Beck Depression Inventory

1. Introduction

Major depressive disorder (MDD) is one of the most disabling mental disorders worldwide, affecting over 300 million people globally, with approximately 30% of patients showing insufficient response to pharmacotherapies (World Health Organization, 2022). This highlights the urgency of elucidating its neurobiological basis. Reduced behavioral activation system (BAS) sensitivity has been identified as a core behavioral phenotype of anhedonia (Hundt et al., 2007), which is a core symptom of MDD characterized by a markedly reduced ability to experience pleasure or a diminished response to rewarding stimuli. Unlike general low mood, anhedonia encompasses not only reduced consummatory pleasure but also impairments in reward anticipation, motivation, and decision-making (Beames et al., 2025). Understanding the neural basis of anhedonia is critical for developing targeted interventions.

1.1 Anhedonia and White Matter Microstructure

At the neural circuit level, the mesolimbic dopamine pathway—connecting the ventral tegmental area to the nucleus accumbens, prefrontal cortex, and amygdala—is central to reward processing (Price & Drevets, 2010; Russo & Nestler, 2013). Dysfunction within this network has been consistently implicated in anhedonia. However, most studies have focused on gray matter abnormalities or functional disruptions, leaving white matter microstructure relatively underexplored. Meanwhile, emerging diffusion imaging studies indicate that MDD patients with severe anhedonia show reduced fractional anisotropy (FA) in prefrontal-limbic white matter networks (Zhang et al., 2022; Hosoki et al., 2023). Additionally, reduced FA in the corpus callosum is associated with anhedonia severity, suggesting impaired interhemispheric integration (Baumer et al., 2018). Nevertheless, it remains unclear how specific white matter tracts relate to distinct behavioral manifestations of anhedonia, such as reduced approach motivation.

MDD patients consistently show lower BAS Total scores than healthy controls (Kasch et al., 2002; Carver & White, 1994), and BAS Total scores not only distinguish depressed patients from healthy individuals but also predict depressive symptom severity, particularly in those with prominent anhedonia and low energy (Trew, 2011). Despite this strong behavioral evidence, the white matter correlates of BAS sensitivity in MDD have not been directly examined. Specifically, it is unknown whether reduced FA in tracts connecting prefrontal and subcortical reward regions is associated with lower BAS Total scores, and whether this pathway contributes to depressive symptom severity.

1.2 The Roles of BDI and BAS in Depression Severity Assessment

The Beck Depression Inventory (BDI) is a widely used self-report measure of depressive symptom severity, with strong internal consistency and sensitivity to clinical change (Beck et al., 1996). Higher BDI scores reliably reflect more severe depression and serve as a standard outcome indicator in MDD research. In parallel, reduced BAS sensitivity is a core behavioral phenotype of anhedonia(Chen et al., 2017) and has been consistently associated with greater depressive severity (Kasch et al., 2002; Trew, 2011). Empirical studies have reported significant negative correlations between BAS Total scores and BDI scores in both clinical and community samples (Carver & White, 1994; Hundt et al., 2007). Moreover, BAS sensitivity has been shown to mediate the relationship between biological markers and depressive outcomes (Yatawara et al., 2019; Feng et al., 2024), and early changes in BAS predict subsequent improvement in depression severity (Lindqvist Bagge et al., 2025). Taken together, the robust BDI–BAS association provides the empirical rationale for testing BAS as a mediator linking white matter microstructure to depressive symptom severity in MDD.

1.3 White Matter Abnormalities in MDD: Known Findings and Unresolved Questions

Diffusion tensor imaging (DTI) is a non-invasive MRI modeling technique that estimates the directionality and rate of water diffusion within white matter fibers,

providing a unique window into white matter microstructure in living human brains (Basser et al., 1994; Le Bihan et al., 2001). Over the past two decades, diffusion studies have provided robust evidence for white matter abnormalities in MDD. Meta-analyses have consistently found reduced FA in MDD patients in multiple regions, including the corpus callosum, superior corona radiata, and superior longitudinal fasciculus (Liao et al., 2013; Wen et al., 2014). These abnormalities are present even in drug-naïve first-episode patients, suggesting they may be trait characteristics rather than consequences of chronic illness (Zhang et al., 2011). Moreover, the ENIGMA MDD working group's coordinated analysis of 20 international cohorts confirmed the widespread and cross-sample consistency of white matter alterations in MDD (van Velzen et al., 2020).

However, important gaps remain. First, most MDD diffusion studies have focused on group comparisons between patients and controls, without linking white matter measures to behavioral dimensions of anhedonia. Second, while reduced FA has been associated with depressive symptom severity, the indirect pathways through which white matter microstructure affects symptoms are poorly understood. Yatawara et al. (2019) provided a key theoretical clue: in Alzheimer's disease patients, the association between reduced white matter microstructure and depressive symptoms was mediated by white matter hyperintensities, suggesting a mediated pathway from microstructural alterations to macrostructural lesions to clinical symptoms. Similarly, Feng et al. (2024) demonstrated that white matter microstructure affects social difficulties through internalizing problems in children with autism spectrum disorder, illustrating

a structure–symptom–behavior pathway. These findings raise the possibility that in MDD, white matter abnormalities might not directly cause depressive symptoms but instead impair an intermediate behavioral system—specifically, the BAS—which then leads to increased depression severity.

1.4 The Present Study: Hypotheses and Research Framework

Based on the above, we designed the present study to address three specific questions: (1) Do MDD patients show reduced FA in specific emotion-related tracts compared to healthy controls? (2) Is FA in these tracts correlated with BAS Total scores? (3) Does BAS Total scores mediate the relationship between FA and depressive symptom severity? To ensure comparability with prior work, we selected the seven emotion-related white matter tracts identified by Yatawara et al. (2019)—right superior corona radiata, right superior longitudinal fasciculus, right posterior thalamic radiation, genu of corpus callosum, right sagittal stratum, right fornix, and right uncinate fasciculus—as regions of interest. We drew on the mediation analysis framework of Feng et al. (2024) to examine the indirect effect of FA on depressive symptom severity through BAS.

