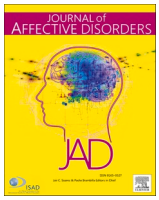
Journal of Affective Disorders 408 (2026) 120733



Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad



Review article



Examining the relationship between pre-treatment anhedonia and treatment outcomes in individuals with anxiety or depression: A systematic review

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ARTICLE INFO

Keywords:
Anhedonia
Depression
Anxiety
Treatment prediction

ABSTRACT

Anxiety and depressive disorders are the most common mental health conditions globally, contributing to substantial functional impairment across social and occupational domains. Despite the efficacy of first-line psychosocial (e.g., cognitive behavioral therapy) and biological (e.g., pharmacotherapy, transcranial magnetic stimulation) interventions, approximately half of patients fail to achieve clinically significant improvement. Identifying predictors of treatment outcomes is crucial for enhancing therapeutic efficacy and addressing limitations of current treatments. This systematic review aimed to synthesize the literature on the relationship between pre-treatment anhedonia and treatment response in individuals receiving psychotherapy, pharmacotherapy, or neuromodulation for anxiety or unipolar depressive disorders. Studies were included that assessed the clinical symptom of anhedonia using subjective measures and, secondarily, subjective, neural, or behavioral indicators of reward sensitivity. Of the 28 articles meeting criteria for this review, nine (32.1 %) indicated higher anhedonia/lower reward sensitivity was associated with worse treatment response. Four studies (14.3 %) found it was linked to better outcomes, eleven (39.3 %) reported mixed results, and four (14.3 %) found no significant relationships. Definitive conclusions cannot be drawn given inconsistent findings and because most studies involved secondary analyses that were often inadequately powered, and there was substantial heterogeneity in treatment types, study designs, measurement approaches, and outcomes. Prospective studies explicitly designed and powered to test anhedonia as a treatment predictor are needed. Future research should also clarify the direction, strength, and clinical relevance of the relationship between anhedonia – including its subcomponents and various units of analysis – and treatment outcomes in depression, anxiety, and related conditions.

1. Introduction

Anxiety and depressive disorders are the most prevalent mental health conditions worldwide and pose a major public health challenge (Baxter et al., 2013; Kessler et al., 2015; Stein et al., 2017; WHO, 2017). These conditions are associated with high rates of psychological and medical comorbidities, significant functional impairment and disability, increased health care utilization, and diminished quality of life (Friedrich, 2017; Greenberg et al., 2021; Liu et al., 2020; Rapaport et al., 2005; Szuhany and Simon, 2022). Despite considerable empirical support for the effectiveness of established first-line psychosocial (e.g., cognitive behavioral therapy; CBT) and pharmacological interventions for anxiety and depressive disorders, only around half of patients report clinically significant improvement following treatment (Arch et al., 2012; Bystritsky, 2006; Corey-Lisle et al., 2004; Cuijpers et al., 2021; Cuijpers et al., 2020; Loerinc et al., 2015). Response rates are comparable for more novel interventions, such as transcranial magnetic stimulation (TMS) for depression (Fitzgerald et al., 2016). Identifying predictors of poorer depression and anxiety treatment outcomes may help guide treatment selection and personalization and inform potential intervention targets that may increase efficacy. Anhedonia may be one such characteristic.

Anhedonia is characterized by a lack of interest in pursuing and/or diminished responsiveness to pleasurable or meaningful experiences. It

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https://doi.org/10.1016/j.jad.2025.120733
Received 21 July 2025; Received in revised form 17 September 2025; Accepted 16 November 2025
Available online 21 November 2025
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is thought to reflect underlying deficits in reward processing (i.e., hyposensitivity across various reward components; Craske et al., 2016, 2024; Taylor et al., 2022). Anhedonia has long been recognized as a core feature of depression (Clark and Watson, 1991). Indeed, loss of interest or pleasure is one of two key symptoms (at least one of which is required) for a DSM-5 diagnosis of major depressive disorder (MDD). Approximately 70 % of individuals with MDD experience anhedonia, which is linked to greater severity, more frequent and longer episodes, and more persistent course of depression (Serretti, 2023). Anhedonia also predicts suicidal ideation beyond overall depression severity (Ducasse et al., 2018). More recently, anhedonia has been recognized as a feature of some anxiety disorders, including social anxiety disorder (SAD; Craske et al., 2024; Kashdan, 2007; Taylor et al., 2022) and generalized anxiety disorder (GAD) (Prenoveau et al., 2010; Seager et al., 2019); however, the empirical base in anxiety disorders is smaller (cf. depression). Although high comorbidity between anxiety and depressive disorders may contribute to these findings, research suggests it does not fully explain the link between anxiety and anhedonia (e.g., in the case of SAD; Kashdan, 2007). To the extent that anhedonia may disrupt central processes that support recovery from depression and anxiety (e.g., by perpetuating avoidance despite rewards, exaggerating threat reactivity, inhibiting behavior change through positive reinforcement, or interfering with new learning), it is possible that higher pre-treatment anhedonia levels may impede successful treatment (Taylor et al., 2022).[1]

Anhedonia has primarily been assessed in clinical psychology research using global self-report measures capturing individuals' subjective capacity for hedonic experiences (Der-Avakian and Markou, 2012; Treadway and Zald, 2011). Although self-report instruments can identify conscious components of anhedonia (e.g., desire, enjoyment), they are limited in assessing unconscious processes or the mechanisms hypothesized to give rise to the subjective experience of anhedonia (Thomsen, 2015). Given the field's shift toward identifying and elucidating how specific symptoms map onto behavioral, physiological, and neurobiological processes, researchers have increasingly examined the reward-related processes thought to underlie anhedonia through the application of behavioral paradigms (e.g., probabilistic reward tasks) and neuroimaging techniques (e.g., electroencephalogram [EEG] and functional magnetic resonance imaging [fMRI]; Craske et al., 2024; Der-Avakian and Markou, 2012; Insel et al., 2010; Rizvi et al., 2016; Thomsen, 2015; Thomsen et al., 2015). Imaging studies have focused on both the brain's electrical responses to rewarding stimuli – captured through event-related potentials (ERPs) using EEG – and neural activation and connectivity patterns using fMRI, particularly within corticostriatal circuits involved in reward processing and modulated in part by dopaminergic signaling (e.g., ventromedial prefrontal cortex [vmPFC], anterior cingulate cortex [ACC], nucleus accumbens [NAcc], and dorsal striatum [caudate and putamen]; for reviews, see: Treadway and Zald, 2011; Der-Avakian and Markou, 2012; Rizvi et al., 2016). Neural and behavioral studies typically examine one or more reward processing stages: (1) anticipatory anhedonia/reward valuation—reduced pleasure in anticipation and impaired prediction of reward value or effort; (2) consummatory anhedonia/reward responsiveness—reduced pleasure during reward; and (3) reward learning—difficulty updating behavior based on expected versus actual outcomes.

Several studies have linked anhedonia and reduced reward sensitivity to worse outcomes in both psychotherapeutic and pharmacological treatments for depression and anxiety (e.g., Khazanov et al., 2020; McMakin et al., 2012; Papalini et al., 2019; Sequeira et al., 2021). However, no comprehensive reviews on this topic currently exist. Filling this gap in the literature may facilitate treatment personalization based on an individual's particular characteristics (e.g., levels of certain traits, such as anhedonia) and inform treatment targets with potential to improve outcomes (e.g., Insel, 2014). Consistent with the mental health field's growing emphasis on understanding psychopathology in terms of varying degrees of dysfunction within key psychological and biological systems, this review takes a transdiagnostic, symptoms-based approach (e.g., Craske et al., 2024; NIMH, n.d.; Rizvi et al., 2016). For comprehensiveness, it includes studies that measured anhedonia as a clinical symptom (clinician-rated or self-report measures), as well as subjective, neural, and behavioral markers of reward sensitivity deficits. Although the clinical symptom of anhedonia is not synonymous with blunted reward sensitivity, the two are highly related and are hypothesized to reflect underlying dysfunction in the reward system (e.g., Craske et al., 2024). A concurrent examination of both the clinical symptom and its underlying component processes, therefore, aims to provide a more holistic, multi-level understanding of how deficits in hedonic processing may impact treatment outcomes. This approach is consistent with contemporary research frameworks like the Research Domain Criteria (RDoC), which encourage investigation across different units of analysis (Insel et al., 2010). Given that reward-related brain circuits develop throughout childhood and accelerate during adolescence—and that most anhedonia research focuses on adults—this review includes studies across developmental stages, as anhedonia may relate differently to treatment outcomes in youth due to distinct neurocognitive, physical, and social factors (Gupta et al., 2024). Conclusions from the present review may help elucidate *why* some individuals with anxiety or depression do not benefit from treatment (e.g., due to elevated anhedonia), thus informing more effective and personalized treatment planning (e.g., that specifically targets anhedonia) prior to or alongside other interventions.

1.1. Present review

This review aims to critically assess and synthesize the available evidence examining pre-treatment anhedonia in relation to treatment response in individuals receiving psychosocial, pharmacological, or neuromodulation interventions for anxiety or unipolar depressive disorders.[2] The following questions will be addressed: 1) Are pre-treatment levels of anhedonia and its underlying reward sensitivity deficits related to anxiety or depression treatment outcomes, and do these relationships vary based on 2) how anhedonia/hedonic processing is measured (i.e., using self- or clinician-reported anhedonia symptom measures, or subjective, neural, or behavioral indicators of reward sensitivity), 3) the type of treatment administered, 4) diagnosis, or 5) developmental stage?

2. Methods

2.1. Search strategy and identification of studies

The present systematic review adhered to the PRISMA guidelines (Page et al., 2021). Searches were conducted in four electronic databases: PubMed, PsycInfo, Web of Science, and Embase. Search terms combined field searches for (1) anxiety or depressive disorders (2) empirical treatments (e.g., CBT, antidepressant, TMS), and (3)

[1] Although post-traumatic stress disorder (PTSD) shares symptom overlap with depression and anxiety, it is etiologically distinct - requiring exposure to a Criterion A trauma - and is characterized by discrete neurobiological mechanisms, with unique patterns of neural structure and circuitry alterations, genetic risk, neurocognitive functioning deficits, and hypothalamic-pituitary-adrenal axis dysregulation (Bromis et al., 2018; Daskalakis et al., 2024; Koopowitz et al., 2021; Stupin et al., 2021). Thus, PTSD was not included in this review.

[2] Only unipolar depressive disorders were included in the present review given that, unlike research on MDD, findings in bipolar disorder have not consistently demonstrated reduced reward-related activity in the striatum or other brain regions. While additional studies are needed, current evidence suggests that the underlying mechanisms of anhedonia may differ between unipolar and bipolar mood disorders (Whitton and Pizzagalli, 2022).

anhedonia or reward processing. No restrictions were imposed on publication dates to ensure a more comprehensive review of the available literature. Gray literature and unpublished studies were excluded to maintain a focus on peer-reviewed sources and uphold methodological rigor and consistency. Full search terms are listed below:

("anxiety" OR "anxious" OR "anxiety disorder" OR "panic disorder" OR "agoraphobia" OR "specific phobia" OR "generalized anxiety disorder" OR "GAD" OR "social anxiety disorder" OR "SAD" OR "social phobia" OR "depression" OR "depress*" OR "depressive disorder" OR "major depressive disorder" OR "MDD" OR "major depression" OR "persistent depressive disorder" OR "dysthymia" OR "dysthymic disorder") AND ("therapy" OR "psychotherapy" OR "treatment" OR "intervention" OR "cognitive behavioral therapy" OR "CBT" OR "psychosocial treatment" OR "psychosocial intervention" OR "mindfulness-based stress reduction" OR "MBSR" OR "acceptance and commitment therapy" OR "ACT" OR "exposure therapy" OR "cognitive processing therapy" OR "antidepressant" OR "medication" OR "pharmacotherapy" OR "medication management" OR "selective serotonin reuptake inhibitor*" OR "SSRI" OR "monoamine oxidase inhibitor" OR "MAOI" OR "selective norepinephrine reuptake inhibitor" OR "SNRI" OR "neuromodulation" OR "electroconvulsive therapy" OR "ECT" OR "ketamine" OR "transcranial magnetic stimulation" OR "TMS") AND ("anhedonia" OR "inability to experience pleasure" OR "loss of interest" OR "diminished pleasure" OR "blunted positive*" OR "low positive*" OR "pleasure deficit" OR "lack of interest" OR "reward*" OR "reward respons*" OR "neural reactivity to reward" OR "reward reactivity" OR "reward learning" OR "reward processing" OR "pleasure respons*" OR "positive affect" OR "positive emotion*" OR "approach*" OR "approach motivation" OR "approach temperament")

Two independent evaluators screened the titles and abstracts of publications retrieved from the searches. Duplicate citations were first removed using the reference management software EndNote. The remaining titles and abstracts were then uploaded into Rayyan, a web-based tool that facilitates systematic review screening (Ouzzani et al., 2016). Articles were flagged for full-text review if their titles or abstracts addressed the relationship between pre-treatment anhedonia levels (assessed via self-report or clinician-administered measures, or using neural or behavioral indicators of anhedonia) and treatment outcomes in human samples with anxiety or depression, or if they lacked sufficient information to determine relevance. Studies were excluded at this stage if titles or abstracts indicated they were non-empirical (e.g., reviews) or did not implement a treatment or intervention. Full text articles marked for review were retrieved and evaluated for accordance with the pre-established inclusion and exclusion criteria (provided below). Following Wohlin's (2014) guidelines, backward (i.e., examining references cited by the selected articles) and forward snowballing (i.e., identifying articles that cite the selected studies) were used to ensure comprehensive coverage of the literature. The first author conducted the initial search in November 2024, followed by a second search by the second author in February 2025.

2.2. Inclusion and exclusion criteria

Full texts of articles were reviewed to determine if they met the following inclusion criteria: (1) peer-reviewed empirical studies in English; (2) samples included individuals with a principal or co-principal diagnosis of at least one anxiety disorder (i.e., GAD, SAD, panic disorder (PD), agoraphobia, separation anxiety disorder, or specific phobia) or unipolar depressive disorder (i.e., MDD or persistent depressive disorder [PDD]; formerly dysthymic disorder) as determined by clinical diagnostic interview; (3) involved an evidence-based psychotherapeutic, pharmacological, or neuromodulation intervention (i.e., one that has demonstrated efficacy based on randomized controlled clinical trials [RCTs] or meta-analyses; American Psychological Association, 2005; Katz, 2004; Wampold et al., 2011; Westen et al., 2004); (4) included a pre-treatment measure of the clinical symptoms of anhedonia (self-report, clinician-administered, or parent-rated instrument), or a measure of subject, neural, or behavioral reward sensitivity indexing hedonic processing; (5) included pre- and post-treatment scores or a change index for one or more treatment outcomes (i.e., anxiety or depression symptom severity or remission status); (6) examined pre-treatment anhedonia levels as a predictor of treatment outcome(s). Studies were included only if all these criteria were met.

Exclusion criteria were: (1) studies that did not include pre-treatment anhedonia or reward sensitivity as a *predictor* of treatment outcomes; (2) studies that did not report on subacute or long-term treatment response outcomes; (3) samples that did not include individuals with a principal or co-principal diagnoses of at least one anxiety or unipolar depressive disorder; (4) studies that did not administer a psychotherapeutic, pharmacological, or neuromodulation intervention; (5) studies published in languages other than English; and (6) non-empirical studies, such as case studies, book chapters, theoretical papers, narrative or meta-analytic reviews, qualitative studies, conference abstracts, clinical guidelines, or study protocols.

To maintain conceptual specificity in the present review, studies were excluded that measured state or trait positive affect more generally (e.g., PANAS). Broad self-report measures of positive affect that combine high and low arousal emotions without distinguishing the core motivational (interest) and affective (pleasure) deficits of anhedonia may lack the specificity needed to capture this construct accurately. Consequently, including these measures may misrepresent general positive mood fluctuations as the clinical symptom of anhedonia – a condition that specifically includes motivational (reduced ability to experience interest) and affective (reduced ability to experience pleasure) components (Craske et al., 2024; Taylor et al., 2022), potentially leading to less accurate conclusions. We therefore opted to exclude from the current review studies that included only broad measures of positive emotional states (e.g., PANAS, which includes items such as: strong, alert, relaxed, calm, serene, confident) and include those with the more narrowly defined concepts of anhedonia and reward sensitivity. Although this approach may have reduced the breadth of included studies and somewhat limited generalizability, we prioritized conceptual precision to ensure more accurate and specific conclusions could be drawn about anhedonia's potential impact on treatment outcomes.

