Journal of Affective Disorders 368 (2025) 872–887

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Review Article

Brain functional effects of cognitive behavioral therapy for depression: A systematic review of task-based fMRI studies

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ARTICLE INFO

Keywords:
fMRI
Psychotherapy
Depression
Cognitive behavioral therapy
Neuroimaging
Brain function

ABSTRACT

Background: Depressive disorders are associated with alterations in brain function, affecting processes such as affective and reward processing and emotion regulation. However, the influence of Cognitive Behavioral Therapy (CBT) on the neuronal patterns remains inadequately understood. Therefore, this review systematically summarizes longitudinal fMRI brain activity changes in depressive patients treated with CBT and their association with symptom remission.

Methods: This systematic review was conducted according to the PRISMA statement. Out of 2149 results of the literature search, $N = 14$ studies met the inclusion criteria (e.g., diagnosis of a current depressive disorder, assessment of longitudinal task-based fMRI, and the analysis of functional changes before and after CBT).

Results: The findings reveal (1) diminished limbic reactivity following CBT across various tasks, (2) increased striatal activity during reward processing, but decreased activity during affective processing and future thinking, and (3) alterations in cingulate and prefrontal cortex activity across tasks. Partially, these results are associated with symptom remission, especially in the subgenual anterior cingulate cortex.

Limitations: There are heterogenous results especially in cortical areas that might partially be due to methodological issues like differences across the studies in terms of task content, statistical evaluation, and interventions. Thus, future research should focus on the standardization of methodologies.

Conclusions: The results indicate that CBT partially normalizes the neural patterns of depressive patients, particularly within regions involved in affective and reward processing and the development of negative cognitive biases. Overall, potential neural mechanisms underlying CBT were identified, underscoring its effectiveness on an objective neurobiological basis.

1. Introduction

Major depressive disorder (MDD) is one of the most prevalent psychiatric disorders globally, accounting for the largest proportion of mental disorder disability-adjusted life-years (DALYs) in 2019 (GBD 2019 Mental Disorders Collaborators, 2022). In light of this data and the high risk of relapse, suicide rates, and substantial economic costs caused by this disease (American Psychiatric Association, 2013; GBD 2019 Mental Disorders Collaborators, 2022), further investigation of the mechanisms of MDD and especially its effective treatments is necessary.

Following Beck's (1967) cognitive theory of depression, patients with depressive disorders suffer from the so-called cognitive triad of a negative view of themselves, the world, and their future and, therefore, have a mood-congruent negative bias. Consequently, this results in impairments in information and emotion processing and regulation (Joormann and Quinn, 2014). Over the last decades, the conceptualization of MDD has progressively added a more biological framework: animal models (e.g., Deussing, 2006) and neurobiological models of depression emerged (Mayberg, 2003; Phillips et al., 2003; Willner et al., 2013), accompanied by supportive evidence from imaging studies (Beck, 2008; for reviews, see: Borsini et al., 2020 (reward processing); Krause et al., 2021 (facial emotion processing); Villalobos et al., 2021 (cognitive control/emotion regulation)). Disner et al. (2011) postulate an integrated cognitive neurobiological model of depression, explaining

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https://doi.org/10.1016/j.jad.2024.09.084
Received 23 April 2024; Received in revised form 26 August 2024; Accepted 14 September 2024
Available online 17 September 2024

the negative cognitive biases in depressive patients assumed by Beck (1967) (comprising biased attention, processing, memory, and rumination) by dual-process-models of bottom-up limbic hyperactivity in combination with decreased top-down cognitive control, thereby resulting in functional alterations in predominantly limbic, striatal, cingulate and prefrontal areas.