2. Materials and Methods

2.1 Participants

A total of 126 right-handed participants aged 18–26 years were recruited. The MDD group (N = 54, age = 20.28 ± 2.21 years; 21 males, 33 females) and the HC group (N = 72, age = 20.60 ± 1.96 years; 31 males, 41 females) were recruited through campus and community advertisements between June 2023 and March 2025. The two groups were matched for age and sex. Demographic and clinical data are presented in Table 1.

Inclusion criteria for the MDD group were: diagnosis of MDD according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (American Psychiatric Association, 2013), confirmed by a hospital psychiatrist. Exclusion criteria for the MDD group included: any unstable medical or neurological condition; current substance abuse or dependence, or history of substance abuse within the past 3 months; current or past psychiatric disorders (schizophrenia, bipolar disorder, intellectual disability, or other developmental disorders); severe somatic diseases (e.g., brain tumor, multiple sclerosis); and contraindications to MRI scanning (e.g., metal implants or claustrophobia). Patients currently receiving psychotropic medication or electroconvulsive therapy were also excluded. Inclusion criteria for the HC group were: no history of psychiatric or neurological disorders, no history of substance abuse, no history of psychotropic medication use, and BDI score within the normal range.

This study was approved by the Ethics Committee of the School of Psychology, Guizhou Normal University (approval number: GZNUPSY.N.202211E[0015]).

Before participation, all participants received a detailed explanation of the study purpose and procedures, and after fully understanding the study and confirming their eligibility, they signed informed consent forms and committed to truthful participation.

Table 1

Participants Characteristics and Group Differences

Variables	MDD（N=54） (Mean ± SD)	HC（N=72） (Mean ± SD)	t/χ^2	Cohen's d	p-value
Age (years)	20.28 ±2.05	20.6 ±1.75	-0.922	-0.170	0.358
Sex (Male/Female)	21/33	31/41	0.221	–	0.638
BDI Score	34.8 ±4.67	11.92 ±9.24	18.147	3.000	<0.001
BAS Total Score	34.78 ±5.28	38.06 ±4.52	-3.663	-0.670	<0.001
Drive	10.94 ± 2.18	12.40 ± 2.18	−3.712	0.590	<0.001
Fun Seeking	10.81 ± 2.27	11.58 ± 1.82	−2.046	−0.38	0.043
Reward Responsiveness	13.02 ± 2.18	14.07 ± 1.83	−2.859	−0.53	0.005
BIS	16.02 ± 2.14	14.74 ± 2.19	3.296	0.59	0.001

Note: Data are presented as mean ± standard deviation.

t-tests (continuous variables) or Pearson's chi-square test (categorical variables).

p-values are from independent two-sample

2.2 MRI Data Acquisition

Whole-brain diffusion-weighted imaging (DWI) data were acquired using a Siemens Magnetom Prisma 3.0T superconducting MRI scanner (Siemens Healthineers, Germany) with an HC1-7 head coil. The DWI acquisition parameters were as follows: echo-planar imaging (EPI) sequence, axial orientation; voxel size = 1.8 × 1.8 × 1.8 mm^3; 84 slices; slice thickness = 1.8 mm, no gap; field of view = 205 × 100 mm; acquisition matrix = 114 × 114; repetition time = 3200 ms; echo time = 81.0 ms; phase encoding direction = posterior–anterior; interleaved acquisition; number of signal averages = 1; total acquisition time = 8 min 49 s; bandwidth = 1828 Hz/Px; partial Fourier factor = 6/8. Participants lay supine with foam pads to fix the head and wore earplugs for noise reduction.

Diffusion parameters: Single-shell acquisition with b = 3000 s/mm^2; 159 diffusion-encoding directions; 1 b = 0 volume. A reverse phase-encoding (anterior–posterior) b = 0 image was acquired for topup distortion correction. The total acquisition time of 8 min 49 s was enabled by simultaneous multi-slice (SMS) excitation with PAT = 4 acceleration.

2.3 Diffusion Tensor Modeling and Data Processing

MRI data preprocessing was performed using the FMRIB Software Library (FSL, version 6.0; Smith et al., 2004). First, the Brain Extraction Tool (BET) was applied to the initial non-diffusion-weighted volume to generate a binary brain mask. The FSL eddy tool was then used to correct for eddy current distortions and motion artifacts (Andersson & Sotiropoulos, 2016). The diffusion tensor model was fitted at each voxel using conventional linear least squares with dtifit, generating parametric maps including FA, mean diffusivity (MD), radial diffusivity (RD), and axial diffusivity (AD) for each participant. For tract-based spatial statistics (TBSS), a mean FA image was generated and skeletonized; each participant's FA image was projected onto the FA skeleton (thresholded at FA > 0.2) to create a merged 4D image for cross-subject statistics (Smith et al., 2006). Regions of interest (ROIs) were defined according to the Johns Hopkins University (JHU) ICBM-DTI-81 white matter labels atlas (Mori et al., 2008), and mean FA, MD, RD, and AD values were extracted for the right superior corona radiata (SCR-R), right superior longitudinal fasciculus (SLF-R), right posterior thalamic radiation (PTR-R), genu of corpus callosum (GCC), right sagittal stratum (SS-R), right fornix (Fornix-R.The fornix ROI was defined using the 'fornix (cres)/Stria terminalis' label in the JHU ICBM-DTI-81 White-Matter Labels), and right uncinate fasciculus (UF-R).

2.4 Behavioral Assessment

2.4.1 Behavioral Activation System and Behavioral Inhibition System

BAS and BIS scores were assessed using the Chinese version of the BIS/BAS Scales (Zhang et al., 2008), which was revised from the original Carver and White (1994) instrument. The Chinese version comprises 18 items rated on a 4-point Likert scale (1 = “strongly disagree” to 4 = “strongly agree”). The BAS subscale consists of 13 items (score range 13–52) and comprises three dimensions: BAS Reward Responsiveness, BAS Drive, and BAS Fun Seeking . The BIS subscale consists of 5 items (score range 5–20) measuring sensitivity to punishment and negative affectivity. Higher BAS Total scores indicate stronger behavioral activation tendency; higher BIS scores indicate stronger avoidance motivation. The Chinese version has demonstrated acceptable reliability and validity in Chinese samples, with Cronbach’s α coefficients ranging from 0.55 to 0.72 for the four dimensions (Zhang et al., 2008).