2.3. Study selection and data extraction

Prior to conducting the literature search and review, a structured extraction table was created. The table captured the following information: (a) bibliographic details (title, authors, year, country); (b) sample characteristics (e.g., anxiety or depression diagnosis, age, sex/gender, race/ethnicity, sample size); (c) study methodology (e.g., recruitment and sampling procedures, study design); (d) intervention details (e.g., type of treatment, dosage and frequency, intervention format); (e) assessment tools used for anhedonia or reward sensitivity; and (f) measurement tools used to assess treatment outcomes. All studies that met inclusion criteria were systematically coded, with relevant data entered into the extraction table. Extracted information was then reviewed to ensure accuracy and completeness. The PRISMA flow diagram presented in Fig. 1 outlines the process of evaluation for study inclusion. Table 1 summarizes study and sample characteristics; Table 2 details study designs and findings.

2.4. Study rigor

The Quality In Prognosis Studies (QUIPS) tool (Hayden et al., 2013) was used to assess the risk of bias for the included studies across six domains: (1) study participation, (2) study attrition, (3) prognostic factor measurement, (4) outcome measurement, (5) study confounding, and (6) statistical analysis and reporting. Each domain is rated as low, moderate, or high risk of bias. This tool was developed to evaluate risk of bias in prognostic factor studies and is applicable to both randomized

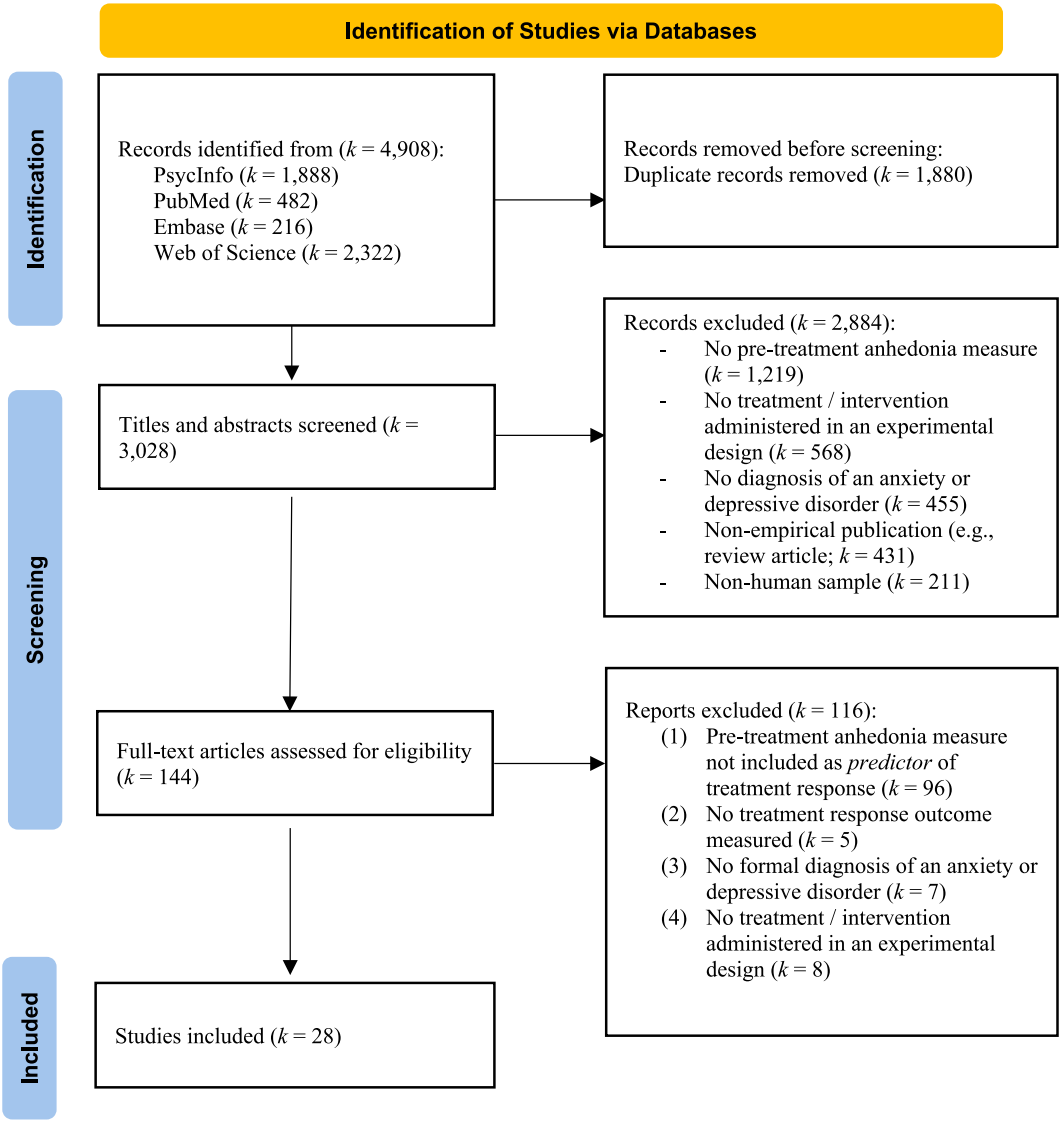

Fig. 1. Flowchart of included studies.

and non-randomized designs (Hayden et al., 2013). Each domain includes specific criteria to evaluate potential sources of bias, including adequacy of sample selection, completeness of follow-up, validity and reliability of prognostic factor and outcome measurements, control for important confounders, and appropriateness and transparency of the statistical analyses performed.

3. Results

3.1. Screening and selection of studies

A total of 28 articles met inclusion criteria for the present review. Study selection procedures are outlined in Fig. 1. Several included studies were derived from the same or partially overlapping samples. Specifically, Ang et al. (2020), Giles et al. (2023), and Greenberg et al. (2020) all utilized data from the EMBARC trial, while Rezaei et al. (2021, 2023) drew on partially overlapping participant samples. These studies were retained as they examined distinct outcomes or employed different methodologies, contributing unique information to the review.

3.2. Sample characteristics

Sample characteristics for each study are summarized in Table 1; full details are available in the Supplemental Materials.

3.3. Study design characteristics

Tables 1 and 2 summarize study design characteristics. A detailed description of treatment types, dosages, anhedonia assessments, and outcome measures is available in the Supplemental Materials.

3.4. Study rigor

Risk of bias ratings for each included study are presented in Table 3. The most common sources of potential bias were insufficient reporting of attrition, incomplete control for relevant confounding variables, and, in a limited number of studies, the use of individual outcome measure items as predictors (although this was generally mitigated by including other subcomponents of the measure as covariates). Overall, the risk of bias assessment indicated that the included studies demonstrated acceptable rigor.

A small number of included studies were derived from the partially

Table 1
Descriptive characteristics of included studies.

Study	Country	Principal or co-principal diagnosis	Adults vs. children	Type of treatment	Sample size *(N)*	Age[a] *M (SD)*	Age range (years)	Sex (% female)	Race/ethnicity (% White)	Recruitment setting
Allen et al., 2019	Canada	MDD	Adults	Medication (escitalopram)	N = 210	35.22 (12.62)	18–61	63%	NP	NP
Alsayednasser et al., 2022	United Kingdom	MDD	Adults	Psychotherapy (BA or CBT)	N = 440 (n=221 BA; n=219 CBT)	43.48 (14.06)	18+	65.9%	91.1%	Outpatient clinics
Ang et al., 2020	USA	MDD	Adults	Medication (sertraline or bupropion)	N = 87	39.9 (13.8)	18–65	64.4%	NP	Outpatient clinics
Barch et al., 2020	USA	MDD	Children	Psychotherapy (PCIT-ED)	RewP: N = 60; LPP: N = 44	RewP: 5.46 (0.84) LPP: 5.64 (0.81)	4–6.9	RewP: 35%; LPP: 36%	22%	Outpatient clinics & community
Brandt et al., 2021	Denmark	MDD	Adults	Medication (escitalopram)	N = 90	27.1 (8.43)	NP	71.1%	NP	Outpatient clinics
Burkhouse et al., 2016	USA	Anxiety disorder (SAD, PD, GAD) &/or MDD	Adults	Psychotherapy (CBT)	N = 52	23.94 (6.54)	18–47	76.9%	61.5%	Outpatient clinics
Burkhouse et al., 2018	USA	Anxiety disorder (GAD, SAD, PD, PTSD) &/or Depressive Disorder (MDD, PDD)	Adults	Medication (various SSRIs) or Psychotherapy (CBT)	N = 63 (n=34 CBT; n=29 SSRI)	28.70 (9.55)	NP	74.6%	68.3%	Outpatient clinics and community
Carl et al., 2016	USA	MDD	Adults	Psychotherapy (BA)	N = 33	33.2 (6.5)	21–45	66.7%	NP	Outpatient clinics & community
Dickey et al., 2023	USA	MDD	Adolescents	Psychotherapy (group CBT)	N = 70	15.81 (1.46)	14–18	65.7%	87.1%	Outpatient clinics & community
Dunlop et al., 2023	Canada	MDD	Adults	Medication (escitalopram)	N = 87	33.61 (11.46)	NP	66.7%	NP	Outpatient clinics
Forbes et al., 2010	USA	MDD	Adolescents	Psychotherapy (CBT) with or without Medication (citalopram or fluoxetine)	N = 13	12.9 (2.3)	10–16	69.2%	92.3%	Outpatient clinics
Giles et al., 2023	USA	MDD	Adults	Medication (sertraline)	N = 195	37.2 (13.1)	18–65	66.2%	63.6%	Outpatient clinics and community
Greenberg et al., 2020	USA	MDD	Adults	Medication (sertraline)	N = 110	36.84 (13.17)	NP	73%	65%	Outpatient clinics & community
Hou et al., 2018	China	MDD	Adults	Medication (various SSRIs, SNRIs, &/or mirtazapine)	N = 81	48.0 (14.01)	NP	72.8%	NP	Outpatient clinics
Khazanov et al., 2020	USA	MDD	Adults	Medication (unspecified antidepressants) or Medication + Psychotherapy (CT)	N = 433	43.36 (13.03)	NP	58%	NP	Outpatient clinics
Krepel et al., 2020	Netherlands	MDD	Adults	rTMS	N = 196	43.62 (NP)	18–78	50.5%	NP	Outpatient clinics & Community
Kujawa et al., 2019	USA	GAD or SAD	Children & Adolescents	Medication (sertraline) or Psychotherapy (CBT)	N = 27	13.07 (4.05)	7–19	40.7%	25.9%	Outpatient clinics & Community
McMakin et al., 2012	USA	MDD	Adolescents	Medication (various SSRIs or venlafaxine) or Medication + Psychotherapy (CBT)	N = 334	16 (1.6)	12–18	70%	84%	Outpatient clinic
Norris et al., 2021	USA	Anxiety Disorder (GAD, SAD, Separation Anxiety, SAD, PD, agoraphobia, illness anxiety)	Children & Adolescents	Psychotherapy (CBT)	N = 136	12.18 (3.12)	7–17	51.5%	79%	Outpatient clinic
Papalini et al., 2019	Netherlands	Specific Phobia	Adults	Psychotherapy (group exposure therapy or PMR)	N = 44	20.5 (2.4)	16–25	90.9%	NP	Outpatient clinics & Community
Rezaei et al., 2021	Iran	MDD	Adults	tDCS	N = 116	40.52 (11.56)	NP	65.5%	NP	Outpatient clinics
Rezaei et al., 2023	Iran	MDD	Adults	tDCS	N = 182	49.92 (NP)	19–69	56.6%	NP	Outpatient clinics
Sequeira et al., 2021	USA	Anxiety Disorder (GAD, SAD, Separation Anxiety)	Children & Adolescents	Psychotherapy (CBT or CCT)	N = 72	11.01 (1.52)	9–14	52.8%	NP	Outpatient clinics and community
Sewart et al., 2019	USA	SAD	Adults	Psychotherapy (CBT or ACT)	N = 80	28.3 (6.7)	18–60	50%	46.8%	Outpatient clinics and community
Straub et al., 2015	Germany	MDD	Adolescents	Psychotherapy (group CBT)	N = 18	16.47 (1.36)	13–18	NP	77.3%	Outpatient clinic
Walsh et al., 2017	USA	MDD	Adults	Psychotherapy (BA)	N = 33	33 (7.1)	21–45	66.7%	NP	Outpatient clinic
Webb et al., 2021	USA	MDD	Adolescents	Psychotherapy (CBT)	N = 36	28.3 (6.7)	13–18	100%	72.4%	Community
Whitton et al., 2020	USA	MDD	Adults	Medication (pramipexole)	N = 25	26.5 (6.3)	NP	40%	52%	Outpatient clinics

Note. A small number of studies involved partially overlapping datasets: (1) Ang et al. (2020), Giles et al. (2023), and Greenberg et al. (2020) – highlighted in light blue; (2) Rezaei et al. (2021, 2023) – highlighted in light green. MDD = major depressive disorder; SAD = social anxiety disorder; PD = panic disorder; GAD = generalized anxiety disorder; PTSD = post-traumatic stress disorder; PDD = persistent depressive disorder; rTMS = repetitive transcranial magnetic stimulation; tDCS = transcranial direct current stimulation; NP = not provided; RewP = reward positivity; LPP = late positive potential; BA = behavioral activation; CBT = cognitive behavioral therapy; SSRI = selective serotonin reuptake inhibitor; BA = behavioral activation; CBT = cognitive behavioral therapy; PCIT-ED = parent-child interaction therapy – emotion disorders; CT = cognitive therapy; PMR = progressive muscle relaxation; CCT = child-centered therapy; ACT = acceptance and commitment therapy.

overlapping samples, which may introduce bias to this narrative synthesis, as findings from shared participants could be overrepresented. To enhance transparency, studies with overlapping data are highlighted in Tables 1–3 and identified throughout the review.

3.5. Findings from included studies

3.5.1. Are pre-treatment anhedonia or underlying reward sensitivity levels related to treatment outcomes?

Table 2 presents the results for each study. Of the 28 studies included in this review, 46.4 % ($k = 13$) demonstrated that any/all pre-treatment anhedonia or reward sensitivity measures were significantly related to treatment outcomes, with considerable variability in the direction and magnitude of effects (from small to large; several studies only reported unstandardized estimates). Nine of these studies indicated that higher pre-treatment anhedonia/lower reward sensitivity was related to poorer treatment outcomes (Alsayednasser et al., 2022; Ang et al., 2020; Greenberg et al., 2020; Khazanov et al., 2020; Krepel et al., 2020; McMakin et al., 2012; Norris et al., 2021; Sequeira et al., 2021; Walsh et al., 2017), whereas the remaining four studies suggested higher pre-treatment anhedonia/lower reward sensitivity was related to superior treatment outcomes (Burkhouse et al., 2016; Hou et al., 2018; Rezaei et al., 2021, 2023).[3] Eleven of the 28 studies (39.3 %) reported mixed findings on the relationship between pre-treatment anhedonia/reward sensitivity and treatment outcomes, with some measures within the same study showing significant associations, while others did not. Specifically, higher pre-treatment anhedonia/lower reward sensitivity predicted worse outcomes on *at least one* measure in six studies (Barch et al., 2020; Dickey et al., 2023; Dunlop et al., 2020; Straub et al., 2015; Webb et al., 2021; Whitton et al., 2020); the opposite pattern was found in 2 studies (i.e., higher pre-treatment anhedonia/lower reward sensitivity predicted better outcomes; Burkhouse et al., 2018; Kujawa et al., 2019); and three studies reported associations in *both* directions (Carl et al., 2016; Forbes et al., 2010; Papalini et al., 2019). The remaining four studies (14.3 %) found that pre-treatment anhedonia and/or reward sensitivity indicators were not significantly associated with treatment response (effects sizes were generally small or not reported; Allen et al., 2019; Brandt et al., 2021; Giles et al., 2023; Sewart et al., 2019).