Treatment guidelines for MDD recommend either pharmacotherapy, psychotherapy, or a combination of both treatments (American Psychological Association, 2019). It is argued that the neural mechanisms engaged in both modalities may differ (DeRubeis et al., 2008; Quidé et al., 2012). Additionally, Kalsi et al. (2017) empirically demonstrated different neurobiological outcomes between both treatments in patients with anxiety and depressive disorders in a meta-analysis. While the efficacy of both treatments is well established and candidate neural mechanisms of action of pharmacotherapy have been widely studied (e.g., alteration of neurotransmitter systems and long-term stimulation of neurogenesis; Willner et al., 2013), the examination of the effects of psychotherapy has often been limited to behavioral markers and self-report (Sankar et al., 2018). However, effective psychotherapy should also manifest neurobiologically (Kandel, 1998). CBT, as one of the most common forms of psychotherapy and in the context of mood disorders mainly influenced by Hollon and Beck (1979), is based on the interplay of dysfunctional behavior and cognitions and aims to identify and modify these (cognitive restructuring and behavioral activation) by skill acquisition and subsequent learning processes. Consistent with the dual-process models, DeRubeis et al. (2008) postulated that effective CBT for MDD may normalize emotion regulation by increasing prefrontal cortex activity, indicative of increased cognitive control exerting a top-down influence on reducing limbic hyperactivity.

However, neurobiological studies examining the effects of psychotherapy have yielded highly inconsistent results (Barsaglini et al., 2014), and the neurobiological mechanisms underlying CBT still remain unclear, which may in part be due to the wide heterogeneity of imaging methods used (e.g., SPECT, PET, sMRI, fMRI, task-based or resting-state approaches). Among these techniques, fMRI is the most widely used non-invasive method for investigating neural activity. By detecting changes in deoxyhemoglobin, the blood oxygen level-dependent (BOLD) contrast, fMRI delineates local alterations in the demand for oxygenated blood, thereby inferring changes in brain activity (Villringer and Dirnagl, 1995) during rest (resting-state fMRI) or task completion (task-based fMRI).

Prior reviews have often compared different imaging methods (Chalah and Ayache, 2018; Franklin et al., 2016). In order to reduce this heterogeneity and answer the question whether disparate results are merely a methodological artifact (Barsaglini et al., 2014), the present review will exclusively compare longitudinal task-based fMRI studies with samples of patients diagnosed with MDD or dysthymia (objective 1). However, in research about neurobiological mechanisms, treatment response emerges as a variable that could influence outcomes. Hence, the second objective of this review is to explore the relationship between longitudinal alterations in brain activity and improvements in clinical symptoms. Thus, the aim of this review is to provide a systematic overview of

(1) the effects of CBT in depressed patients on brain activity and
(2) the association of these neural changes with symptom improvement

in order to contribute to a better understanding of the neurobiological mechanisms of CBT in depressive disorders.

2. Methods

2.1. Search strategy

Studies investigating CBT effects on brain activity with task-based fMRI were identified through systematic database research on PubMed using the terms ('depressive disorder' OR 'depression') AND ('fMRI' OR 'functional MRI' OR 'functional magnetic resonance imaging') AND ('psychotherapy' OR 'psychotherapeutic' OR 'cognitive-behavioral therapy' OR 'cognitive-behavioural therapy' OR 'CBT'). The research focused on articles published before 8 February 2023. Furthermore, reference lists of included studies and retrieved reviews and meta-analyses were examined to identify additional relevant studies.

This systematic review was conducted and reported following the PRISMA guidelines (Page et al., 2021). The study selection process is illustrated in Fig. 1.

2.2. Eligibility criteria

Following the PICO framework (Page et al., 2021), studies meeting the following criteria were included in this review:

2.2.1. Participants

Only studies with participants suffering from an acute major depressive episode or acute dysthymia as primary diagnosis assessed by a clinical interview were included. Comorbidity was accepted except for bipolar disorder, psychosis, or substance dependency. Studies including samples with patients with other psychiatric disorders were included if the depressed sample was investigated separately. Studies were included if patients fell into the age range between 13 and 69, while studies only investigating late-life depression were excluded because neurobiological correlates of late-life depression seem to differ from those of early-onset depression (Bora et al., 2012). Single-case-studies were excluded. Different studies investigating overlapping samples were included if different tasks were used.