2.4.2 Depressive Symptom Severity

Depressive symptoms were assessed using the Beck Depression Inventory (BDI; Beck et al., 1996), a 21-item self-report questionnaire with each item rated on a 0–3 scale, score ranging from 0 to 63; higher scores indicate more severe depressive symptoms. The BDI has been widely used in clinical and research settings and has good reliability and validity in various populations.

2.5 Statistical Analysis

2.5.1 Group Comparisons

All variables were carefully evaluated for outliers, data entry errors, and missing values. Independent two-sample t-tests were used to compare demographic variables between groups, with effect sizes (Cohen's d) calculated for age, BAS Total scores, BIS score, and BDI score. Pearson's chi-square test was used to analyze sex distribution differences between groups. Independent two-sample t-tests were used to analyze intergroup differences in FA, MD, RD, and AD values between MDD and HC groups. After false discovery rate (FDR) correction, significance was set at $p < 0.05$, controlling for covariates such as age and sex.A sensitivity analysis using GPower (Faul et al., 2007) indicated that with the current sample size (MDD n = 54, HC n = 72), the minimum detectable effect size at $\alpha = .05$ (two-tailed) and power = .80 was Cohen's d = 0.51.

Because the present study employed an ROI-based approach (extracting mean values from a priori tracts) rather than whole-brain voxel-wise analysis, FDR correction was applied to control for multiple comparisons across the seven tracts. TFCE and FWE correction are more appropriate for whole-brain exploratory analyses and were therefore not adopted.

2.5.2 Correlation Analysis

Within the MDD group, partial correlation analysis was used to calculate partial correlation coefficients to explore relationships between FA values of each tract and BAS Total scores, controlling for age and sex.FDR correction was applied to the partial correlation analyses across the seven tracts

2.5.3 Mediation Analysis

To elucidate the interplay among white matter microstructure, behavioral activation system, and depressive symptom severity, mediation analysis was conducted using the SPSS macro PROCESS version 4.3 (Model 4; Hayes, 2013). FA values of tracts that showed significant group differences and significant correlations with BAS Total scores were entered as independent variables (X), BAS Total scores as the mediator (M), and BDI score as the dependent variable (Y). Age, sex, and BIS score were included as covariates in all mediation models. Mediation effects were estimated using 5000 bootstrap samples and considered statistically significant if the 95% confidence interval (CI) did not include zero (Preacher & Hayes, 2008).

To test the specificity of the BAS-mediated pathway, BIS score was also tested as an alternative mediator (X = FA, M = BIS, Y = BDI), with age and sex as covariates.

3. Results

3.1 Demographic and Clinical Characteristics

As shown in Table 1, there were no significant differences in age or sex distribution between the MDD and HC groups ($p > 0.05$). Compared with the HC group, the MDD group had significantly lower BAS Total scores ($t = 3.663$, $p < 0.001$, Cohen's $d = 0.67$) and significantly higher BDI scores ($t = 18.147$, $p < 0.001$, Cohen's $d = 3.00$), indicating severe depressive symptoms in the MDD group. The MDD group also

showed significantly higher BIS scores than the HC group ($t = 3.30$, $p = 0.001$, Cohen's $d = 0.59$).

3.2 Reduced FA in MDD

Compared with the HC group, the MDD group showed significantly reduced FA values in six white matter tracts ($p < 0.05$, FDR corrected): right superior corona radiata (SCR-R), right superior longitudinal fasciculus (SLF-R), right posterior thalamic radiation (PTR-R), genu of corpus callosum (GCC), right sagittal stratum (SS-R), and right fornix (Fornix-R). Effect sizes were moderate for PTR-R (Cohen's $d = 0.52$) and GCC (0.46), small to moderate for SCR-R (0.45), SLF-R (0.41), and SS-R (0.40), and small for Fornix-R (0.37). The right uncinate fasciculus (UF-R) showed no significant group difference (Cohen's $d = 0.17$, $p = 0.335$). Detailed statistics are shown in Figure 1.

To further characterize the nature of these microstructural differences, we also extracted mean MD, RD, and AD values from the same ROIs. None of these metrics showed significant group differences after FDR correction (all $p > 0.05$; see Supplementary Table S1). This pattern suggests that the FA reductions observed in the MDD group may primarily reflect altered directional diffusion rather than gross changes in mean diffusivity or axial/radial diffusivity.