3.5.1.1. Summary of findings by direction. Over half of the studies (53.6 %, $k = 15$) reported higher pre-treatment anhedonia/lower reward sensitivity predicted worse treatment outcomes on *at least* one measure. Six studies found the opposite pattern. Three studies reported associations in both directions, and four found no significant associations. Sample sizes (ranging from $N = 13$ to 440) and effect sizes (small to large) varied widely, with no consistent relationships emerging between these factors and patterns of findings (e.g., direction or significance).

3.5.2. Do findings vary based on how anhedonia or underlying hedonic processing deficits are measured?

3.5.2.1. Subjective symptom measures of anhedonia. Four of the 9 studies using self-reported anhedonia symptom measures (44.4 %) and the only study using a clinician-administered measure (McMakin et al., 2012) found that higher pre-treatment anhedonia was associated with poorer treatment outcomes (Alsayednasser et al., 2022; Dunlop et al., 2020; Khazanov et al., 2020; Krepel et al., 2020). In a study of BA or CBT for MDD, Alsayednasser et al. (2022) revealed individuals with higher pre-treatment anhedonia on the SHAPS reported smaller reductions in depression symptoms (irrespective of treatment group; small-medium effect) and fewer depression-free days following BA but not CBT (medium-large effect). Dunlop et al. (2020) showed that lower pre-treatment anhedonia on the DARS predicted greater depression improvement in individuals with MDD after 8 weeks of escitalopram (small-medium effect). In a study of adults with MDD receiving either antidepressants alone or combined with cognitive therapy, higher pre-treatment anhedonia on the MASQ predicted longer time to both remission and recovery over follow-up (small-medium effect; Khazanov et al., 2020). Similarly, in a trial of antidepressants with or without adjunctive CBT for treatment-resistant adolescent MDD, McMakin et al. (2012) found that higher clinician-rated anhedonia was the only pre-treatment symptom dimension on the CDRS-R to predict longer time to remission and fewer depression-free days (small-medium effect). Finally, Krepel et al. (2020) found that non-responders (cf. responders) to rTMS for MDD reported higher pre-treatment anhedonia (BDI-II loss of pleasure/interest items) with a small-medium effect in the discovery sample and large effect in the replication sample, and that pre-treatment anhedonia was negatively correlated with symptom improvement (small effect in both samples).

Three of the studies using self-report anhedonia measures (33.3 %) found that higher pre-treatment levels of this trait were associated with superior treatment responses (Carl et al., 2016; Rezaei et al., 2021, 2023). Carl et al. (2016) found that in a behavioral activation trial for adults with MDD, pre-treatment self-reported anhedonia (BDI-II loss of pleasure/interest items) moderated symptom change over time, accounting for substantial between-person variability in treatment response (large effect), though this result should be interpreted cautiously given the high risk of bias due to confounding (see Table 3; Carl et al., 2016). Two studies by Rezaei et al. (2021, 2023) using partially overlapping transcranial Direct Current Stimulation (tDCS) treatment datasets in adults with MDD indicated that responders (cf. non-responders) endorsed higher pre-treatment anhedonia (on both the SHAPS [small-medium effect] and BDI-II loss of pleasure/interest items [large effects]), with anhedonia emerging as the only significant predictor of tDCS response accounting for related factors (e.g., rumination).

The remaining studies using self-report anhedonia symptom measures (including the SHAPS and a combined MASQ-PANAS scale) found no significant relationship between pre-treatment anhedonia and treatment outcomes ($k = 2$; 22.2 %; Papalini et al., 2019; Sewart et al., 2019). Effect sizes were small or not reported.

3.5.2.2. Subjective measures of reward sensitivity. Three studies (Allen et al., 2019; Dickey et al., 2023; Norris et al., 2021) assessed hedonic processing using self-reported sensitivity of the behavioral approach system (BAS), a motivational system that regulates reward-seeking behavior and pursuit of desirable or pleasurable outcomes (Carver and White, 1994). Of these studies, two (66.7 %) found no significant relationship between pre-treatment subjective reward sensitivity and treatment outcomes (Allen et al., 2019; Dickey et al., 2023; effect sizes were small or not reported). The third study (33.3 %) found that higher pre-treatment reward sensitivity predicted more favorable treatment outcomes. Specifically, Norris et al. (2021) found that among youth with anxiety disorders receiving CBT, higher pre-treatment reward responsiveness (BIS/BAS-C) predicted lower post-treatment anxiety and depression severity (small-medium effect), improved global functioning (medium effect), and greater likelihood treatment responder status (large effect).

3.5.2.3. Neural markers of hedonic processing. Of the reward processing phases (anticipation, responsiveness, learning), most EEG and fMRI studies focused on the reward *response* phase. These generally found that greater reward responsiveness (i.e., lower anhedonia) predicted better treatment outcomes (small to large effects; Carl et al., 2016; Sequeira et al., 2021; Straub et al., 2015) or showed mixed findings with partial support (Ang et al., 2020; Barch et al., 2020; Dunlop et al., 2020; Forbes

[3] Note that Ang et al. (2020) and Greenberg et al. (2020) are both drawn from the EMBARC trial, and Rezaei et al. (2021, 2023) include partially overlapping participant samples.

Table 2
Design and findings of included studies.

Study	Sample	Treatment	Dose (# sessions, daily medication dosage, or neuromodulation specifications)	Duration (weeks)	Anhedonia/reward measure(s)	Outcome measure(s)	Results	Summary of findings
Allen et al., 2019	Adults with MDD *N* = 210	Escitalopram	10–20 mg	8	**BIS/BAS scales: BAS total** & **reward responsiveness** (RR), **drive** (DR), & **fun-seeking** (FS) **subscale scores**	Post-treatment depression symptoms on **MADRS** & **QIDS-SR** (controlling for pre-treatment symptom levels)	**Approach:** Multiple regressions examining whether pre-treatment BAS total & subscale scores predicted week 8 depression. Controlled for age, sex, & pre-treatment scores on outcome measures for each model. Applied Bonferroni correction of *alpha* = 0.0063 for multiple comparisons. **Predictor = BAS total:** **MADRS:** β = 0.13, SE = 0.07, p = .06 **QIDS-SR:** β = 0.11, SE = 0.07, p = .09 **Predictor = BAS RR:** **MADRS:** β = 0.10, SE = 0.34, p = .78 **QIDS-SR:** β = 0.06, SE = 0.17, p = .71 **Predictor = BAS DR:** **MADRS:** β = −0.14, SE = 0.35, p = .69 **QIDS-SR:** β = 0.01, SE = 0.17, p = .95 **Predictor = BAS FS:** **MADRS:** β = 0.66, SE = 0.34, p = .049 **QIDS-SR:** β = 0.20, SE = 0.16, p = .21	Pre-treatment BAS scores (total & subscales) were not significantly associated with post-treatment depression symptoms. Pre-treatment BAS fun-seeking was associated with attenuated depression on the MADRS, but did not survive the adjusted alpha level for Bonferroni correction.
Alsayednasser et al., 2022	Adults with MDD *N* = 440	Behavioral Activation (*n* = 221) or CBT (*n* = 219)	≤ 20 sessions (Average BA = 11.5, average CBT = 12.5)	≤ 26	Self-reported anhedonia on **SHAPS**	Change in depression symptoms ("depression repair") on **PHQ-9** assessed at intake, 6 months, 12 months, and 18 months, and number of **depression-free days** across follow-up period (measure of sustained benefit from treatment)	**Approach:** Moderation analyses using Generalized Estimating Equations (GEEs). Controlled for pre-treatment depression on PHQ-9. **PHQ-9:** A significant interaction between pre-treatment SHAPS and time indicated reductions in PHQ-9 were less marked in those with more severe baseline SHAPS (B = −0.08, SE = 0.02, 95% CI = −0.13 to −0.04, $Wald\ \chi^2$ = 13.32, p < .001). This moderation effect did not vary as a function of BA vs. CBT treatment group (non-significant 3-way interaction: B = 0.01, SE = 0.01, 95% CI = −0.01 to 0.02, $Wald\ \chi^2$ = 0.27, p = .61) **Depression-free days:** In the **BA group**, individuals with greater pre-treatment SHAPS severity experienced fewer cumulative depression-free days during the follow-up period (B = −6.87, SE = 1.97, 95% CI = −10.77 to −2.98, t = 3.50, p < .001). In the **CBT group**, there was no significant association between pre-treatment SHAPS and depression-free days (B = 1.73, SE = 2.18, 95% CI = −2.59 to 6.06, t < 1, p > .05).	Individuals with higher pre-treatment anhedonia (on SHAPS) showed a smaller reduction in depression symptoms over time, irrespective of treatment group (BA vs. CBT). Individuals with higher pre-treatment anhedonia (on SHAPS) experienced fewer depression-free days following treatment in the BA group, but not the CBT group.
Ang et al., 2020	Adults with MDD **Stage 1:** *N* = 296 with MDD **Stage 2:** *N* = 125 (*n* = 87 with MDD vs. *n* = 38 HC)	**Stage 1:** Sertraline (*n* = 146; data could be analyzed for 116) or Placebo (*n* = 150) **Stage 2:** Sertraline (*n* = 49) or Bupropion (*n* = 38); no interventions for HC	Sertraline: ≤ 200 mg; Bupropion: ≤ 450 mg	**Stage 1:** 8 **Stage 2:** 8: Responders continued with another 8-week course of same intervention; non-responders crossed over to 8 weeks of sertraline or bupropion, respectively	**Behavioral reward sensitivity** (immediate behavioral impact of reward - analyzed in terms of response bias or the preference for a more frequently rewarded stimulus) **& neural resting state functional connectivity (RSFC)** (fMRI; connectivity between bilateral NACC & rACC)	Binary depression treatment response on **HDRS;** considered treatment responders if completed at least 4 weeks of treatment + showed HDRS decrease ≥ 50%	**Approach:** Using Stage 2 data, 2-way treatment (sertraline vs. bupropion) × response (responder vs. non-responder on HDRS) ANOVA assessing differences based on pre-treatment behavioral reward sensitivity & RSFC, respectively. Note that responders did not differ from non-responders on HDRS at baseline. **Reward Sensitivity:** $F_{1,83}$ = 7.12, p < .05, η_p^2 = .079, BF_{10} = 5.15 **Reward Sensitivity Follow-up Tests:** ***Bupropion:*** p < .05, d = 0.87, BF_{10} = 7.48 ***Sertraline:*** p > .05, d = 0.29, BF_{10} = 0.36 **Comparisons to HC:** Reward sensitivity for bupropion responders was similar to HC (t_{52} =	Higher pre-treatment reward sensitivity and greater resting-state functional connectivity between the bilateral NAcc and the rostral ACC were associated with better response to bupropion, but not to sertraline.

					activation in the win vs. loss contrast during MID)		Pre-treatment activation in the sgACC was negatively correlated with pre-to-follow-up change in BDI-II scores (left sgACC: $r = -0.56$, $p = .02$, right sgACC: $r = -0.59$, $p = .01$). There were no significant associations between pre-treatment sgACC activation and change in CDRS-R scores (p's > .05).	reduction in response to CBT group on the BDI-II, but not the CDRS-R.
Walsh et al., 2017	Adults with MDD $N = 33$	Behavioral Activation Treatment for Depression	≤ 15 sessions	≤ 15	**Neural reward sensitivity** (fMRI; neural connectivity during MID reward trials, with specific focus on changes in frontostriatal connectivity between task runs)	Change in depression symptoms on **BDI-II** across treatment	**Approach**: Hierarchical linear models During reward anticipation, greater connectivity between the left caudate seed and the right paracingulate gyrus (BA24/32) was related to greater reductions in depression symptoms (BDI) over the course of treatment ($\gamma_{Connectivity*Treatment\ Week} = -0.39$, SE = 0.19, $t(186) = -2.02$, $p = .045$). Pseudo-R^2 calculations showed this connectivity metric accounted for ~7.6% of the between-person variance in the within-person effect of treatment week (time) on BDI scores. In the anticipation phase, less connectivity attenuation between the right putamen seed and right OFC/temporal pole (BA47) was related to greater reductions in depression symptoms (BDI) during treatment ($\gamma_{Connectivity\ Difference\ *Treatment\ Week} = 0.40$, SE = 0.14, $t(185) = 2.80$, $p < .0001$). These differences accounted for 16% of the between-person variance in change in BDI scores during treatment. During the reward outcome phase, greater connectivity attenuation between the left NAcc seed and paracingulate	Higher pre-treatment frontostriatal functional connectivity during reward processing on the MID task predicted better response to behavioral activation treatment.
							gyrus (BA 32) was related to larger declines in depression symptoms (BDI) during treatment ($\gamma_{Connectivity\ Difference\ *Treatment\ Week} = -0.40$, SE = 0.16, $t(185) = -2.51$, $p = .0013$). These differences accounted for 4.7% of the between-person variance in change in BDI scores during treatment. During reward anticipation, greater connectivity attenuation between the right frontal medial cortex seed and paracingulate gyrus (BA 32) predicted larger reductions in depression symptoms (BDI) during treatment ($\gamma_{Connectivity\ Difference\ *Treatment\ Week} = -0.36$, SE = 0.14, $t(185) = 2.58$, $p = .010$). These differences accounted for 11% of the between-person variance in change in BDI scores during treatment.	
Webb et al., 2021	Female Adolescents with MDD $N = 36$	CBT	12 sessions	12	**Neural reward sensitivity** (EEG; **RewP** & **LPP** during monetary reward gambling task; evaluated global connectivity (i.e., across task runs) and connectivity attenuation (i.e., reductions in connectivity from run 1 to run 2)	Change in depression symptoms on **BDI-II** across treatment	**Approach**: Multilevel modeling Adolescents with a greater pre-treatment LPP responses to wins showed larger reductions in depressive symptoms (i.e., the LPP_{wins} × time interaction was significant: ($B = 0.81$, $t_{27.6} = 2.38$, $p = .024$). . Pre-treatment RewP did not predict change in depression symptoms (i.e., the $RewP_{wins}$ × time & $RewP_{loss}$ × time interactions were non-significant; p's > .61).	During the pre-treatment monetary reward task, higher *sustained* (LPP) - but not *initial* (RewP) - reward responsiveness predicted greater reduction in depression symptoms.
Whitton et al., 2020	Adults with MDD ($N = 25$)	Pramipexole	0.5 mg/day, titrated to maximum of 2.5 mg/day	6	**Behavioral reward sensitivity** (probabilistic reward task [PRT], modeled reward learning and reward sensitivity)	Post-treatment depression symptoms and rate of change across treatment on **HDRS,** and global illness severity on clinician-rated **CGI-**	**Approach:** Multiple regressions to assess whether pre-treatment reward processing on probabilistic reward task (reward learning, sensitivity, and prediction error signals) predicted post-treatment scores on the HDRS (controlling for baseline scores) and	Behavioral reward sensitivity and learning on the PRT did not predict depression symptom reduction or global illness severity.

					Neural reward sensitivity (fMRI; ventral striatum activation during the reinforcement learning task, modeled prediction error signaling during gain and loss trials)	**Change Scale.**	CGI-C. Also tested moderating effects of behavioral and neural reward sensitivity (i.e., PRT Reward Response × Week interaction) on symptom improvement and global illness severity across the 6 weeks in treatment. **Behavioral Predictors:** Pre-treatment PRT performance (reward learning or sensitivity) did not significantly predict post-treatment HDRS or CGI-C scores ($p > .10$). There were no significant Reward Learning × Week nor Reward Sensitivity × Week interactions in predicting HDRS or CGI-C improvement across time in treatment (p's > .10). **Neural Predictors:** Pre-treatment ventral striatal gain or loss prediction error signals on the PRT did not predict post-treatment scores on the HDRS ($p > .10$). The Gain Prediction Error × Week interaction was marginal/non-significant in the model predicting HDRS scores ($B = -0.32$, 95% CI = −0.68 to 0.04, $p = 0.08$). A significant Gain Prediction Error × Week interaction in the model predicting CGI scores emerged: stronger gain prediction error signals predicted larger improvements in global illness severity across treatment ($B = -0.08$, 95% CI = −0.13 to −0.02, $p = 0.004$).	Neural (ventral striatal) reward-related activation on the PRT predicted greater improvements in global illness severity (but not self-reported depression symptoms) across the course of treatment.