2.2.2. Intervention

Studies describing treatment with CBT between baseline- and follow-up-MRI-assessment were included. All types of CBT were possible, including sub-forms like Cognitive Behavioral Analysis System of Psychotherapy (CBASP; McCullough, 2003) or Behavioral Activation Therapy (BAT; Sturmey, 2009). Studies investigating group CBT or computerized CBT were included as well. Randomization to treatment was not necessary for inclusion. Additional treatment with antidepressants was allowed because the treatment guidelines for depression of moderate severity and above recommend a combination of psychotherapy and pharmacotherapy, and combination treatment thus more closely reflects the clinical practice under naturalistic conditions (Gelenberg et al., 2010; National Institute for Health and Care Excellence, 2022).

2.2.3. Comparison

Comparison groups were not required for inclusion because longitudinal changes within the depressed patients were investigated.

2.2.4. Outcome

For the first objective, studies were included if brain activity changes in the whole brain or region of interest (ROI) were assessed using task-based fMRI pre and post treatment with CBT. Regarding the second objective, inclusion criteria were an assessment of brain activity changes using task-based fMRI pre and post CBT treatment and, in addition, the measurement of clinical symptom severity pre and post intervention. Studies were included if they reported the association of brain activity changes and clinical symptom severity changes pre and post therapy.

Only task-based fMRI studies were included, and resting state studies were excluded to reduce heterogeneity because brain activity deriving from unconstrained thinking during resting state is assumed to differ from activity during instructed tasks (Rayner et al., 2016).