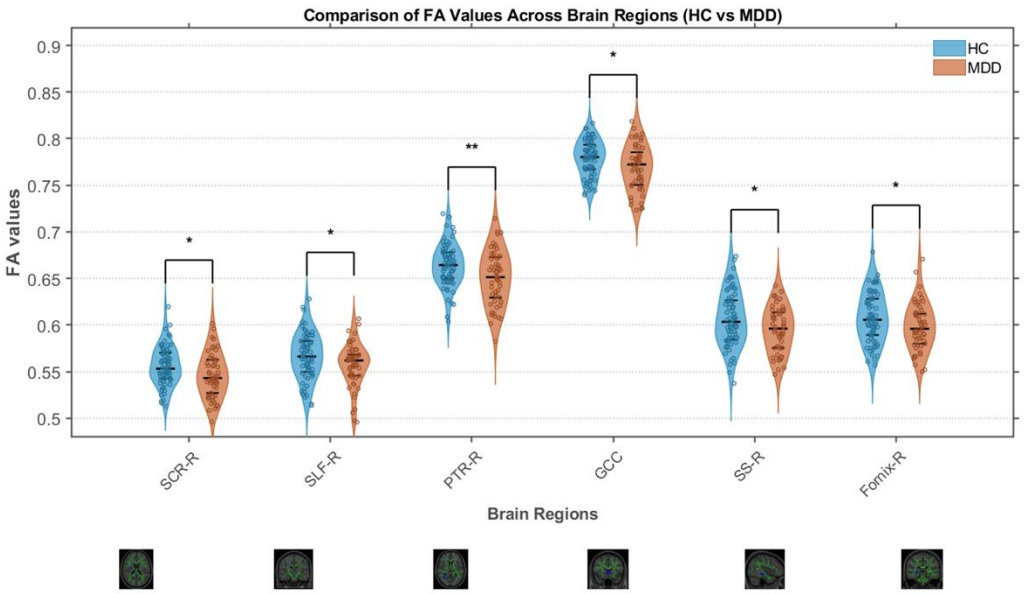


Figure 1.Comparison of FA Values Between MDD and HC Groups Across White Matter

Tracts. Bars represent mean FA values ± standard error. Asterisks indicate significant group differences after FDR correction ($p < 0.05$, $p < 0.01$). The MDD group showed significantly lower FA in six tracts: SCR-R (Cohen's d =0.45, p=0.012), SLF-R (d=0.41, p=0.018), PTR-R (d=0.52, p=0.004), GCC (d=0.46, p=0.009), SS-R (d=0.40, p=0.021), and Fornix-R (d=0.37, p=0.036). No significant difference was found for UF-R (d=0.17, p=0.335). Abbreviations: SCR-R, right superior corona radiata; SLF-R, right superior longitudinal fasciculus; PTR-R, right posterior thalamic radiation; GCC, genu of corpus callosum; SS-R, right sagittal stratum; Fornix-R, right fornix; UF-R, right uncinate fasciculus.

*Note: Bars represent mean FA values ± standard error. *$p < 0.05$, **$p < 0.01$.

3.3 Correlation Between BAS Total scores and FA Values

Within the MDD group, after controlling for age and sex, partial correlation analysis revealed that BAS Total scores were significantly positively correlated with FA values(Figure 2.) of SCR-R ($r = 0.361$, $p = 0.007$), SLF-R ($r = 0.326$, $p = 0.016$), PTR-R ($r = 0.302$, $p = 0.026$), and SS-R ($r = 0.323$, $p = 0.017$). The R^2 values suggested that FA values explained approximately 9–13% of the variance in BAS Total scores. Correlations with GCC ($r = 0.207$, $p = 0.134$), Fornix-R ($r = 0.150$, $p = 0.278$), and UF-R ($r = 0.208$, $p = 0.130$) did not reach statistical significance.After FDR correction, the correlations with SCR-R, SLF-R, PTR-R, and SS-R remained significant (all $p < 0.05$).

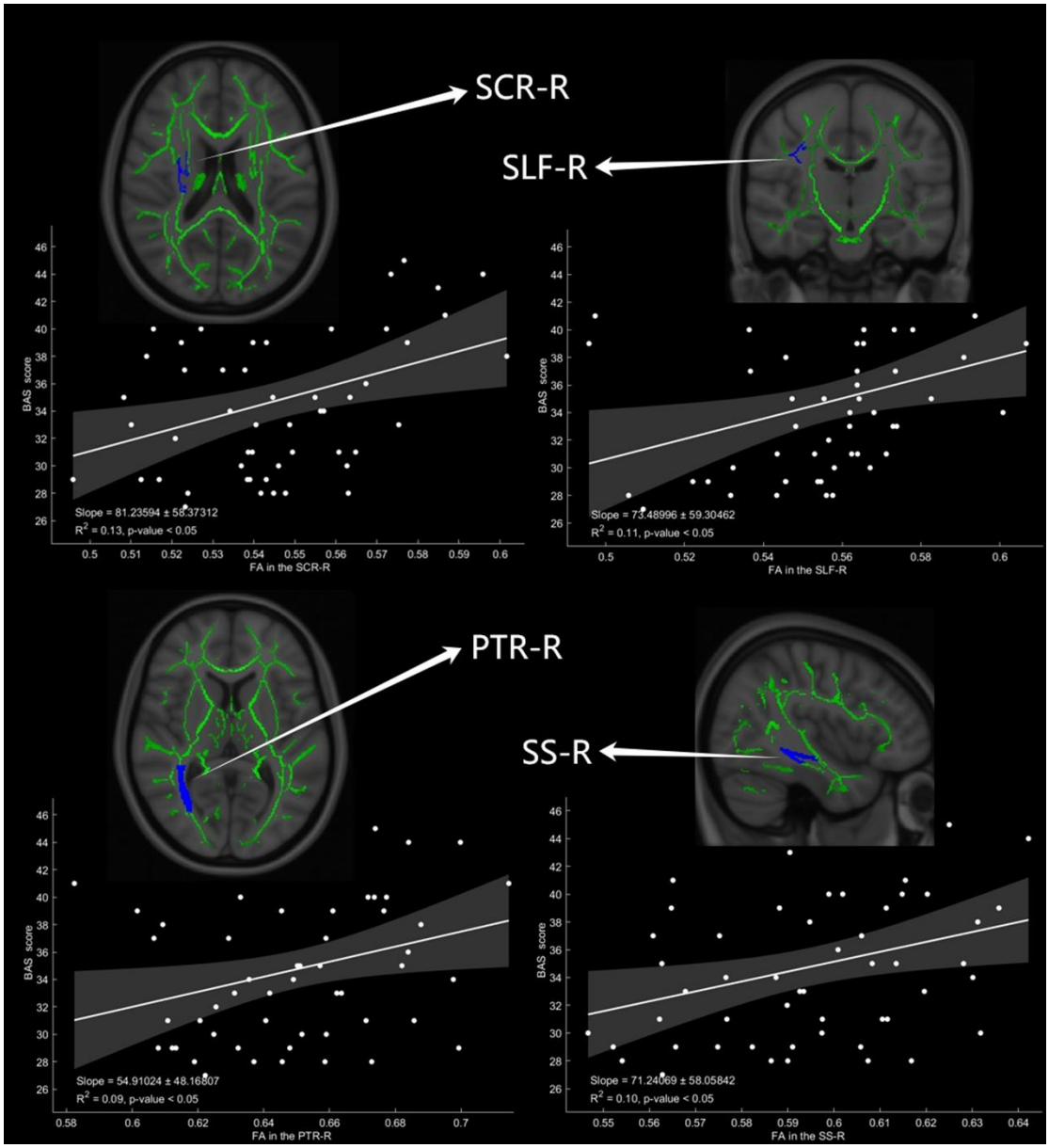


Figure 2.Relationship Between FA Values and BAS scores. Scatter plots show significant positive partial correlations (controlling for age and sex) between FA values of four tracts and BAS scores: (A) SCR-R (r=0.361, p=0.007), (B) SLF-R (r=0.326, p=0.016), (C) PTR-R (r=0.302, p=0.026), and (D) SS-R (r=0.323, p=0.017). Each point represents one participant. Shaded areas indicate 95% confidence intervals for the regression lines.