							0.82, $p > .05$, $d = 0.26$, $BF_{10} = 0.39$), but reward sensitivity for non-responders was lower than HC ($t_{58} = -2.14$, $p < .05$, $d = 0.59$, $BF_{10} = 1.75$) **RSFC:** Whole brain analyses revealed significant interaction between medication type & RSFC between NACC and rACC: peak at x = −6, y = 30, z = 12, maximum $t = 5.76$, $k = 170$ voxels, clustering threshold $p < .001$, false discover rate $p < .05$ **RSFC Follow-up Tests:** ***Bupropion:*** $t_{34} = 4.48$, $p < .01$, $d = 1.21$, $BF_{10} > 100$ ***Sertraline:*** $T_{46} = 4.48$, $p < .01$, $d = 0.93$, $BF_{10} = 37.47$ Behavioral reward sensitivity was positively correlated with NACC–rACC RSFC ($r = 0.22$, $p < .05$), showing greater fronto-striatal connectivity related to higher reward sensitivity. **Comparisons to HC:** ***Bupropion:*** NACC-rACC RSFC for bupropion responders was significantly larger than HC ($t_{51} = 3.64$, $p < .001$, $d = 1.05$, $BF_{10} = 44.25$), whereas that for non-responders was lower at a trend level ($t_{55} = -1.84$, $p = .07$, $d = 0.51$, $BF_{10} = 1.10$) ***Sertraline:*** NACC-rACC RSFC for sertraline responders was significantly lower than HC ($t_{60} = -3.70$, $p < .001$, $d = 0.97$, $BF_{10} = 58.92$), whereas there was no difference between non-responders &	
							HC ($t_{58} = 0.83$, $p > .05$, $d = 0.21$, $BF_{10} = 0.36$) Within each medication group, separate voxelwise analyses converged with the full-group results & indicated NACC–rACC RSFC was particularly related to treatment response for the bupropion group. Buproprion responders showed higher NACC–rACC RSFC, while there were no significant differences in NACC-rACC RSFC within the sertraline group. **Replicating Sertraline Findings with Stage 1 sample:** Sertraline responders and non-responders in stage 1 did not differ in reward sensitivity ($t_{114} = -0.15$, $p > .05$, $d = 0.03$, $BF_{10} = 0.20$), or NACC–rACC RSFC ($t_{110} = 1.53$, $p > .05$, $d = 0.29$, $BF_{10} = 0.57$)	
Barch et al., 2020	Children with MDD RewP: PCIT-ED $n = 60$, waitlist $n = 58$; LPP: PCIT-ED $n = 44$, waitlist n = 55	PCIT-ED	18 sessions	18	**Neural reward sensitivity** (EEG; **RewP** in Doors Task; **LPP** in Picture Task)	Binary depression treatment response on clinician-rated **K-SADS-EC**: MDD remission defined as no longer meeting diagnostic criteria; MDD non-remission defined as still meeting criteria Change in depression symptoms on clinician-rated **K-SADS-EC** from pre- to post-treatment	**Approach:** Binary logistic regressions & linear regressions to examine whether pre-treatment RewP or LPP (residual scores reflecting variability in response to wins not accounted for by loss responses) predicted MDD remission status or depression symptom reduction Pre-treatment RewP responses did not predict remission status or change in MDD symptoms (p's > .18) Pre-treatment LPP responses predicted MDD remission: $B = 0.30$; $SE = 0.15$; $OR = 1.35$; $p = .04$, but not MDD symptom reduction ($p > .41$)	At pre-treatment, RewP did not predict depression remission status or symptom reduction Greater LPPs to positive pictures predicted higher likelihood of MDD remission, but did not predict depression symptom reduction
Brandt et al., 2021	Adults with MDD $N = 90$	Escitalopram	5–20 mg Option for duloxetine (30–120 mg) for those with severe side	8	**Neural reward sensitivity** (fMRI; striatum, mPFC, & anterior insula activation in card-guessing task)	Primary binary depression treatment response on **HDRS-6** (remitter if early response (i.e., > 50% reduction in HDRS-6	**Approach:** Logistic regression models using 5-fold cross-validation Pre-treatment reward-related brain responses from all contrasts did not	Pre-treatment reward-related brain responses did not predict antidepressant treatment response

			effects at week 4 onwards			at week 4 & HDRS-6 < 5 at week 8); non-responder if no early response (i.e., < 25% reduction in HDRS-6 at week 4 & < 50% HDRS-6 reduction at week 8)) Secondary binary depression treatment response on **HDRS-17** (responder if ≥50% reduction in HDRS-17 at week 8; remitter if HDRS-17 ≤ 7 at week 8) Change in depression symptoms on **HDRS-6**	improve the classification of binary depression treatment response groups nor continuous treatment response (p's > 0.39)	
Burkhouse et al., 2016	Adults with Anxiety Disorders N = 52 (n = 30 with Pure Anxiety; n = 22 with Comorbid Anxiety & Depression)	CBT	12 sessions	12	**Neural reward sensitivity** (EEG; **RewP** & **SPN** in guessing reward task)	Overall treatment response on clinician-rated **CGI-I;** considered responders if score of 1 "very much improved" or 2 "much improved Change in depression symptoms on **BDI-II** from pre- to post-treatment	**Approach:** Hierarchical logistic regressions & hierarchical linear regressions Lower RewP predicted CBT response on CGI-I: $Wald$ = 4.63, p = .03, OR = 1.18 [1.02, 1.38]; not moderated by diagnostic group (p = .19). Lower RewP predicted BDI-II symptom change in comorbid group: $t(19) = 2.73$, p = .01, B = 1.13, vs. pure anxiety group: t(27) = −0.18, p = .86, B = −0.14 SPN did not predict response to CBT or symptoms change (p's ≥ .42)	Individuals with lower pre-treatment RewP were more likely to be treatment responders. Lower pre-treatment RewP was correlated with a greater reduction in depressive symptoms for those with comorbid anxiety & depression, but not pure anxiety.
Burkhouse et al., 2018	Adults with Anxiety &/or Depressive Disorders N = 63	CBT (n = 34) or SSRI (n = 29; sertraline, fluoxetine, paroxetine, escitalopram, or citalopram)	CBT: 12 sessions SSRI: Flexible dosages based on tolerability (reaching maximum by week 8)	12	**Neural reward sensitivity** (EEG; **RewP** in guessing reward task)	Change in depression symptoms (**HDRS & BDI-II composite**) from pre- to post-treatment	**Approach:** Hierarchical linear regression models (Entered pre-treatment symptoms, RewP, & treatment group (CBT vs. SSRI) at step 1 and 2-way interaction between pre-treatment RewP and treatment group in step 2.	Individuals with blunted RewP at pre-treatment were more likely to exhibit depression symptom reduction following SSRI treatment, but not CBT.
						Change in anxiety symptoms (**HARS & BAI composite**) from pre- to post-treatment	Attenuated pre-treatment RewP predicted greater depression symptom improvement for SSRI group: (β = −0.39, t = −2.04, p < .05), but not CBT group: (β = 0.14, t = 0.75, p = .46), No main effects of pre-treatment RewP on anxiety symptom change for CBT or SSRI group (p's > .05)	Pre-treatment RewP did not predict anxiety symptom reduction for SSRI or CBT group.
Carl et al., 2016	Adults with MDD N = 33	Behavioral Activation Therapy for Depression	8–15 sessions	8–15	Self-reported anhedonia on **BDI-II** **Reaction time** on monetary incentive delay (MID) task **Neural reward sensitivity** (fMRI; activation during MID in response to reward)	Change in depression symptoms on **BDI-II** from pre- to post-treatment	**Approach:** Hierarchical linear regression models Significant interaction effect between pre-treatment self-reported anhedonia & treatment week in predicting change in BDI ($\gamma_{\text{Anhedonia Subscale * Tx Week}}$ = −0.16, SE = 0.035, t(173) = −4.60, p < .0001); pre-treatment self-reported anhedonia accounted for 43% of between-person variance in the within-person effect of treatment week on BDI. Significant interaction effect between reaction time on MID at pre-treatment & treatment week in predicting change in BDI ($\gamma_{\text{Reaction Time Change Rate * Tx Week}}$ = −0.02, SE = 0.001, t(185) = −2.41, p = .02); change in reaction time during MID accounted for 15% of between-person variance in the within-person effect of treatment week on BDI. Changes in right NAcc activation from runs 1 to 2 during reward trials did not predict treatment response (p > .05). Sustained overall ACC activation (less decrease) from runs 1 to 2 was associated with larger reductions in depression symptoms during treatment ($\gamma_{\text{Change in ACC Activation * Tx Week}}$ = .46, SE = 0.20, t(200) = −2.38, p = .02); change in	Individuals with higher pre-treatment anhedonia showed greater reductions in depression symptoms across treatment. Greater declines in reaction time (i.e., increased speed) from runs 1 to 2 during reward trials in the MID task was associated with larger decreases in depression symptoms during treatment. Greater sustained activation in the ACC during reward trials at pre-treatment predicted greater reductions in BDI symptoms following treatment.

							ACC activation accounted for 5.6% of between-person variance in the within-person effect of treatment week on BDI.	
Dickey et al., 2023	Adolescents with MDD *N* = 70	Group CBT: Coping with Depression Course for Adolescents	16 sessions	8	**Neural reward sensitivity** (EEG; **RewP** & **LPP** during monetary reward task) **BIS/BAS scales: Reward Responsiveness (RR) subscale**	Overall treatment response on clinician-rated **CGI-I** Post-treatment depression symptoms on **MFQ**	**Approach:** Hierarchical linear regression models (intent-to-treat). Controlled for pre-treatment depression on MFQ. Attenuated RewP predicted lower post-treatment depression symptoms on MFQ (accounting for pre-treatment symptoms; $B = 0.91$, SE = 0.42, $\beta = 0.23$, $z = 2.16$, $p = .031$), but not clinician-rated improvement ($p = .680$) Although LPP did not predict clinician-rated improvement in the intent-to-treat analyses ($p = .137$), larger LPP residuals did predict greater clinician-rated improvement for treatment *completers* ($B = -0.04$, SE = 0.02, $\beta = -0.32$, $z = -2.13$, $p = .033$). Reappraisal-related LPPs did not predict change in depression symptoms (p's > .709) Self-reported reported reward responsiveness on BIS/BAS scale did not predict post-treatment depression symptoms or clinician-rated improvement (p's > .371).	Lower RewP amplitudes at pre-treatment predicted reduced depression symptoms following treatment. Larger LPP residuals during reappraisal predicted greater clinician-rated improvement. Self-reported reward responsiveness on BIS/BAS at pre-treatment did not predict depression symptoms or clinician-rated improvement.
Dunlop et al., 2020	Adults with MDD *N* = 87	Escitalopram	10–20 mg	8	Self-reported anhedonia on **DARS** & **SHAPS** **Neural reward sensitivity** (fMRI; ventral striatal functional connectivity (VS-FC) during MID in anticipation & response to reward) **Behavioral reward sensitivity** (response time during MID task)	Change in depression symptoms on **MADRS** from pre- to post-treatment	**Approach:** Mixed effects linear regression models Lower DARS (but not SHAPS, $p = .053$) anhedonia severity at pre-treatment was associated with greater MADRS improvement at week 8 ($r = 0.27 +/- 0.10$, FDR-corrected $p = .04$, df = 81, 95% CI: 0.07, 0.47). BOLD response & VS-FC during reward anticipation and consumption phases of the MID task at pre-treatment were not associated with change in depression symptoms on MADRS at week 8 (p's > .05). After controlling for age, sex and recruitment site and for multiple comparisons, faster response time at pre-treatment was associated with greater antidepressant improvement at week 8 for non-incentivized miss trials ($r = -0.27 \pm 0.11$ SE [95% CI: −0.47, −0.05], FDR-corrected $p = .04$) but no other trial conditions (p's > .05)	Lower self-reported anhedonia severity (on DARS) and faster response time during incentivized misses on the MID task at pre-treatment were associated with greater depression symptom improvement at week 8 (on MADRS). Neither pre-treatment BOLD activity, VS-FC during anticipation nor consumption of reward on the MID task were correlated with depression symptom improvement at week 8.
Forbes et al., 2010	Adolescents with MDD *N* = 13 (10 of whom endorsed comorbid GAD)	CBT ($n = 7$) or CBT + SSRI ($n = 6$); groups were combined for analyses due to small sample sizes	CBT: 8 sessions citalopram: 10–40 mg; fluoxetine: 5–25 mg	8	**Neural reward sensitivity** (fMRI; striatal & mPFC reactivity during anticipation of & response to reward trials on card-guessing monetary reward task)	Clinician-rated global severity on **CGI-S** & clinician-rated global improvement on **CGI-I** at post-treatment Change in anxiety symptoms on **SCARED** from pre- to post-treatment Change in depression symptoms on **MFQ** from pre- to post-treatment	**Approach:** Linear growth models **CGI-S:** Striatal reactivity in response to (but not anticipation of) reward outcome at pre-treatment predicted post-treatment general clinical severity (CGI-S) ratings ($B = 0.26$, $SE = 0.08$, $p < .01$). **SCARED:** Striatal reactivity in anticipation of reward at pre-treatment was inversely associated with post-treatment anxiety symptoms on SCARED ($B = -4.70$, $SE = 2.29$, $p < .05$). Greater striatal reactivity in anticipation of reward at pre-treatment was associated with faster rate of reduction in anxiety symptoms on SCARED across treatment ($B = -0.64$, $SE = 0.24$, $p < .01$). Greater mPFC reactivity in anticipation of reward at pre-treatment was associated with slower rate of reduction in anxiety symptoms on SCARED across treatment ($B = 4.21$, $SE = 1.50$, $p < .01$).	Greater reward-related striatal reactivity on the reward task prior to treatment was associated with greater clinical severity at post-treatment, but also with lower anxiety symptoms, and faster improvement of anxiety symptoms. Higher mPFC reactivity on the reward task prior to treatment was associated with slower improvement in anxiety symptoms.