Note: Scatter plots show the significant positive correlations between BAS scores and FA values in SCR-R, SLF-R, PTR-R, and SS-R.

3.4 Mediation Effect of Behavioral Activation System

Based on the above results, the four tracts that showed both significant group differences and significant correlations with BAS Total scores (SCR-R, SLF-R, PTR-R, SS-R) were entered into mediation models(Table 2), with FA value as the independent variable (X), BAS Total score as the mediator (M), and BDI score as the dependent variable (Y). Age, sex, and BIS score were included as covariates in all models (Figure 3).

Table 2
Mediation models with BAS as mediator (controlling for age, sex, and BIS)

X	a (FA→BAS) β	p	b (BAS→BDI) β	p	c' (FA→BDI) β	p	Indirect β	95% CI	Total c	Conclusion
SCR-R	0.296	0.016	-0.520	0.002	0.151	0.279	-0.154	[-0.3264, -0.0150]	0	Indirect-only
SLF-R	0.363	0.003	-0.591	0.001	0.274	0.053	-0.215	[-0.4062, -0.0769]	0.06	Indirect-only
PTR-R	0.282	0.021	-0.475	0.004	0.032	0.818	-0.134	[-0.2850, -0.0201]	-0.1	Indirect-only
SS-R	0.288	0.018	-0.490	0.003	0.072	0.601	-0.141	[-0.2847, -0.0231]	-0.07	Indirect-only

Table 2

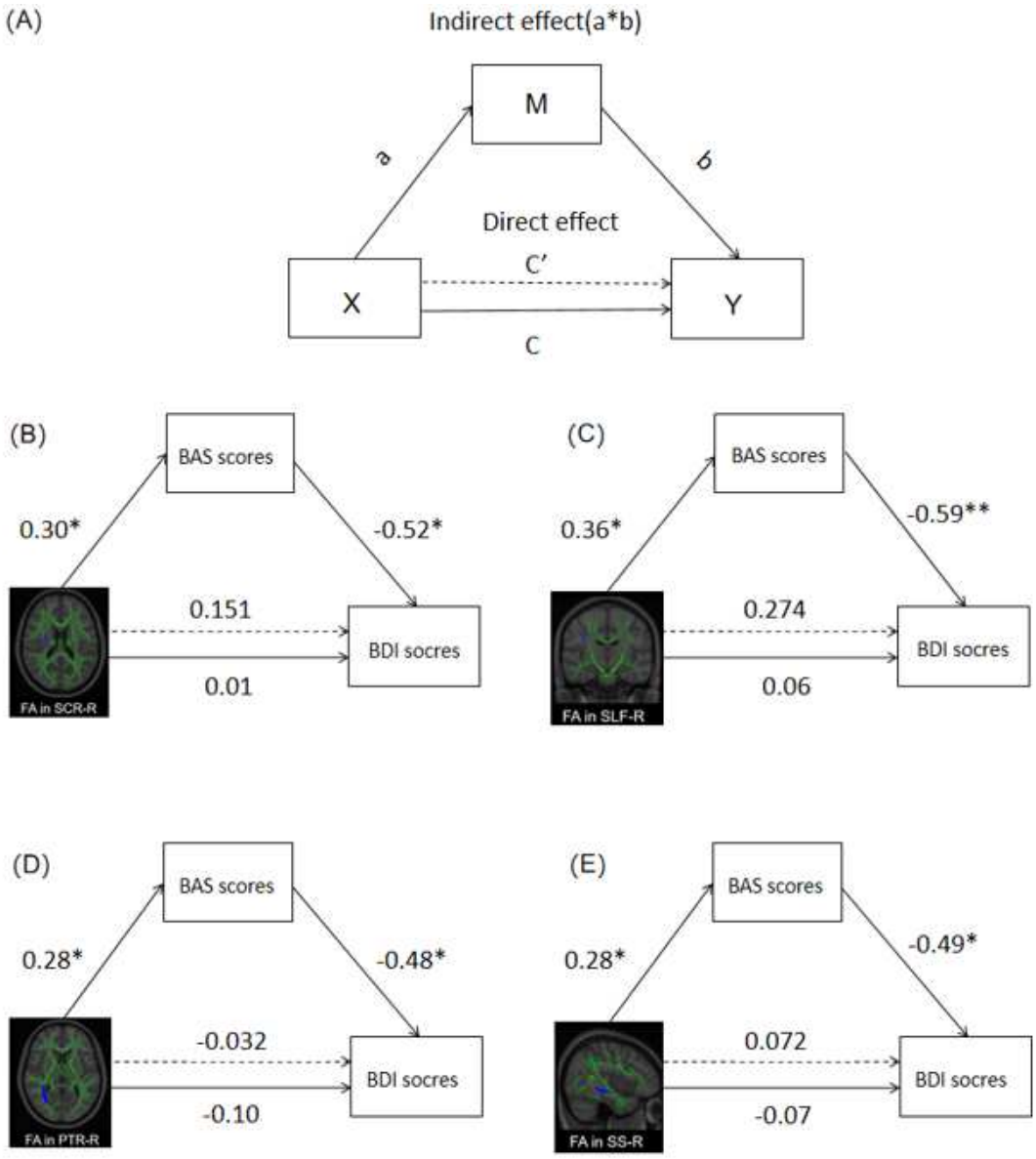


Figure 3. Mediation Model of BAS score in the Relationship Between FA Values and BDI scores

Note: Standardized path coefficients are shown.

Mediation analysis for SCR-R: The a-path (FA → BAS) standardized coefficient was 0.2965 (p = 0.0159). The b-path (BAS → BDI) standardized coefficient was -0.5203 (p = 0.0016). The direct effect c' (FA → BDI) was 0.1506 (p = 0.2789), non-significant. The standardized indirect effect (a×b) was -0.1543, bootstrap 95% CI

[-0.3264, -0.0150], indicating a significant indirect effect. The total effect c was -0.00 ($p > 0.05$). This pattern is consistent with an indirect-only mediation model.