							CGI-I & MFQ Neither striatal nor mPFC reactivity in anticipation or response to reward at pre-treatment predicted post-treatment depression symptoms or rate of change, nor general clinician-rated improvement (*p*'s > .05)	
Giles et al., 2023	Adults with MDD *N* = 195	Sertraline or Placebo (group sample sizes NP)	≤ 200mg	8	Reward behavior disengagement (RBD) on the **probabilistic reward learning task;** binary categorization as "reward task engaged" or "disengaged"	Change in depression symptoms on **HDRS** across treatment	**Approach:** Repeated-measures linear mixed-models There was a significant 3-way interaction between time (8 timepoints), treatment group (sertraline vs. placebo), and RBD (reward task engaged vs. disengaged) such that reward task disengaged individuals showed greater reductions HDRS scores as treatment progressed when on sertraline compared to placebo, whereas reward task engaged individuals responded to both sertraline or placebo (i.e., no group differences in slope of change on HDRS; $F(1293) = 4.33$, $p = .038$). *Note that SHAPS scores did not significantly predict RBD classification.*	Participants who were classified as reward task *disengaged* showed greater reductions in HDRS depression symptoms in the sertraline (vs. placebo) group. In contrast, participants who were classified as reward-task *engaged* did not differ in depression reduction between the sertraline or placebo groups.
Greenberg et al., 2020	Adults with MDD *N* = 222	Sertraline (*n* = 110; Placebo *n* = 112)	≤ 200mg	8	**Neural reward sensitivity** (fMRI; ventral striatal (VS) reward index in **probabilistic reward learning task**; calculated temporal change in VS activation for outcome-locked (i.e., prediction error; PE) & cue-locked (i.e., reward expectancy; RE)	Post-treatment depression symptoms on HDRS (for general predictor effects) Depression symptom reduction on **HDRS** from pre- to post-treatment (estimated by interaction between variable and treatment group assignment on estimated week 8 HDRS scores)	**Approach:** Multilevel linear models estimating both symptom trajectories and week-8 outcomes. No general predictor effect of pre-treatment VS reward index on depression scores at week 8 ($p = .58$, right VS; $p = .47$ left VS). Both right ($F_{(1,198)} = 9.67$, $p = .0004$) and left ($F_{(1,193)} = 12.93$, $p = .002$) VS reward indices moderated treatment effects, with lower reward index values being associated with lower estimated week 8 depression scores in the sertraline vs. placebo groups.	Pre-treatment activity in the left VS (indicating the degree to which changes in response to RE and PE followed the pattern suggested by reinforcement learning models) moderated response to sertraline (vs. placebo). Specifically, lower reward index values (i.e., more abnormal VS functioning) were associated with lower depression symptoms at week 8 in the sertraline (vs. placebo) group.
Hou et al., 2018	Adults with MDD *N* = 81	SSRIs (*n* = 48), SNRIs (*n* = 26), or antidepressant combinations of SSRIs, SNRIs, &/or mirtazapine (*n* = 7)	Flexible dosages; unspecified min/max	2	**Neural reward network functional connectivity** (fMRI; resting-state functional connectivity (FC) of NAcc-based networks)	Binary early depression treatment response on **HDRS** based on reductive rate (RR) = ($HDRS_{pre\text{-}treatment} - HDRS_{week\ 2}$)/$HDRS_{pre\text{-}treatment}$); considered responsive depression (RD; *n* =44) if RR < 50%; considered non-responding depression (NRD; *n* = 37) if RR ≥ 50%	**Approach:** ANCOVA within the gray matter mask, controlling for whole brain GMV, age, gender, and education level. Within the left NAcc reward network, FC in the right superior frontal gyrus (area under curve (AUC) = 0.837, *p* <.001) and left para hippocampus (AUC = 0.770, *p* <.001) differentiated NRD from RD participants, with the RD group showing decreased positive FC in these areas. Within the right NAcc reward network, FC of the left superior frontal gyrus (AUC = 0.827, $p < .001$) differentiated NRD from RD participants, with the RD group showing decreased positive FC in this area.	The early responder (RD) and non-early responder (NRD) groups showed distinct FC patterns within the NAcc-based reward network at pre-treatment. RD participants exhibited reduced connectivity
Khazanov et al., 2020	Adults with MDD *N* = 433	Antidepressants (unspecified from several classes; *n* = 217) or Antidepressants + Cognitive Therapy (CT; *n* = 216)	Flexible dosages; unspecified min/max	≤ 182.5 (i.e., up to 42 months)	Self-reported anhedonia on **MASQ**	Depression treatment response on **HDRS; Remission** defined as HDRS ≤ 8 & LIFE ratings ≤ 2 for 4 consecutive weeks (after 12 months, criteria relaxed & partial remission was met with 4 weeks of HDRS ≤ 12 and LIFE ratings ≤ 3); **Relapse** defined as HDRS ≥ 16 or LIFE ≥ 5 for 2 consecutive weeks or more; **Recovery** defined as meeting criteria for remission and not relapsing for another 26 consecutive weeks First outcome = **time to remission within**	**Approach**: Cox regression (survival) analyses. Controlled for pre-treatment depression severity on HDRS. Higher pre-treatment anhedonia on MASQ predicted longer time to remission within one year ($\beta = -0.23$, $p < .001$, HR = 0.79, NNT = 8.68) and recovery within three years ($\beta = -0.20$, $p < .001$, HR = 0.82, NNT = 10.09), even after controlling for pre-treatment depression severity. When both distress and anhedonia were included in the same model, distress remained a predictor of longer times to remission and recovery, but anhedonia did not (remission: $\beta = -0.09$, $p = .163$, HR = 0.91, NNT = 21.68; recovery: $\beta = -0.05$, $p = .392$, HR = 0.95, NNT = 37.39). Anhedonia interacted with treatment condition in the prediction of time to	Higher pre-treatment anhedonia predicted longer times to remission within 1 year and recovery within 3 years. Interactions with treatment condition showed individuals with higher anhedonia benefited from receiving CT in addition to medication, whereas there was no added benefit of CT for individuals with lower anhedonia.

						first year of study Second outcome = **time to recovery within 3 years** (duration of study)	remission (β = 0.24, p = .036, HR = 1.27, NNT = −8.32) and recovery (β = 0.30, p = .007, HR = 1.35, NNT = −6.79). Treatment outcomes were equivalent for low pre-treatment anhedonia across conditions, whereas those with higher anhedonia took longer to remit within the first year and to recover within 3 years when receiving antidepressants only (vs. receiving combined antidepressants + CT).	
Krepel et al., 2020	Adults with MDD N = 196 (n = 119 Discovery sample; n=77 Replication)	rTMS	Right low frequency (1 Hz) or left high frequency (10 Hz) rTMS at the dorsolateral prefrontal cortex	Unspecified number of weeks/sessions in protocol; reported average = 22.3(8.0) for Discovery sample & 19.0(6.0) for Replication sample	Self-reported anhedonia on **BDI-II**	Binary depression treatment response on **BDI-II;** considered responders if ≥50% decrease on BDI-II score from intake to outtake; considered non-responders if < 50% decrease Change in depression symptoms on **BDI-II**	**Approach**: Generalized linear model univariate analyses, followed by tests of sensitivity, specificity, PPV, & NPV Pre-treatment anhedonia (from BDI-II) was significantly higher in non-responder (cf. responder) group in both the Discovery (d = 0.36, p = .072, *alpha* = 0.1) & Replication samples (d = 0.76, p = .005, *alpha* = 0.05). Pre-treatment anhedonia was correlated with percent change in BDI score with treatment in both the Discovery (r = −0.221; p = .023; r^2 = 4.9%) & Replication samples (r = −0.224; p = .025; r^2 = 6.0%). A discriminant analysis in the Discovery set using anhedonia and age was significant (p = .034; *Wilks' λ* = 0.937; $\chi 2$= 6.771; *df* = 2), with sensitivity of 62.5% and specificity of 53.7%. PPV was 44.6% & NPV was 70.6%. Area under the curve of the ROC, regressed on non-response, was 0.643. This model also reached significance when repeated in the Replication set (p = .018; *Wilks' λ* = 0.880; $\chi 2$ = 8.024; *df* = 2), with sensitivity of 73.9% & specificity of 74.4%. PPV was 60.7% & NPV was 80.0%. Area under the ROC	Non-responders (cf. responders) to rTMS treatment exhibited higher pre-treatment anhedonia. Pre-treatment anhedonia was negatively correlated with total BDI percentage change over time in treatment. Pre-treatment anhedonia was marginally predictive of rTMS response. Neither PPV nor NPV reached the level of clinical relevance (i.e., >75%)
							curve was 0.726 In assessing clinical relevance in the combined Discovery & Replication samples, the PPV and NPV did not reach the a-priori determined value of 75%, & thus are not considered to meet clinically relevance.	
Kujawa et al., 2019	Children & Adolescents with GAD or SAD N = 27	CBT (n = 16) or Sertraline (n = 11); Groups were combined for analyses due to small sample sizes	CBT: ≤ 18 sessions Sertraline: 12.5–200 mg	CBT: ≤ 18 Sertraline: ≤ 12	**Neural reward sensitivity** (EEG; **RewP** during monetary reward task)	Change in anxiety symptoms on **PARS** from pre- to post-treatment Change in depression symptoms on **CDI** from pre- to post-treatment	**Approach**: Hierarchical multiple regression analyses RewP was not a significant predictor of change in anxiety symptoms (p's > .14). Reduced pre-treatment RewP to reward feedback predicted greater reduction in depression symptoms (t(21) = −2.10, p < .05), even after accounting for pre-treatment symptom severity (B = −0.29, SE = 0.14, p < .05). Although underpowered for treatment group comparisons, preliminary exploratory analyses of the effect of RewP predicting change in depressive symptoms approached significance in the CBT group (*partial* r = −0.54, t(10) = −2.02, p = .07, but not in the Sertraline group (partial r = −0.02, t(5) = −0.05, p = .96.	Reduced reward responsiveness (RewP) at pre-treatment predicted greater reduction in depression (but not anxiety) symptoms following treatment. Exploratory analyses suggest the effects were more salient for CBT (vs. SSRIs). RewP at pre-treatment did not predict change in anxiety symptoms following treatment.
McMakin et al., 2012	Adolescents with SSRI Treatment-resistant MDD N = 334	Medication switch (different SSRI or venlafaxine) or Medication switch + CBT (unspecified sub-group sample sizes)	SSRI: ≤ 40 mg for SSRI; venlafaxine: ≤ 225mg CBT: 12 sessions + up to 6 booster sessions	24 (12 weeks acute treatment, 12 weeks continuation treatment)	Clinician-rated symptoms on anhedonia dimension of **CDRS-R**	Time to remission on clinician-rated **A-LIFE**; remission defined as 3+ consecutive weeks without clinically significant depression symptoms. Depression-free days based on **CDRS-R**	**Approach**: Cox proportional hazards were used to predict time to remission; linear regression models were used to predict depression-free day Multivariate analyses simultaneously examining all 5 depression symptom dimensions on the CDRS-R (reported depressed mood, anhedonia, somatic symptoms, morbid thoughts, observed depression) revealed that higher pre-treatment anhedonia was the only dimension to predict longer **time to**	Higher pre-treatment anhedonia uniquely predicted longer time to remission and fewer depression-free days across treatment.

							remission (HR = 0.91, 95% CI = 0.84–0.99, $p < .05$), and the sole dimension to predict fewer **depression-free days** (β = −4.355, SE = 1.18; partial correlation = −0.23, $p < .001$). When pre-treatment anhedonia and total CDRS score were examined simultaneously, higher anhedonia remained a unique predictor of longer time to remission (**Anhedonia:** HR = 0.90, 95% CI 0.83–0.97, $p < .01$; **CDRS-R total score**: HR = 0.99, 95% CI = 0.97–1.01, $p = .30$) and fewer depression-free days (**Anhedonia**: β = 3.16, SE = 1.16, $p < .01$, partial correlation = 0.16; **CDRS-R total score:** HR = 0.96, SE = 0.29, $p < .01$, partial correlation = 0.20).	
Norris et al., 2021	Children & Adolescents with Anxiety Disorders $N = 136$	CBT: Coping Cat protocol	16 sessions	16	**BIS/BAS-C: Reward Responsiveness (RR) subscale**	Post-treatment anxiety symptoms (**MASC-C**) Post-treatment depressive symptoms (**MFQ-C**) Post-treatment clinician-rated global functioning (**CGAS**) Binary clinician-rated treatment responder status (**CGI-I**)	**Approach**: Hierarchical regression models; pre-treatment age and sex were entered at level 1, pre-treatment depression (MFQ-C), anxiety (MASC-C), & functioning (CGAS) were entered at level 2; pre-treatment RR (BAS) was entered at level 3 The inclusion of RR accounted for an additional 4% of the variance in post-treatment anxiety symptoms (MASC-C), $Wald\ \chi^2(1) = 5.09$, $p = .02$, $\Delta R^2 = 0.04$. Lower RR [$B = -0.16$, $SE = 0.07$, $z = -2.26$, $p = .02$] & greater pre-treatment anxiety [$B = 0.45$, $SE = 0.12$, $z = 3.75$, $p < .001$] significantly predicted more severe post-treatment anxiety. RR accounted for an additional 6% of the variance in post-treatment depression symptoms (MFQ-C), $Wald\ \chi^2(1) = 7.58$, $p = .01$, $\Delta R^2 = 0.06$. Lower RR [$B = -0.13$, $SE = 0.05$, $z = -2.75$, $p = .01$] & greater pre-treatment depressive symptoms [$b = 0.29$, $SE = 0.10$, $z = 2.99$, $p = .003$] significantly predicted more severe post-treatment depressive symptoms. RR accounted for an additional 11% of the variance in post-treatment functioning, $Wald\ \chi^2(1) = 13.84$, $p < .001$, $\Delta R^2 = 0.11$. Higher RR [$B = 6.08$, $SE = 1.63$, $z = 3.72$, $p < .001$], greater pre-treatment functioning [$B = 0.50$, $SE = 0.16$, $z = 3.23$, $p = .001$], & lower pre-treatment anxiety [$B = -6.44$, $SE = 2.72$, $z = -2.37$, $p = .02$] predicted increased post-treatment. RR accounted for an additional 19% of outcome variance, $Wald\ \chi^2(1) = 10.28$, $p < .001$, $\Delta R^2 = 0.19$. Higher RR [$B = 1.43$, $SE = 0.45$, $z = 3.21$, $p = .001$], greater pre-treatment functioning [$B = 0.508$, $SE = 0.04$, $z = 1.98$, $p = .05$], & lower pre-treatment anxiety [$B = -1.60$, $SE = 0.72$, $z = -2.21$, $p = .03$] predicted responder status. For every one unit increase in RR, the odds of responding to treatment increased by 4.17-fold (CI: 1.74−10.01).	Higher pre-treatment reward responsiveness predicted lower post-treatment anxiety and depression symptom severity, better global functioning, and greater likelihood of being a treatment responder.
Papalini et al., 2019	Adults with Specific Phobia (Spiders) $N = 44$	Group-based Exposure Therapy ($n = 25$) or PMR ($n = 19$)	Single session	N/A (Single Session)	**Neural reward sensitivity** (fMRI; NAcc, vmPFC, VTA, & whole brain activation during anticipation & response to reward in the MID task) **Behavioral responses** during MID (reaction times & accuracy on reward trials) Self-reported anhedonia on **SHAPS**	Change in spider phobia symptoms (**FSQ**) from pre- to post-treatment	**Approach:** Regression analyses Region of Interest analyses: there were no significant associations between pre-treatment neural activation in the regions of interest during reward anticipation or consumption and reduction in spider phobia (FSQ) following either treatment (NAcc: $p > .70$; VTA & vmPFC: p's > .20). Whole-brain analyses: In the exposure therapy (but not PMR) group, better treatment outcome (greater ΔFSQ) was associated with higher pre-treatment reward-anticipation-related brain	Overall, while activation in the brain regions of interest were not related to therapy outcome, regions involved in *attentional processing of reward cues* were predictive of phobia symptom change following exposure therapy, but not PMR. Slower reaction times to reward cues and less activation in the left posterior cingulate cortex during reward

							activity in the frontal pole (BA 10), extending into the ventrolateral PFC ($p = .04$). In the exposure therapy (but not PMR) group, there were strong negative associations found between treatment outcome (greater ΔFSQ) and reward consumption-related activation in three distinct clusters: left posterior cingulate cortex (PCC, $p < .001$), left superior temporal gyrus (STG, $p < .001$), and right precuneus ($p = .02$). In the exposure therapy (but not PMR) group, greater reduction in FSQ was associated with lower reward consumption-related activation in the left PCC (Partial $r = -0.464$, $p = .03$), but not in the right precuneus (Partial $r = -0.23$, $p = .31$) or in the left superior temporal gyrus ($r = -0.17$, $p = .46$). Better therapy outcome (greater ΔFSQ) was associated with lower reward consumption-related activation in the right lingual gyrus ($p < .001$), left middle temporal gyrus ($p < .001$), and medial PFC ($p < .001$) in the exposure therapy (but not PMR) group. Behavioral responses: The exposure therapy (cf. PMR) group showed a stronger positive correlation between median reward RT and treatment outcome was found, as indicated by a significant interaction between group and median RTs on change in FSQ ($\beta = 2.82$, $p = .04$). Slower reward RTs correlated with a greater reduction in phobia symptoms for the exposure group (Partial $r = 0.528$, $p = .01$), but not in the PMR group (Partial $r = -0.085$, $p = .75$).	consumption were associated with spider phobia symptom reduction following exposure therapy (but not PMR). In the exposure therapy group, increased pre-treatment activation in the vmPFC during reward anticipation, and decreased activation in the mPFC during reward consumption were correlated with greater symptom reduction. Self-reported hedonic capacity did not correlate with reduction in spider phobia symptoms following treatment.
							No significant interaction between group and task accuracy on change in FSQ (ΔFSQ; $\beta = -0.817$, $p = .61$). No significant correlation between accuracy & FSQ change in the exposure group (Partial $r = -0.178$, $p = .44$) or PMR group (Partial $r = 0.08$, $p = .76$). No association between hedonic capacity (SHAPS) & change in spider phobia (FSQ) for either the exposure group (Partial $r = -0.070$, $p = .75$) or PMR group (Partial $r = 0.315$, $p = .22$).	
Rezaei et al., 2021	Adults with MDD $N = 116$	tDCS of the prefrontal cortex (Anodal electrode located over the left DLPFC; cathode located over the right supraorbital region)	Completed one of the following tDCS protocols: 1) 10 daily 20-minute sessions of 2 mA tDCS within 2 weeks ($n = 84$) *or* 2) 10 twice daily 20-min sessions of 2 mA tDCS within 2 weeks ($n = 32$)	2	Loss of pleasure & loss of interest items on **BDI-II**	Binary depression treatment response on **BDI-II;** considered responder if ≥50% reduction from the pre-treatment score	**Approach**: Independent-samples t-tests & binary logistic regression analyses, including all variables that differed between groups as predictors of tDCS response (from BDI-II: cognitive-affective factors of BDI-II, loss of pleasure & interest items, & sleep problems; history of treatment) Responders (cf. non-responders) exhibited significantly higher scores on the pre-treatment BDI-II questions regarding loss of pleasure ($t = -8.76$, $p = .001$) & loss of interest ($t = -4.48$, $p = .001$). Higher pre-treatment scores for loss of pleasure ($\beta = 1.44$, SE = 0.39, Wald = 13.61, $p = .001$) and loss of interest ($\beta = 0.83$, SE = 0.41, Wald = 4.07, $p = .044$) predicted response to tDCS. The Wald criterion showed that loss of pleasure and loss of interest were significant predictors of tDCS response for both dosing protocols (p's < 0.01).	Higher pre-treatment levels of loss of pleasure & loss of interest predicted greater reduction in overall depression symptoms (i.e., responder status on BDI-II) after tDCS
Rezaei et al., 2023	Adults with MDD $N = 182$	tDCS of the prefrontal cortex (Anodal electrode located	10 daily 20-minute sessions of 2 mA tDCS within 2 weeks	2	Self-reported anhedonia on **SHAPS**	Binary depression treatment response on **HDRS-17;** considered responder if ≥50%	**Approach**: Independent-samples t-tests & binary logistic regression analyses Responders (cf. non-responders)	Higher pre-treatment anhedonia predicted greater reduction in overall depression symptoms (i.e.,