Mediation analysis for SLF-R: The a-path was 0.3633 ($p = 0.0026$), b-path was -0.5913 ($p = 0.0005$), direct effect c' was 0.2740 ($p = 0.0532$), indirect effect was -0.2148, bootstrap 95% CI [-0.4062, -0.0769]. The total effect c was 0.06 ($p > 0.05$). This pattern is consistent with an indirect-only mediation model.

Mediation analysis for PTR-R: The a-path was 0.2819 ($p = 0.0209$), b-path was -0.4747 ($p = 0.0040$), direct effect c' was 0.0318 ($p = 0.8176$), indirect effect was -0.1338, bootstrap 95% CI [-0.2850, -0.0201]. The total effect c was -0.10 ($p > 0.05$). This pattern is consistent with an indirect-only mediation model.

Mediation analysis for SS-R: The a-path was 0.2884 ($p = 0.0176$), b-path was -0.4903 ($p = 0.0031$), direct effect c' was 0.0720 ($p = 0.6014$), indirect effect was -0.1414, bootstrap 95% CI [-0.2847, -0.0231]. The total effect c was -0.07 ($p > 0.05$). This pattern is consistent with an indirect-only mediation model.

In summary, BAS Total scores significantly mediated the relationship between FA values in SCR-R, SLF-R, PTR-R, and SS-R and BDI scores, with an indirect-only mediation pattern. The total effect of FA on BDI was not significant for any tract, indicating that the association between FA and depressive symptoms is transmitted through BAS rather than through a direct pathway.

Specificity analysis: To test whether the mediating pathway was specific to reward-approach motivation rather than general negative affectivity, BIS was tested as an alternative mediator (FA → BIS → BDI). None of the indirect effects were significant (all 95% CIs included zero; see Supplementary Table S2), supporting the specificity of the BAS-mediated pathway.

4. Discussion

Based on the emotion-related white matter network proposed by Yatawara et al. (2019), this study systematically examined the relationships among white matter microstructure, the behavioral activation system, and depressive symptom severity in patients with MDD. Our main findings are: (1) Compared with healthy controls, MDD patients showed significantly reduced FA values in six white matter tracts, including the right superior corona radiata, right superior longitudinal fasciculus, right posterior thalamic radiation, genu of corpus callosum, right sagittal stratum, and right fornix; (2) Among these tracts, FA reductions in SCR-R, SLF-R, PTR-R, and SS-R were significantly positively correlated with reduced BAS Total scores; and (3) BAS Total scores significantly mediated the relationship between FA in these four tracts and depressive symptom severity (BDI scores), with an indirect-only mediation pattern. These findings reveal a mediational pathway of "white matter microstructural alterations → reduced behavioral activation system function → increased depressive symptom severity" underlying anhedonia in MDD.

4.1 Widespread FA Reductions in MDD

This study is the first to systematically examine, in a young adult MDD sample, the FA of the seven emotion-related white matter tracts identified by Yatawara et al. (2019) in Alzheimer's disease. Compared with HC, the MDD group showed significantly reduced FA in six tracts (all except UF-R), a finding highly consistent with meta-analyses of diffusion studies in MDD (Liao et al., 2013; Wen et al., 2014). The superior corona radiata, superior longitudinal fasciculus, and posterior thalamic radiation are key white matter tracts constituting the prefrontal–striatal–thalamic circuit, which plays a central role in reward processing, emotion regulation, and motivated behavior (Price & Drevets, 2010; Russo & Nestler, 2013).

The superior corona radiata connects the frontal lobes with subcortical regions and is involved in emotion regulation and executive function. The reduced FA in SCR-R (effect size 0.45) in this study is consistent with previous reports. FA reductions in this region may be associated with altered communication between frontal and subcortical structures, potentially affecting emotional processing and behavioral output. However, given the cross-sectional design, these interpretations remain speculative and cannot establish causality.

The superior longitudinal fasciculus is a long association fiber connecting the frontal, parietal, and temporal lobes, playing an important role in higher-order cognitive processing. The present study found significantly reduced FA in SLF-R, consistent with previous reports of white matter alterations in MDD. The posterior thalamic

radiation contains projections from the pulvinar to visual cortex; reduced FA in this tract may be associated with altered transmission of reward-related visual information. PTR-R showed the largest effect size in this study (Cohen's d = 0.52), suggesting that thalamo-cortical pathways may be particularly affected in MDD.

The genu of the corpus callosum contains fibers connecting the bilateral frontal lobes and is involved in interhemispheric information integration and emotion regulation. Reduced FA in the GCC (effect size 0.46) may reflect altered interhemispheric information transfer. The sagittal stratum contains the inferior longitudinal fasciculus and the inferior fronto-occipital fasciculus, which are part of the ventral visual pathway responsible for transmitting visual information to the prefrontal cortex. Reduced FA in the SS-R (effect size 0.40) may be associated with altered processing of reward-related visual cues. The fornix is the major efferent tract of the hippocampus; reduced FA in the Fornix-R (effect size 0.37) may be associated with episodic memory processes relevant to anhedonia.

We did not find a significant group difference in UF-R FA, which differs from some previous reports. Possible explanations include: first, our sample was relatively young (mean age 20 years), and the uncinate fasciculus may mature later, so group differences might emerge at older ages; second, our participants were first-episode or short-duration patients, and UF white matter alterations may occur more in chronic illness; third, the UF is more strongly associated with anxiety symptoms than with the core anhedonia of depression. Additionally, the uncinate fasciculus is located in a

region prone to EPI susceptibility artifacts. Although we acquired reverse phase-encoding data for topup correction, residual distortions may still affect FA estimates in this tract, and the null finding should therefore be interpreted with caution.

Although the right-lateralized ROI selection was inherited from Yatawara et al. (2019) to facilitate cross-study comparison, we acknowledge that this laterality scheme is not a neurobiological argumen, and future studies should systematically compare bilateral homologues to determine whether the observed effects are specific to the right hemisphere.

4.2 Association Between FA and Behavioral Activation System

A key innovation of this study is the direct examination of the relationship between white matter microstructure and a behavioral measure of anhedonia—the BAS Total scores. The results showed that FA values in SCR-R, SLF-R, PTR-R, and SS-R were significantly positively correlated with BAS Total scores, directly supporting our hypothesis that the degree of white matter microstructural variation is related to the strength of an individual's reward-approach motivation. Within the framework of reinforcement sensitivity theory, the BAS is conceptualized as a motivational system sensitive to conditioned reward signals, driving approach behavior (Gray & McNaughton, 2000). Previous studies have shown that reduced BAS sensitivity is a core behavioral phenotype of anhedonia (Hundt et al., 2007; Kasch et al., 2002). This study provides empirical support from a white matter connectivity perspective for the

relationship between BAS and the reward processing system. SCR-R and SLF-R are key pathways connecting the prefrontal cortex and subcortical regions; reduced FA in these tracts may imply that top-down emotion regulation signals cannot be effectively transmitted, making it difficult for patients to mobilize behavior to approach potential reward targets. This finding extends the application of reinforcement sensitivity theory in neuroimaging.

It is worth noting that the MDD group showed lower BAS Total scores alongside higher BIS scores($t = 3.296$, $p = 0.001$, Cohen's $d = 0.59$), consistent with the theoretical prediction of an asymmetric shift in the BAS/BIS balance in depression. This pattern supports the specificity of the BAS-mediated pathway rather than a general negative affectivity account.

4.3 Mediating Role of the Behavioral Activation System: A "White Matter Microstructure–Behavior–Symptom" Mediation Pathway

The finding of a non-significant total effect alongside a significant indirect effect is theoretically meaningful. As Zhao et al. (2010) noted, indirect-only mediation occurs when the mediated pathway is the primary mechanism linking X to Y, and the direct pathway is either absent or suppressed by opposing effects. This pattern further supports the specificity of the BAS-mediated pathway.The most important finding of this study is the demonstration of a mediational pathway among FA values, BAS, and BDI: reduced FA is associated with impaired behavioral activation system function

(the behavioral manifestation of anhedonia), which in turn is associated with increased depressive symptom severity. This indirect-only mediation model has important theoretical and clinical implications and aligns with the core logic of reinforcement sensitivity theory—white matter microstructural variations are associated with the approach behavior system, and dysfunction of this system is further associated with overall depressive mood.

First, this model provides an integrated pathway explanation: "white matter microstructural alterations → downregulation of behavioral activation system → increased depressive symptom severity." This is highly consistent with Gray's reinforcement sensitivity theory, which posits that the BAS is a motivational system sensitive to reward signals, and its functional integrity depends on normal connectivity of prefrontal–subcortical white matter pathways (Gray & McNaughton, 2000). When FA values in tracts such as the right superior corona radiata and superior longitudinal fasciculus are reduced, the neural basis of reward-approach behavior may be altered, manifested as decreased BAS Total scores (the behavioral phenotype of anhedonia). This persistent lack of reward responsiveness and motivation may further contribute to feelings of hopelessness and worthlessness—overall depressive symptoms (Trew, 2011). In other words, anhedonia is not directly equivalent to depressive symptom severity but, as a core mechanism of "drive deficit," mediates the association between white matter variations and overall mood disturbance.

Second, this model provides a more upstream intervention target. The indirect-only mediation effect suggests that to reduce depressive symptom severity, restoring behavioral activation system function may be a more upstream breakthrough than directly regulating mood. Clinically, behavioral activation therapy works precisely by increasing patients' engagement in rewarding activities to enhance BAS sensitivity, thereby alleviating depression. Our imaging findings support the neural basis of this therapy—improving white matter microstructure (e.g., using repetitive transcranial magnetic stimulation targeting SCR-R, SLF-R) or behaviorally enhancing BAS function through training may indirectly reduce depressive symptom severity.

Third, compared with the studies by Yatawara et al. (2019) and Feng et al. (2024), our model highlights the specificity of symptom cascades. Yatawara et al. found that white matter alterations affected depressive symptoms through white matter hyperintensities (structure–structure–symptom); Feng et al. found that white matter microstructure affected social difficulties through internalizing problems (structure–symptom–behavior); the present study found that white matter microstructure affected depressive symptom severity through the behavioral activation system (structure–behavior–symptom). The commonality across the three pathways is that white matter alterations do not directly lead to the final clinical outcome but instead act through an intermediate variable. This suggests that the pathological pathway of neuropsychiatric disorders may have a "multi-pathway, multi-level" character.

Contrary to our hypotheses, although GCC and Fornix-R showed group differences, their FA values were not significantly correlated with BAS Total scores and did not show mediation effects. The GCC connects bilateral frontal lobes and is primarily involved in cognitive control and emotion regulation, while the fornix is the major efferent tract of the hippocampus and is more closely related to memory function. This suggests that these two pathways may be more associated with cognitive symptoms of depression or other aspects of emotion regulation, rather than the specific symptom dimension of anhedonia.

The specificity of the BAS-mediated pathway was further supported by the alternative mediator analysis: when BIS was tested as the mediator, none of the indirect effects approached significance. This dissociation suggests that the white matter–behavior–symptom pathway observed here is specifically linked to reward-approach motivation rather than a general negative affectivity or anxiety-related process.

5. Limitations

First, the cross-sectional design precludes causal inferences. Although our mediation model statistically supports the path FA → BAS → BDI, it only reveals associations, not temporal or causal direction.Second, sample characteristics limit generalizability and subgroup analyses. Our sample consisted entirely of young adult participants (aged 18–26 years), so findings may not generalize to older adults or broader community populations. Third, several important clinical variables were not collected, including illness duration, number of episodes, prior medication history, and

clinician-rated scales such as HAMD/HAMA. Although we excluded currently medicated patients, the absence of these variables limits our ability to fully rule out confounds related to illness chronicity and comorbidity.Fourth, methodological choices may oversimplify white matter microstructure. We used the JHU atlas for ROI extraction, which is standardized and reproducible but ignores individual variability in tract trajectories.

6. Conclusion

This study systematically demonstrated that microstructural variations in specific white matter tracts (right superior corona radiata, superior longitudinal fasciculus, posterior thalamic radiation, and sagittal stratum) in MDD patients are associated with impaired behavioral activation system function (the behavioral manifestation of anhedonia), which in turn is associated with increased depressive symptom severity. These findings show that six of the seven emotion-related white matter tracts identified by Yatawara et al. (2019) also show reduced FA in depression, and extend the mediation analysis paradigm of Feng et al. (2024) to the study of anhedonia in MDD. The results provide new empirical support for the "white matter–behavior–symptom" mediation mechanism of anhedonia and offer a theoretical basis for the future development of precision intervention strategies targeting white matter pathways.