		over the left DLPFC; cathode located over the right supraorbital region)				reduction from the pre-treatment score	endorsed higher pre-treatment anhedonia (t = 2.93, p = .004). Logistic regression models including all variables that differed between groups as predictors of tDCS response were then run. Among the predictor variables (i.e., anhedonia, rumination, brooding, & reflective pondering), only anhedonia significantly predicted the response to tDCS (β = 0.27, SE = 0.07, Wald = 16.44, p = .0001)	responder status on HDRS-17) following tDCS
Sequeira et al., 2021	Children & Adolescents with Anxiety Disorders N = 72 (also included n = 37 HC)	CBT (Coping Cat Protocol; n = 50) or Child-Centered Therapy (CCT; n = 22)	16 sessions	16	**Neural reward sensitivity** (fMRI; mPFC & striatal reactivity during reward trials on card-guessing monetary reward task)	Binary depression treatment response on **PARS**; considered responder if ≥35% reduction in diagnostician-rated anxiety severity from pre- to post-treatment	**Approach**: One-way ANOVAs & planned comparisons with sensitivity analyses Compared to non-responders, treatment responders showed greater pre-treatment activation in a cluster extending from the left and right subgenual anterior cingulate cortex (sgACC) into the nucleus accumbens (NAcc) at a voxel-wise threshold of p < .005 (cluster size = 1520 mm^3; peak activation, MNI coordinates = 4, 16, −6 [additional peak at −2, 8, −10]; t = 3.64, df = 106, p < .001). Findings held after controlling for pre-treatment depression & anxiety symptoms (p's < .001). Sensitivity analyses confirmed findings did not vary based on type of treatment.	Treatment responders showed greater neural activation in a cluster encompassing the sgACC & NAcc during the monetary reward task at pre-treatment
Sewart et al., 2019	Adults with SAD N = 80	CBT (n = 45) or ACT (n = 35)	12 sessions	12 (range: 11–18 due to scheduling conflicts)	Self-reported dispositional positive affect measured by combining the **positive affect subscale** of **PANAS** & high positive emotion items from the **MASQ** using Z-score transformations	Change in social anxiety symptoms from pre- to post-treatment measured by combining (following Z-score transformation) **LSAS-SR, SIAS, & SPS** Change in quality of life (QOL) from pre- to post-treatment	**Approach:** Multilevel modeling Omnibus three-way interactions (time × condition × pre-treatment PA) revealed that pre-treatment PA did not moderate reduction in social anxiety symptoms for either CBT or ACT from pre- to post-treatment (β = 0.04, 95% CI [−0.4, 0.5], p = .88) or from pre-treatment to 12-month follow-up assessment (β = 0.2, 95% CI [−0.1, 0.4], p = .30).	Pre-treatment PA did not moderate the effect of treatment group on outcomes (i.e., social anxiety severity or quality of life). Pre-treatment PA was a non-treatment-specific predictor of QOL in both the CBT and ACT groups, such that those with low to
						(**QOLI**)	When testing pre-treatment PA as a non-treatment-specific predictor (i.e., combining groups), the relationships remained non-significant for post-treatment and follow-up (β = –0.1, 95% CI [–0.4, 0.1], p = .28; b = –0.01, 95% CI [–0.1, 0.4], p = .27). Omnibus three-way interactions (time × condition × pre-treatment PA) revealed that pre-treatment PA did not moderate QOL for either CBT or ACT from pre- to post-treatment (β = –0.2, 95% CI [–1.0, 0.5], p = .54) or from pre-treatment to 12-month follow-up assessment (b = 0.2, 95% CI [–0.2, 0.7], p = .28). However, when testing pre-treatment PA as a non-treatment-specific predictor (i.e., combining groups), PA did predict change in QOL from pre- to post-treatment (β = –0.6, 95%CI [–1.0, –0.2], p = .002), but not from pre-treatment to 12-month follow-up (β = 0.1, 95%CI [–0.2, 0.2], p = .99). Simple effects tests showed that among participants with low (1 SD below mean) and average PA, the slope change in QOL was significant (low PA slope = 1.1, 95%CI [0.6, 1.6], p < .001; average PA slope = 0.5, 95% CI [0.3, 0.9], p b .001). Slope change was not significant for those with high PA (1 SD above the mean; slope = 0.05, 95%CI [–0.4, 0.5], p = .82). This could be due to the fact that individuals with greater pre-treatment PA already endorsed high QOL at pre-treatment.	average levels of pre-treatment PA experienced greater improvements in QOL (cf. individuals with high pre-treatment PA). This could, however, be due to a ceiling effect.
Straub et al., 2015	Adolescents with MDD N = 18	CBT Group	5 sessions + 1 booster session 1.5–6.5 weeks after intervention	5	**Neural reward sensitivity** (fMRI; sgACC, NAcc, amygdala, & hippocampus	Change in depression symptoms on **BDI-II** and **CDRS-R** from pre- to post-treatment	**Approach:** Correlated sgACC activation during pre-treatment MID with pre-to-follow-up changes in BDI-II and CDRS-R scores in in all participants who completed CBT group	Higher pre-treatment sgACC activation in the win vs. loss contrast on the MID was associated with greater depression symptom

Note. A small number of studies involved partially overlapping datasets: (1) Ang et al. (2020), Giles et al. (2023), and Greenberg et al. (2020) – highlighted in light blue; (2) Rezaei et al. (2021, 2023) – highlighted in light green. Studies involving the administration of medication followed standardized titration protocols or applied flexible dosages based on medical clinician judgment; β = standardized coefficient, whereas B = unstandardized coefficient; MDD = major depressive disorder; HC = healthy controls; GAD = generalized anxiety disorder; SAD = social anxiety disorder; RewP = reward positivity; LPP = late positive potential; PCIT-ED = Parent-Child Interaction Therapy-Emotion Development; BA = Behavioral Activation; CBT = Cognitive Behavioral Therapy; SSRI = selective serotonin re-uptake inhibitor; SNRIs = serotonin-norepinephrine reuptake inhibitors; CT = cognitive therapy; rTMS = repetitive transcranial magnetic stimulation; PMR = progressive muscle relaxation; tDCS = transcranial direct current stimulation; DLPFC = dorsolateral prefrontal cortex; ACT = acceptance and commitment therapy; N/A = not applicable; BIS/BAS = Behavioral Inhibition System/Behavioral Activation System Scales (Carver and White, 1994); fMRI = functional magnetic resonance imaging; mPFC = medial prefrontal cortex; SPN = stimulus-preceding negativity; BDI-II = Beck Depression Inventory-Second Edition (Beck et al., 1996); MID = monetary incentive delay; DARS = Dimensional Anhedonia Rating Scale (Rizvi et al., 2015); SHAPS = Snaith-Hamilton Pleasure Scale (Snaith et al., 1995); MASQ

= Mood and Anxiety Symptom Questionnaire (Watson and Clark, 1991); CDRS-R = Child Depression Rating Scale-Revised (Poznanski et al., 1984); BIS/BAS-C = Behavioral Inhibition and Behavioral Activation System Scales for children (Muris et al., 2005); NAcc = bilateral nucleus accumbens; vmPFC = ventromedial prefrontal cortex; VTA = ventral tegmental area; PANAS = Positive and Negative Affect Schedule (Watson et al., 1988); EEG = electroencephalogram; MADRS = Montgomery-Asberg depression rating scale (Montgomery and Åsberg, 1979); QIDS-SR = Quick inventory of depressive symptomatology-self report (Rush et al., 2003); HDRS (also referred to as HDRS-17 or HAMD in some studies) = Hamilton Rating Scale for Depression (Hamilton, 1960); PHQ-9 = Patient Health Questionnaire (Kroenke et al., 2001); K-SADS-EC = Schedule for Affective Disorders and Schizophrenia for School-Age Children-Early Child Version (Kaufman et al., 1997); HDRS-6 = 6-item Hamilton Rating Scale for Depression (Bech et al., 1981); CGI-I = Clinical Global Impression Rating Scale - Improvement (Busner and Targum, 2007); HARS = Hamilton Anxiety Rating Scale (Bruss et al., 1994); BAI = Beck Anxiety Inventory (Beck et al., 1988); MFQ = Mood and Feelings Questionnaire (Angold et al., 1995); SCARED = Screen for Childhood Anxiety Related Emotional Disorders (Birmaher et al., 1997); CGI-S = Clinical Global Impression Rating Scale – Severity (Busner and Targum, 2007); CGI-C = Clinical Global Impression – Change Score (Guy, 1976); PARS = Pediatric Anxiety Rating Scale (The Research Units on Pediatric Psychopharmacology Anxiety Study Group, 2002); CDI = Children's Depression Inventory (Kovacs, 1992); A-LIFE = Adolescent Longitudinal Interval Follow-up Evaluation (Keller, 1993); MASC-C = Multidimensional Anxiety Scale for Children (March et al., 1997); MFQ-C = Mood and Feelings Questionnaire – Child Report (Costello and Angold, 1988); CGAS = Children's global assessment scale (Shaffer et al., 1983); FSQ = Fear of Spiders Questionnaire (Szymanski and O'Donohue, 1995); LSAS-SR = Liebowitz Social Anxiety Scale – self-report (Fresco et al., 2001); SIAS = Social Interaction Anxiety Scale (Mattick and Clarke, 1998); SPS = Social Phobia Scale (Mattick and Clarke, 1998); QOLI = Quality of Life Inventory (Frisch et al., 1992); ANOVA = analysis of variance; BF_{10} = Bayes Factor (quantifies amount of evidence supporting the alternative Hypothesis; higher scores from 1 to 100 indicate stronger evidence); ACC = anterior cingulate cortex; HR = hazard ration; NNT = number need to treat; PPV = positive predictive value; NPV = negative predictive value; RBD = reward behavior disengagement; PRT = probabilistic reward task.

et al., 2010; Giles et al., 2023; Papalini et al., 2019; Webb et al., 2021). Fewer studies found mixed or partial support for the opposite pattern—lower responsiveness predicting better outcomes (small to medium effects; Burkhouse et al., 2016, 2018; Dickey et al., 2023; Kujawa et al., 2019). One study found no significant effects (Brandt et al., 2021). Among studies on reward *anticipation,* two supported or partially supported a link between greater anticipatory reward sensitivity and better outcomes (Forbes et al., 2010; Walsh et al., 2017 - small to large effects, depending on brain region), while one showed the reverse (Papalini et al., 2019; small-medium effects), and one showed no effects (Dunlop et al., 2020). Of the two reward *learning* studies, one found mixed results with lower reward learning linked to better outcomes in the medication (but not placebo) group (Greenberg et al., 2020), and one found no significant associations (Whitton et al., 2020). fMRI and EEG findings are summarized below by result patterns and implicated brain regions.

3.5.2.3.1. Resting state functional connectivity. Of the 18 studies using fMRI or EEG techniques to observe neural measures of hedonic functioning, two examined resting state functional connectivity with the NAcc across reward networks (Ang et al., 2020; Hou et al., 2018). Ang et al. (2020) found that among individuals with MDD treated with bupropion (but not sertraline), responders showed higher NAcc–rACC resting state functional connectivity (large effect). In contrast, a study by Hou et al. (2018) found that early depression treatment responders to SSRIs exhibited reduced resting state functional connectivity patterns in the NAcc-based reward networks at pre-treatment (moderate-large effect). The remaining 16 studies described below examined neural reward sensitivity during reward-related tasks or paradigms.

3.5.2.3.2. Significant fMRI findings. Greater reward-related neural activity or connectivity in the ACC and frontostriatal regions during pre-treatment monetary reward tasks was associated with superior treatment outcomes for four studies, each of which examined cognitive behavioral therapies for depression or anxiety (small to large effects; Carl et al., 2016; Sequeira et al., 2021; Straub et al., 2015; Walsh et al., 2017). Specifically, one study in adults with MDD revealed that greater sustained activation in the ACC during reward trials at pre-treatment predicted greater reductions in BDI-II depression symptoms following behavioral activation treatment, and that change in ACC activation across trials accounted for 5.6 % of the variance in reduction in BDI-II over the course of treatment (Carl et al., 2016). In a study of adolescents with MDD who completed 5–6 sessions of group CBT, higher pre-treatment sgACC activation in the win vs. loss contrast on the monetary incentive delay (MID) was associated with greater depression symptom reduction in response to CBT group on the BDI-II, but not the CDRS-R (Straub et al., 2015). Another study of behavioral activation treatment for depression found that higher pre-treatment frontostriatal functional connectivity during reward processing (anticipation and outcome phases) on an MID task predicted better response to treatment, accounting for 4.7–16 % of the variance in the effect of treatment week on BDI-II scores (Walsh et al., 2017). A study in youth with anxiety disorders found that anxiety treatment responders showed greater neural activation in a cluster encompassing the sgACC & NAcc during the monetary reward task at pre-treatment (Sequeira et al., 2021). In contrast, a study by Burkhouse et al. (2016) suggested that *attenuated* reward responsiveness – as measured by RewP during a reward task – was correlated with greater reduction in depressive symptoms on the BDI-II (large effect in comorbid group) and a higher likelihood of responding to treatment (CGI-I; small-medium effect).

3.5.2.3.3. Non-significant fMRI findings. Two studies found that reward-related neural indices during pre-treatment reward tasks were not significantly related to escitalopram treatment response in adults with MDD (Brandt et al., 2021; Dunlop et al., 2020). These studies focused on activation in the striatum, mPFC, and anterior insula (Brandt et al., 2021) and on ventral striatal functional connectivity in anticipation and response to reward (Dunlop et al., 2020) in relation to depression treatment response (assessed using the HDRS and MADRS, respectively).

3.5.2.3.4. Mixed fMRI findings. Other studies also yielded complex findings. In a small study of CBT (with or without SSRIs) for adolescents with MDD and GAD, Forbes et al. (2010) found that greater striatal reactivity on a reward task prior to treatment was associated with greater clinician-rated severity at post-treatment, but also with lower self-reported anxiety symptoms and faster improvement of anxiety symptoms. In contrast, higher mPFC reactivity on the reward task prior to treatment was associated with slower improvement in anxiety symptoms. Neither striatal nor mPFC reactivity in anticipation or response to reward at pre-treatment predicted post-treatment depression symptoms (MFQ) or rate of change in depression, nor general clinician-rated improvement. Greenberg et al. (2020) reported nuanced neural reward findings in adults with MDD treated with sertraline or placebo over eight weeks. They showed that pre-treatment activity in the left ventral striatum during a probabilistic reward learning task (indicating the degree to which changes in response to reward expectancy and prediction error followed the patterns suggested by established reinforcement learning models) moderated response to sertraline compared to placebo. Lower reward index values (i.e., more abnormal VS functioning) were associated with reduced post-treatment depression symptoms in the sertraline (cf. placebo) group. Whitton et al. (2020) found that ventral striatal reward-related activation on a probabilistic reward task predicted greater improvements in clinician-rated global illness severity (CGI), but not self-reported depression symptoms (HDRS) in response to pramipexole treatment in adults with MDD. Finally, a study by Papalini et al. (2019) in adults with spider phobia who completed a single session of group-based exposure therapy or PMR suggested that although activation in the brain regions of interest were not related to therapy outcomes (i.e., changes in spider phobia on the FSQ), regions involved in the *attentional processing of reward cues* –

Table 3
Study risk of bias – assessed using the Quality In Prognosis Studies (QUIPS) tool.

Study	Study participants	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting
Allen et al., 2019	Low	Low	Low	Low	Low	Low
Alsayednasser et al., 2022	Low	Low	Low	Low	Low	Low
Ang et al., 2020	Low	Moderate	Low	Low	Low	Low
Barch et al., 2020	Low	Low	Low	Low	Low	Low
Brandt et al., 2021	Low	Moderate	Low	Low	Low	Low
Burkhouse et al., 2016	Low	Moderate	Low	Low	Moderate	Low
Burkhouse et al., 2018	Low	Low	Low	Low	Low	Low
Carl et al., 2016	Low	Low	Low/moderate	Low/moderate	High	Low
Dickey et al., 2023	Low	Low	Low	Low	Low	Low
Dunlop et al., 2023	Low	Low	Low	Low	Low	Low
Forbes set al., 2010	Moderate	High	Low	Low	Moderate	Low
Giles et al., 2023	Low	Moderate	Moderate	Low	Low	Low
Greenberg et al., 2020	Low	Low	Low	Low	Low	Low
Hou et al., 2018	Low	Moderate	Low	Low	Low	Low
Khazanov et al., 2020	Low	Low	Low	Low	Low	Low
Krepel et al., 2020	Low	Low	Moderate	Moderate	Low	Low
Kujawa et al., 2019	Low	Moderate	Low	Low	Low	Low
McMakin et al., 2012	Low	Low	Low	Low	Low	Low
Norris et al., 2021	Low	Low	Low	Low	Low	Low
Papalini et al., 2019	Moderate	Low	Low	Low	Low	Low
Rezaei et al., 2021	Low	Low	Moderate	Moderate	Low	Low
Rezaei et al., 2023	Low	Low	Low	Low	Low	Low
Sequeira et al., 2021	Low	Low	Low	Low	Low	Low
Sewart et al., 2019	Low	Low	Low	Low	Moderate	Low
Straub et al., 2015	Moderate	Low	Low	Low	Moderate	Low
Walsh et al., 2017	Low	Low	Low	Low	Moderate	Low
Webb et al., 2021	Moderate	Low	Low	Low	Low	Low
Whitton et al., 2020	Moderate	Low	Low	Low	Low	Low

Note. Ratings indicate whether the specified domain reflects low, moderate, or high risk of bias. A rating of "Low/Moderate" indicates that within that domain, some indicators or measures were judged to have low risk of bias, while others were judged to have moderate risk. Studies highlighted in light blue (i.e., Ang et al., 2020; Giles et al., 2023; and Greenberg et al., 2020) utilized overlapping data from the EMBARC trial. Studies highlighted in light green (i.e., Rezaei et al., 2021, 2023) shared somewhat overlapping data.

particularly the left PCCC (medium-large effect) – were predictive of phobia symptom change following exposure therapy (but not PMR). In the exposure group, increased pre-treatment activation in the vmPFC during reward anticipation, and decreased activation in the mPFC during reward consumption were correlated with greater symptom reduction.

3.5.2.3.5. EEG findings. EEG studies of hedonic processing during reward tasks focused on two ERPs: Reward Positivity (RewP), reflecting initial reward response, and Late Positive Potential (LPP), reflecting sustained emotional attention. Most studies yielded mixed findings. Barch et al. (2020) found that, whereas RewP did not predict treatment outcomes in youth receiving parent-child interaction therapy, greater LPP to positive pictures predicted a higher likelihood of MDD remission (defined as no longer meeting diagnostic criteria on the clinician-rated K-SADS-EC; small-medium effect), but did not predict depression symptom reduction (continuous measure of depression symptoms on K-SADS-EC). Consistent with these findings, Webb et al. (2021) found that higher *sustained* (LPP) - but not *initial* (RewP) - reward responsiveness during a pre-treatment monetary reward task predicted greater reduction in depression symptoms on the BDI-II following CBT. A study of group CBT in adolescents with MDD found *attenuated* RewP predicted lower post-treatment depression symptoms on the MFQ (small-medium effect), but did not predict clinician-rated improvement (Dickey et al., 2023). This study also reported that larger LPP residuals predicted greater clinician-rated improvement for treatment completers (medium-sized effect), but not in the intent-to-treat analyses. Two other studies that examined the role of RewP (but not LPP) revealed mixed findings. Burkhouse et al. (2018) found that those with blunted RewP during a pre-treatment reward task were more likely to exhibit depression symptom reduction on an HDRS and BDI-II composite measure following SSRI treatment (medium effect), but not CBT. Pre-treatment RewP did not predict anxiety symptom reduction for the SSRI or CBT group (Burkhouse et al.). Similarly, Kujawa et al. (2019) reported that reduced reward responsiveness (RewP) during a pre-treatment monetary reward task predicted greater reduction in depression (but not anxiety) symptoms following treatment for children with anxiety disorders (small-medium effect). Exploratory analyses suggested this effect was more salient for CBT (cf. SSRIs).

3.5.2.4. Behavioral measures of hedonic processing. Five studies examined behavioral indicators of reward sensitivity (Ang et al., 2020; Carl et al., 2016; Dunlop et al., 2020; Papalini et al., 2019; Giles et al., 2023; Whitton et al., 2020). One study in MDD showed that higher pre-treatment behavioral reward sensitivity (reward-related response bias) was associated with greater likelihood of depression treatment response (symptom improvement $\geq$50 %) to bupropion (large effect), but not sertraline (small-medium non-significant effect; Ang et al., 2020). In an

overlapping sample, Giles et al. (2023) found that reward task disengaged individuals showed greater depression symptom reduction in with sertraline than placebo, whereas reward task engaged individuals showed no treatment group difference. Another study found that greater pre-treatment improvement in reaction time during reward trials on an MID task predicted larger reductions in depression symptoms across treatment, accounting for 15 % of the variance in symptom change (Carl et al., 2016). Dunlop et al. (2020) found faster pre-treatment response time on non-incentivized miss trials of an MID task predicted greater antidepressant response at week 8 in individuals with MDD.[4] Papalini et al. (2019) found slower pre-treatment reward reaction times on reward trials of an MID task predicted greater symptom reduction following exposure therapy for spider phobia (medium effect), but not progressive muscle relaxation training; accuracy was unrelated to symptom change in either group.

Notably, of the five studies examining both self-reported symptom measures of anhedonia in addition to neural or behavioral indicators of hedonic processing as predictors of treatment outcomes, two did not report correlations between these pre-treatment measures (Carl et al., 2016; Dunlop et al., 2020), while the other three found no significant associations between self-reported anhedonia and neural or behavioral data (Dickey et al., 2023; Giles et al., 2023; Papalini et al., 2019).

3.5.3. Do findings vary based on the type of treatment administered?

3.5.3.1. Psychotherapy. Of the twelve psychotherapy studies, four suggested higher anhedonia/lower reward sensitivity was related to poorer treatment outcomes (small to large effects; Alsayednasser et al., 2022; Norris et al., 2021; Sequeira et al., 2021; Walsh et al., 2017), whereas one found the opposite (i.e., it was linked to greater symptom reduction [small-medium effect] and likelihood of treatment response [large effect]; Burkhouse et al., 2016). Six studies revealed mixed within-study findings depending on the specific anhedonia measures and outcome variables examined (with considerable heterogeneity in direction and magnitude of effects; Barch et al., 2020; Carl et al., 2016; Dickey et al., 2023; Papalini et al., 2019; Straub et al., 2015; Webb et al., 2021). Finally, one found no significant relationship between hedonic disposition and treatment outcomes (small/negligible effect size; Sewart et al., 2019). No clear differences emerged based on treatment modality (e.g., CBT vs. pure behavioral activation or cognitive therapy) or delivery format (e.g., group vs. individual).

3.5.3.2. Pharmacotherapy. Of the seven pharmacotherapy studies, two studies from an overlapping EMBARC trial dataset found that higher pre-treatment anhedonia/lower reward sensitivity predicted poorer treatment outcomes (Ang et al., 2020; Greenberg et al., 2020), while one found that lower reward sensitivity (based on resting state reward-related connectivity) was associated with better outcomes (Hou et al., 2018). One study yielded mixed findings (Dunlop et al., 2020) and two others reported no significant relationships (Allen et al., 2019; Brandt et al., 2021). Giles et al. (2023; also drawing on data from the EMBARC trial) found that reward task disengaged participants with MDD showed greater symptom reduction with sertraline compared to placebo, while reward task engaged participants showed no treatment group differences. The only study involving a dopamine agonist (pramipexole) yielded mixed findings, such that pre-treatment behavioral reward sensitivity and learning indices on the PRT did not predict depression symptom reduction or global illness severity, but greater reward-related ventral striatal activation predicted greater improvement in global illness severity (Whitton et al., 2020). Most studies involved SSRIs (and/or SNRIs), limiting conclusions about medication-specific effects, and findings from the two studies using dopamine-enhancing agents (bupropion [Ang et al., 2020] or pramipexole [Whitton et al., 2020]) were mixed, showing no consistent differences from SSRIs.

3.5.3.3. Combination or comparison of pharmacotherapy and psychotherapy. Five studies examined a combination and/or comparison of pharmacotherapy and psychotherapy interventions. Two trials involving medication or medication in conjunction with psychotherapy found that higher pre-treatment anhedonia predicted poorer treatment outcomes (small-medium effects; Khazanov et al., 2020; McMakin et al., 2012). Three studies yielded mixed findings. Specifically, Burkhouse et al. (2018) found lower reward sensitivity predicted greater depression (but not anxiety) symptom reduction following SSRIs (medium effect), but not CBT. Kujawa et al. (2019) similarly reported that lower reward sensitivity predicted greater depression (but not anxiety) reduction following both SSRIs and CBT (small-medium effect), with a stronger effect for CBT. Forbes et al. (2010) found higher pre-treatment striatal reactivity predicted greater clinical severity but faster anxiety improvement, while higher mPFC reactivity predicted slower anxiety improvement; neither predicted depression changes or overall clinical improvement.

3.5.3.4. Neuromodulation. Three studies implemented neuromodulation techniques. In a study of rTMS targeting the dorsolateral prefrontal cortex (DLPFC), Krepel et al. (2020) found that non-responders exhibited higher pre-treatment anhedonia, which was linked to smaller reductions in depression symptoms over treatment (small-medium effects). Two tDCS studies targeting the DLPFC (with partially overlapping datasets) by Rezaei et al. (2021, 2023) suggested the opposite; namely, higher pre-treatment anhedonia predicted greater depression symptom reduction following treatment (small-medium to large effects).

3.5.4. Do findings vary based on diagnosis (anxiety vs. depressive disorders)?

Most studies included samples with MDD ($k = 21$) or MDD and anxiety disorders ($k = 2$; Burkhouse et al., 2016, 2018). The remaining five studies involved samples with anxiety disorders (Kujawa et al., 2019; Norris et al., 2021; Papalini et al., 2019; Sequeira et al., 2021; Sewart et al., 2019). However, only five studies examined *anxiety* treatment response as an outcome (Burkhouse et al., 2018; Forbes et al., 2010; Norris et al., 2021; Papalini et al., 2019; Sewart et al., 2019). The limited number of studies examining anhedonia as a predictor of anxiety (cf. depression) treatment response precludes clear comparisons. Nevertheless, consistent with the studies investigating anhedonia in relation to depression outcomes, the patterns of findings were mixed for studies examining anxiety outcomes. Burkhouse et al. (2018) found that pre-treatment reward responsiveness predicted depression (but not anxiety) symptom reduction following SSRIs (medium effect), but not CBT. In contrast, Forbes et al. (2010) reported that higher striatal reactivity in anticipation and response to reward during a pre-treatment task predicted lower post-treatment anxiety symptoms and faster anxiety symptom reduction, with no significant effects for depression. Norris et al. (2021) found that higher self-reported reward responsiveness predicted lower post-treatment symptom severity for *both* anxiety and depression symptoms (small-medium effects), in addition to improved global functioning (medium effect) and greater likelihood of treatment response (large effect). However, Sewart et al. (2019) reported pre-treatment hedonic disposition did not predict changes in social anxiety severity. Similarly, Papalini et al. (2019) found pre-treatment self-reported hedonic capacity did not predict spider phobia reduction; however, some neural reward processing predictors were significant.

[4] Similar marginally significant trends were observed for incentivized hits ($r = -0.24$, FDR-corrected $p = .06$), incentivized misses ($r = -0.21$, FDR-corrected $p = .07$), and non-incentivized hits ($r = -0.22$, FDR-corrected $p = .07$). Dunlop et al. (2020) interpreted faster response times as general indicators of more *motivated* task engagement, citing research linking higher anhedonia with general psychomotor retardation in MDD (e.g., Drysdale et al., 2017).

3.5.5. Do findings vary by age range/developmental stage?

Of the nine studies comprised of children or adolescent samples, three indicated higher levels of anhedonia/lower reward sensitivity at pre-treatment were associated with poorer treatment outcomes (small to large effects; McMakin et al., 2012; Norris et al., 2021; Sequeira et al., 2021). The remaining six studies yielded mixed within-study findings, with some anhedonia or treatment outcome measures showing significant relationships while others did not (magnitude and direction of effects varied considerably). Specifically, higher pre-treatment anhedonia predicted worse outcomes on *at least* one measure in Barch et al. (2020), Dickey et al. (2023), Straub et al. (2015), and Webb et al. (2021). Kujawa et al. (2019) found the opposite pattern for at least one measure, and Forbes et al. (2010) reported associations in both directions. However, sample sizes were small ($N < 30$) for the latter two studies (i.e., Kujawa and Forbes). Youth samples differed from those with adults in that all child studies yielded at least one significant association between a measure of anhedonia and treatment response (cf. adult studies: Allen et al., 2019; Brandt et al., 2021; Sewart et al., 2019), and no child findings suggested higher anhedonia/lower reward sensitivity was linked to *better* treatment outcomes (cf. adult studies: Burkhouse et al., 2016; Hou et al., 2018; Rezaei et al., 2021, 2023).

4. Discussion

4.1. Summary of results

The purpose of this review was to identify and synthesize the extant literature examining the relationship between pre-treatment anhedonia and treatment response in individuals receiving psychotherapy, pharmacotherapy, or neuromodulation interventions for anxiety or unipolar depressive disorders. To comprehensively examine the role of anhedonia across various units of analysis, studies were included if they measured this construct at the self-report, neural, and/or behavioral levels. Of the 28 articles that met criteria for the current review, results from nine studies reported that higher pre-treatment anhedonia/lower reward sensitivity was related to poorer treatment response (32.1 %), four suggested it was related to superior treatment response (14.3 %), eleven yielded mixed findings (39.3 %), and only four studies found no significant relationships (14.3 %). Of the studies with mixed findings, more than half ($k = 6$) found higher pre-treatment anhedonia/lower reward sensitivity predicted worse response for *at least* one measure, two found the opposite pattern, and three reported associations in both directions. Mixed findings within studies using multiple units of analysis to measure hedonic processing are consistent with evidence suggesting latent constructs of positive valence functioning do not robustly converge across self-report, behavioral, and neuroimaging measures (Peng et al., 2021). Overall, findings from this review were mixed, with slightly less than a third of studies reporting a consistent association between higher pre-treatment anhedonia/lower reward sensitivity and less favorable outcomes. Given the considerable heterogeneity in study designs, treatments provided, participants included (e.g., child/adolescent or adult), measurement approaches, and findings, further research with larger samples, more consistent methodologies, and comprehensive assessments of anhedonia – including its subcomponents and comparisons across different units of analysis – is needed to confirm the insights from this review and clarify the direction and strength of the relationship between anhedonia and treatment response for anxiety and depression.