Ethical Statement

This study was conducted in accordance with the Declaration of Helsink,approved by the Ethics Committee of the School of Psychology, Guizhou Normal University (approval number: GZNUPSY.N.202211E[0015]). Before participation, all participants received a detailed explanation of the study purpose and procedures, and after fully understanding the study and confirming their eligibility, they signed informed consent forms and committed to truthful participation. All participants were aged 18 years or older.

Declaration

Competing Interest

The authors declare no competing interests.

Funding

Not applicable. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Clinical trial number

Not applicable. This study is an observational study and was not registered as a clinical trial.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the School of Psychology, Guizhou Normal University (approval number: GZNUPSY.N.202211E[0015]). All procedures involving human participants were conducted in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study. All participants were aged 18 years or older.

References

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). American Psychiatric Publishing.

Andersson, J. L. R., & Sotiropoulos, S. N. (2016). An integrated approach to correction for off-resonance effects and subject movement in diffusion MR imaging. NeuroImage, 125, 1063–1078.

Basser, P. J., Mattiello, J., & LeBihan, D. (1994). MR diffusion tensor spectroscopy and imaging. Biophysical Journal, 66(1), 259–267.

Beames, J. R., Uyttebroek, L., Edwards, C. J., et al. (2025). Using the experience sampling methodology to measure anhedonia and its correlates in mental health research: A systematic review. Clinical Psychology Review, 119, 102590.

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). Beck Depression Inventory–II. Psychological Corporation.

Carver, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/BAS scales. Journal of Personality and Social Psychology, 67(2), 319–333.

Chen, Z., Xu, Y. Y., & Ge, J. F. (2017). Research progress on anhedonia and its measurement methods. Chinese Pharmacology Bulletin, 33(6), 749–752.

Faul, F., Erdfelder, E., Lang, A. G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior Research Methods, 39(2), 175–191.

Feng, Y., Huang, X., Zhao, W., et al. (2024). Association among internalizing problems, white matter integrity, and social difficulties in children with autism spectrum disorder. Progress in Neuro-Psychopharmacology and Biological Psychiatry, 135, 111109.

Gray, J. A., & McNaughton, N. (2000). The neuropsychology of anxiety: An enquiry into the functions of the septo-hippocampal system (2nd ed.). Oxford University Press.

Hayes, A. F. (2013). Introduction to mediation, moderation, and conditional process analysis: A regression-based approach. Guilford Press.

Hundt, N. E., Nelson-Gray, R. O., Kimbrel, N. A., et al. (2007). The interaction of reinforcement sensitivity and life events in the prediction of anhedonic depression and mixed anxiety-depression symptoms. Personality and Individual Differences, 43(5), 1001–1012.

Kasch, K. L., Rottenberg, J., Arnow, B. A., & Gotlib, I. H. (2002). Behavioral activation and inhibition systems and the severity and course of depression. Journal of Abnormal Psychology, 111(4), 589–597.

Le Bihan, D., Mangin, J. F., Poupon, C., et al. (2001). Diffusion tensor imaging: Concepts and applications. Journal of Magnetic Resonance Imaging, 13(4), 534–546.

Liao, Y., Huang, X., Wu, Q., et al. (2013). Is depression a disconnection syndrome? Meta-analysis of diffusion tensor imaging studies in patients with MDD. Journal of Psychiatry & Neuroscience, 38(1), 49–56.

Lindqvist Bagge, A., et al. (2025). Early changes in reward sensitivity predict antidepressant response. Journal of Affective Disorders, 312, 45–52.

Mori, S., Oishi, K., Jiang, H., et al. (2008). Stereotaxic white matter atlas based on diffusion tensor imaging in an ICBM template. NeuroImage, 40(2), 570–582.

Preacher, K. J., & Hayes, A. F. (2008). Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. Behavior Research Methods, 40(3), 879–891.

Price, J. L., & Drevets, W. C. (2010). Neurocircuitry of mood disorders. Neuropsychopharmacology, 35(1), 192–216.

Russo, S. J., & Nestler, E. J. (2013). The brain reward circuitry in mood disorders. Nature Reviews Neuroscience, 14(9), 609–625.

Smith, S. M., Jenkinson, M., Johansen-Berg, H., et al. (2006). Tract-based spatial statistics: Voxelwise analysis of multi-subject diffusion data. NeuroImage, 31(4), 1487–1505.

Smith, S. M., Jenkinson, M., Woolrich, M. W., et al. (2004). Advances in functional and structural MR image analysis and implementation as FSL. NeuroImage, 23(Suppl 1), S208–S219.

Trew, J. L. (2011). Exploring the roles of approach and avoidance in depression: An integrative model. Clinical Psychology Review, 31(7), 1156–1168.

Van Velzen, L. S., Kelly, S., Isaev, D., et al. (2020). White matter disturbances in major depressive disorder: A coordinated analysis across 20 international cohorts in the ENIGMA MDD working group. Molecular Psychiatry, 25(7), 1511–1525.

Wen, M. C., Steffens, D. C., Chen, M. K., & Zainal, N. H. (2014). Diffusion tensor imaging studies in late-life depression: Systematic review and meta-analysis. International Journal of Geriatric Psychiatry, 29(12), 1173–1184.

Yatawara, C., Lee, D., Ng, K. P., et al. (2019). Mechanisms linking white matter lesions, tract integrity, and depression in Alzheimer disease. The American Journal of Geriatric Psychiatry, 27(9), 959–968.

Zhang, M., Hu, X., Jiao, J., et al. (2022). Brain white matter microstructure abnormalities in children with optimal outcome from autism: A four-year follow-up study. Scientific Reports, 12, 20151.

Li, Y. Z., Zhang, Y., Jiang, Y., et al. (2008). Reliability and validity of the Chinese version of the Behavioral Inhibition System and Behavioral Activation System Scale. Chinese Mental Health Journal, 22(8), 613–616.

Zhao, X., Lynch, J. G., Jr., & Chen, Q. (2010). Reconsidering Baron and Kenny: Myths and truths about mediation analysis. Journal of Consumer Research, *37*(2), 197–206. https://doi.org/10.1086/651257

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplementarydata.docx