4.1.1. Do findings vary based on how anhedonia or underlying hedonic processing deficits are measured?

Patterns of findings were mixed across studies regardless of how anhedonia was measured. Although self-report anhedonia measures were more consistently related to treatment outcomes, these findings come from varied samples, interventions, and study designs. Without direct comparisons of multiple measures within the same samples or intervention, differences cannot be definitively attributed to measurement type alone. Several studies reported differing findings depending on the type of measures used to assess anhedonia and treatment outcomes, even within the same study. Further, the only studies that reported pre-treatment correlational analyses between self-reported measures of anhedonia and brain or behavioral data found no significant associations. These findings are consistent with evidence suggesting different measures of anhedonia may not reflect the same exact construct, but instead represent related, yet distinct, reward-related processes or subconstructs of anhedonia (Rizvi et al., 2016; Kahneman, 1999; Robinson and Clore, 2002). This divergence has important implications for interpreting findings across studies: reliance on a single type of measure may over- or underrepresent specific facets of anhedonia, and comparisons using different assessment modalities should be interpreted with caution. These findings further underscore the need for multi-method approaches in future research to more comprehensively characterize the construct and strengthen conclusions regarding its role in treatment outcomes. Notably, several studies assessed anhedonia using pleasure- or interest-related item(s) from broader depression scales rather than validated instruments specifically designed to measure anhedonia. Although these items capture core aspects of the construct, they may not fully reflect anhedonia and its multidimensional nature, including motivational or anticipatory components. This variation in operationalization limits comparability across studies and may contribute to the mixed findings.

4.1.2. Do findings vary based on the type of treatment administered?

Descriptively, the relationship between anhedonia and treatment outcomes did not vary substantially based on the type of intervention administered. These results align with research suggesting shared emotion-based brain mechanisms and predictors for cognitive behavioral therapy and antidepressant treatments for anxiety and depression (Gorka et al., 2019). Findings related to neuromodulation were mixed, and the dearth of studies in this area precludes definitive conclusions. The lack of a clear pattern across treatment types may reflect the substantial heterogeneity observed among included studies or suggest a true absence of meaningful differences in how pre-treatment anhedonia and hedonic processing predict outcomes for therapy versus pharmacological interventions. More research is needed to clarify these possible explanations.

4.1.3. Do findings vary based on diagnosis (anxiety vs. depressive disorders)?

Most study samples included individuals with MDD, with relatively few targeting anxiety disorders; however, the observed patterns for anxiety appeared comparable to those found for depression outcomes in this review. These findings may support the transdiagnostic relevance of anhedonia and its underlying reward sensitivity deficits, underscoring the commonalities between processes related to anxiety and depression. Nevertheless, the small number of anxiety-focused studies and mixed findings for both diagnostic groups preclude any firm conclusions. Further research on anhedonia is needed in the context of anxiety disorders.

4.1.4. Do findings vary by age range/developmental stage?

Of the eight studies involving children or adolescent samples, all reported that at least one measure of higher anhedonia/lower reward sensitivity at pre-treatment was linked to poorer treatment outcomes. In contrast to adult studies, none of the youth studies reported entirely nonsignificant findings nor suggested that higher anhedonia was associated with better treatment outcomes. This *may* suggest that, unlike in adults, anhedonia in youth might represent a more stable risk factor for poorer treatment efficacy. However, more research is needed. Moreover, research indicates that anhedonia manifesting earlier in life (i.e., during childhood and adolescence) is associated with more severe and persistent clinical severity and course of illness (Gabbay et al., 2015;

Prabhakar et al., 2022), underscoring the need for targeted interventions that address anhedonia to improve longer-term mental health trajectories for children and adolescents.

4.1.5. Clinical relevance

Inconsistent findings across the reviewed studies and limitations of the current evidence base suggest it is premature to make specific recommendations for personalized treatment based on pre-treatment anhedonia. Nevertheless, it is possible that some patients may benefit from interventions directly targeting deficits in reward processing or experiences of pleasure and positive affect. Moreover, future prediction studies could offer more rigorous data using designs in which participants are first randomly assigned to conditions that differentially target anhedonia before proceeding with a full course of standard treatment. We therefore briefly review emerging findings from interventions explicitly targeting anhedonia and reward processing. Clinical trials exploring novel cognitive behavioral treatments targeting the positive valence system in individuals with anxiety and depression have shown promising results in reducing anhedonia and enhancing subjective positive affect (Craske et al., 2019; Craske et al., 2023; LaFreniere and Newman, 2023; Taylor et al., 2017; Taylor et al., 2024), in addition to strengthening reward-related neural connectivity (Kryza-Lacombe et al., 2021). These interventions emphasize strategies that target the mechanisms thought to underlie anhedonia, such as blunted reward sensitivity, diminished valuation, and attentional biases that direct attention toward negative stimuli and away from positive information (Craske et al., 2024). Pharmacological treatments that address neural systems associated with reward processes, such as dopamine signaling, have also been shown to improve responsiveness to reward (Admon et al., 2017) and enhance fear extinction learning (Esser et al., 2021). More recently, TMS and tDCS studies have emerged demonstrating that neuromodulation targeting reward-related brain regions (e.g., anterior DLPFC) using precise neuronavigational techniques has led to significant improvement in anhedonia, even after accounting for changes in overall depression levels (Fukuda et al., 2021; Light et al., 2019; Wang et al., 2021). Further research is needed to determine whether anhedonia-focused interventions are most effective as standalone treatments, modules integrated into existing therapeutic frameworks, or supplementary components for individuals with more significant deficits in positive valence system functioning. Notably, although anhedonia is a serious symptom that warrants direct attention in treatment, the current evidence base is not yet sufficiently robust to guide personalized clinical decisions for anxiety or depression based on individual levels of anhedonia. Further rigorous research, including large-scale treatment prediction studies, is needed to clarify its role and the mechanisms by which it may act as a barrier to treatment response.

4.2. Limitations and future research

4.2.1. Limitations of the extant literature

Findings should be considered within the context of several limitations. Studies included in this review were not explicitly designed (a priori) to test the question of whether pre-treatment anhedonia/lower reward sensitivity predicted outcomes; thus, these exploratory and post-hoc findings should be interpreted with caution. Sample sizes and study designs and statistical approaches varied considerably. The methods used to assess anhedonia were inconsistent, encompassing an array of measures ranging from different self-report questionnaires to behavioral tasks involving evaluation of neural markers of hedonic processing. As such, it was challenging to draw direct comparisons between studies and their findings. Few studies evaluated whether reward-related neural or behavioral markers correlated with clinical phenotypes (i.e., subjective experiences of anhedonia on global self-report measures), and those that did found non-significant relationships (Dickey et al., 2023; Giles et al., 2023; Papalini et al., 2019). This is consistent with research suggesting that anhedonia questionnaires do not always correlate with performance on reward tasks (for a review, see: Rizvi et al., 2016). Such findings may reflect the fact that self-report measures typically evaluate anhedonia either as a broad construct (without disentangling sub-processes) or assess a certain domain of hedonic processing (e.g., consummatory pleasure or motivation), whereas reward paradigms may evaluate specific components of reward functioning (e.g., reward anticipation, immediate response to reward, or sustained reward response). Further, self-report measures are more susceptible to recall bias as individuals tend to rely on self-knowledge when reflecting on the past, often exaggerating the intensity of emotions or symptoms and skewing their reports toward recent experiences rather than a true average (Kahneman, 1999; Thomas and Diener, 1990; Robinson and Clore, 2002). To clarify the definition and neurobiological markers of anhedonia, self-report measures may benefit from distinguishing subcomponents of anhedonia, and behavioral tasks using neuroimaging strategies should clearly define task components for imaging analyses and demonstrate good test-retest and external reliability (Rizvi et al., 2016). The variable findings from this review suggest that future research may benefit from using multiple complementary measures to capture the full complexity of anhedonia, rather than relying on a single modality or proxy, and that the intercorrelations among these measures should be carefully examined and considered.

Another limitation of the current literature is the small number of studies involving samples of individuals with anxiety disorders or focusing on anxiety symptom severity outcomes. Given anhedonia is increasingly recognized as a prominent symptom affecting individuals with clinically impairing anxiety and may pose a potential barrier to recovering from clinical anxiety (Taylor et al., 2022), this represents a crucial area for future research. Although studies controlled for some confounding variables when examining anhedonia as a predictor of treatment outcomes, it is possible that not all relevant factors were accounted for, limiting definitive conclusions about causality. Some studies in this review used specific items (e.g., BDI-II items assessing anhedonia) as predictor variables from the same measure that was also administered to assess changes in the outcome variable (e.g., depression as determined by the BDI-II). Using items from the outcome measure as predictor variables can lead to various methodological biases that can weaken the interpretability of findings, including collinearity, circular reasoning, and reduced validity given the predictor and outcome measures may not be conceptually distinct constructs (Dormann et al., 2013; Podsakoff et al., 2003). Higher scores on the anhedonia items of a depression measure may simply reflect greater overall depression severity at pre-treatment, providing more room for improvement across treatment due to the initial severity. This may help explain why some studies using self-report measures found that individuals with more severe pre-treatment anhedonia responded better to treatment (rather than worse; Carl et al., 2016; Rezaei et al., 2021; but see: Krepel et al., 2020). Notably, two sets of studies involved somewhat overlapping datasets with an undefined number of shared individuals across samples (Giles et al., 2023; Greenberg et al., 2020, and Ang et al., 2020; Rezaei et al., 2021, 2023), precluding the ability to consider the trials independently.

Finally, questions remain regarding anhedonia's *causal* role in treatment outcomes. It remains unclear whether pre-treatment anhedonia exerts a direct influence on treatment outcomes – potentially via neurobiological or motivational mechanisms – or primarily reflects broader illness severity, chronicity, or associated factors such as psychomotor slowing or cognitive impairment that impede recovery. Clarifying these pathways will be critical to determine whether anhedonia should be prioritized as a direct treatment target or regarded chiefly as a prognostic marker within a broader symptom profile.

4.2.2. Limitations of the current review

This review has multiple limitations. This review focused on the relationships between pre-treatment anhedonia measures and treatment outcomes, but did not extend in scope to explore how changes in

anhedonia throughout treatment may relate to outcomes, or whether and the extent to which pre-treatment anhedonia shifts in response to treatment. Although several studies did not explicitly use the term "anhedonia" to describe the reward-related neural or behavioral measures that were administered, we included them in the present review if they met all inclusion and exclusion criteria and measured reward sensitivity/hedonic processing within any of the pre-determined units of analysis. Thus, it is possible that some authors did not intend to specifically evaluate the role of anhedonia, but rather related constructs or sub-constructs. Another limitation of this review is the exclusion of studies that assessed general state or trait positive affect (e.g., PANAS) or broader positive personality traits such as extraversion (e.g., NEO). Although this approach was intended to enhance the conceptual specificity of subjective anhedonia, it may have limited the generalizability of our findings. A recent narrative review by Craske et al. (2024) highlights the relevance of diminished positive affect, anhedonia, and reward processing deficits in the maintenance and treatment of depression, anxiety, and trauma. Further research is needed to build on this important work. Due to substantial heterogeneity in measures of anhedonia and outcomes, variation in study designs, and diverse statistical approaches – many of which were post-hoc and reported varying levels of detail regarding methods, assumptions, and parameters – standardized effect sizes could not be reliably calculated. Thus, the findings from this review are presented as a narrative synthesis. As the literature develops with more consistent, validated measures and comparable study designs, future research could conduct formal meta-analyses to provide more robust estimates of effect sizes and identify potential moderators of treatment outcomes. Another limitation of this review – as with all systematic reviews – is potential publication bias, as studies with null or negative findings may be underrepresented. The restriction to English-language articles may also limit the comprehensiveness and generalizability of the findings. Finally, the authors were unable to assess the degree of overlap between datasets in the two sets of studies that utilized similar samples (Giles et al., 2023; Greenberg et al., 2020; Ang et al., 2020; Rezaei et al., 2021, 2023), which could limit the independence of the evidence base. Nevertheless, removing these datasets from the systematic review would not lead to different conclusions for the current review.

4.2.3. Future directions

Findings from this review raise several important questions and highlight areas for future research. First, the limited number of studies and relatively small sample sizes underscore the need for larger-scale studies, particularly considering the growing evidence that treatment outcome prediction research is frequently underpowered and has limited generalizability to other samples, populations, or contexts (Chekroud et al., 2024). Given that anhedonia is a common transdiagnostic feature across various forms of psychopathology and has been shown to predict higher symptom severity for depression and anxiety symptom clusters (e.g., Guineau et al., 2023), studies are especially needed to further explore the relationship between anhedonia and treatment outcomes for anxiety disorders and other mental health conditions (cf. solely focusing on depression). Researchers might also investigate whether anhedonia interacts with other factors – such as social support, anxiety, or distress tolerance – in shaping treatment outcomes, as these variables may help explain the mixed findings observed to date. Future research is warranted to refine the measurement of anhedonia and disentangle its subcomponents and neurobiological markers to better clarify the nuanced relationship between this construct and treatment outcomes (Rizvi et al., 2016). To enable more sophisticated and robust statistical approaches that allow for a fine-grained and context-sensitive understanding of findings, researchers may also consider implementing ecological momentary assessment approaches. This could help elucidate the dynamic temporal nature of the relationship between anhedonia and symptom improvement across treatment. Building upon the burgeoning research examining treatments specifically targeting anhedonia, future studies may also investigate potential order effects, such as how addressing positive valence processes before, after, or concurrently with negative valence processes may influence treatment outcomes for anhedonia and overall symptom severity.

4.3. Conclusions

Aligned with the goals of precision medicine, this review sought to better understand how individual characteristics – such as anhedonia – may relate to depression or anxiety treatment response. Findings were largely inconsistent, and definitive conclusions cannot be drawn, as most studies were secondary analyses of existing clinical data rather than designed to test anhedonia as a treatment predictor, and there was substantial heterogeneity in treatments, participants, designs, measurement methods, and outcomes. This review suggests that clinical recommendations for personalizing treatment based on pre-treatment anhedonia are premature. More rigorous treatment prediction studies are clearly needed.

CRediT authorship contribution statement

Madeleine Rassaby: Writing – original draft, Visualization, Methodology, Investigation, Data curation, Conceptualization. **Isabella G. Spaulding:** Writing – review & editing, Validation. **Murray B. Stein:** Writing – review & editing, Supervision. **Charles T. Taylor:** Writing – review & editing, Supervision, Funding acquisition.

Funding

Dr. Taylor's research efforts were partially supported by the National Institute of Mental Health (R61MH129380).

Declaration of competing interest

Charles T. Taylor declares that in the past 3 years he has been a paid consultant for Bionomics, atai Life Sciences, and Engrail Therapeutics, and receives payment for editorial work for *UpToDate*. Murray B. Stein declares that in the past 3 years he has received consulting income from Acadia Pharmaceuticals, Aptinyx, atai Life Sciences, BigHealth, Biogen, Bionomics, BioXcel Therapeutics, Boehringer Ingelheim, Clexio, Eisai, EmpowerPharm, Engrail Therapeutics, Janssen, Jazz Pharmaceuticals, Newleos Therapeutics, PureTech Health, Sage Therapeutics, Seaport Therapeutics, Sumitomo Pharma, Roche/Genentech, and Transcend Therapeutics. Dr. Stein has stock options in Oxeia Biopharmaceuticals, EpiVario and Newleos. He has been paid for his editorial work on *Depression and* Anxiety (Editor-in-Chief), *Biological* Psychiatry (Deputy Editor), and *UpToDate* (Co-Editor-in-Chief for Psychiatry). He has also received research support from NIH, Department of Veterans Affairs, and the Department of Defense. He is on the scientific advisory board for the Brain and Behavior Research Foundation and the Anxiety and Depression Association of America. Madeleine M. Rassaby and Isabella G. Spaulding declare no conflicts of interest.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2025.120733.

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