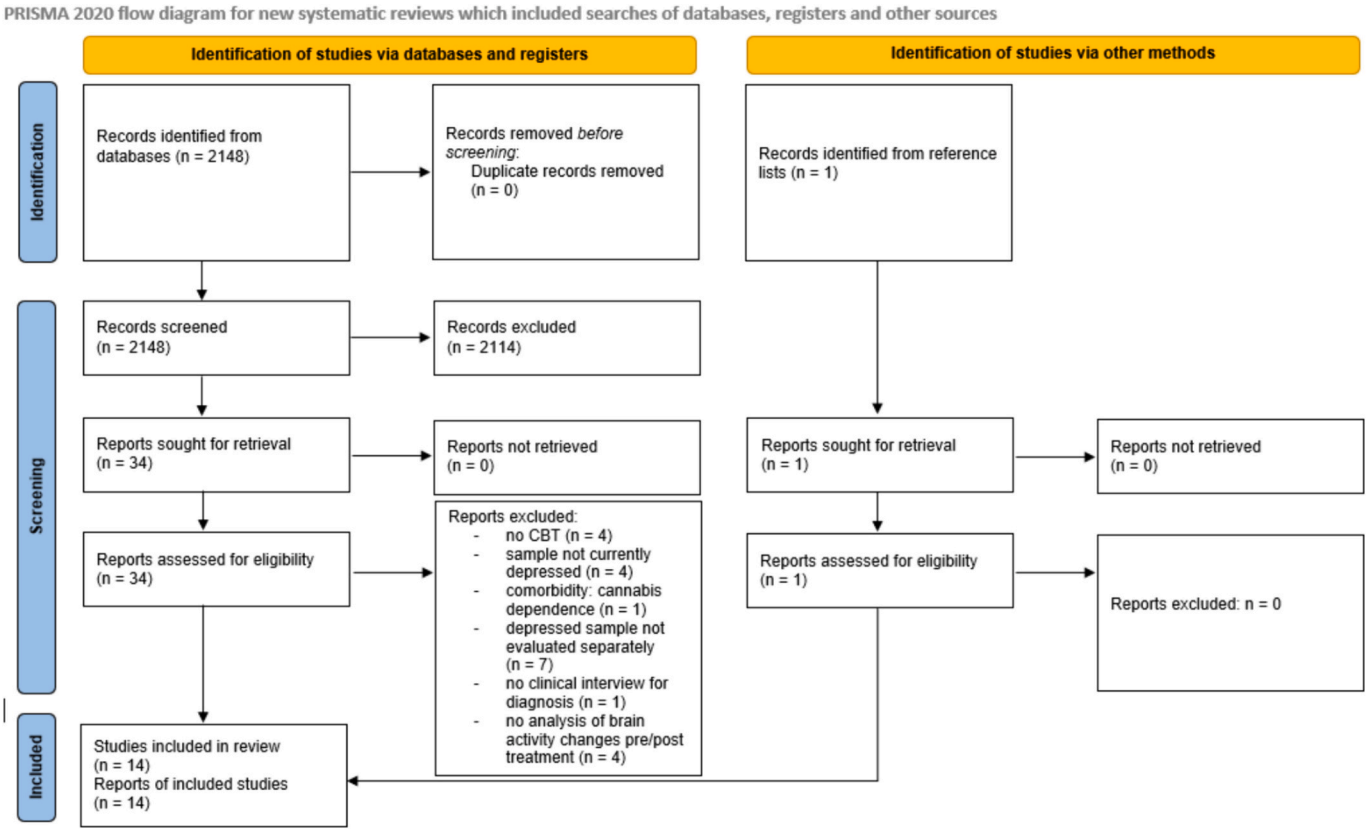

Fig. 1. PRISMA 2020 flow diagram for new systematic reviews.

2.3. Study selection and data collection procedure

The search results were screened by the first author by titles and abstracts. The first author then checked potentially relevant full-text articles for eligibility criteria. To test the reliability of the eligibility process, the third author rated the potentially relevant studies. Interrater reliability was very good with $\kappa = 0.94$, and differing judgment was resolved by consensus. Demographic and clinical characteristics of the samples, forms of CBT, fMRI-tasks, scan intervals, parameters of MRI assessment, and investigated ROIs were extracted.

3. Results

3.1. Characteristics of included studies

The request revealed 2148 results, and one additional article was identified through manual screening of reference lists from included studies and existing reviews and meta-analyses. After screening by title and abstract, 35 full-text articles were checked for eligibility, and 14 studies met the criteria for inclusion in this review. Among these, 12 studies examined longitudinal changes in brain activity (objective 1), while 7 studies additionally investigated these changes in relation to symptom improvement during CBT, and two studies solely explored neural changes associated with symptom improvement, resulting in 9 studies for objective 2.

For details regarding sample and treatment characteristics and fMRI assessment of included articles, see Table 1. All studies investigated patient groups meeting criteria for an acute major depressive episode or dysthymia assessed by a structured clinical interview (Structured clinical interview for DSM-IV (SCID-IV; $n = 11$), First et al., 1996; Clinical Interview Schedule-Revised (CIS-R; $n = 1$), Lewis et al., 1992; Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL; $n = 2$), Kaufman et al., 1997) as the primary diagnosis. Depression severity at baseline and follow-up was either assessed by the Beck Depression Inventory (BDI; Beck and Steer, 1978 or BDI-II; Beck et al., 1996), Hamilton Depression Rating Scale (HDRS-17; Hamilton, 1960), Children's Depression Rating Scale (CDRS; Poznanski and Mokros, 1996), Short Mood and Feelings Questionnaire (SMFQ; Angold et al., 1995) or Snaith-Hamilton Pleasure Scale (SHAPS; Snaith et al., 1995)). Treatment response was defined as a reduction of at least 50 % in depression severity scales post-CBT compared to baseline by the study's authors. $n = 7$ studies investigated classical CBT treatment, $n = 2$ examined group CBT, $n = 2$ computerized CBT, $n = 2$ studies BAT and $n = 1$ studied treatment with CBASP. Treatment durations ranged from 5 to 49 weeks. $N = 11$ studies included a sample of healthy controls, $n = 3$ studies investigated a depressed comparison sample (waiting list or control treatment), and one study lacked a comparison group. The fMRI tasks were mainly affective processing tasks ($n = 7$; Chuang et al., 2016; Dichter et al., 2010; Fu et al., 2008; Klein et al., 2014; Ritchey et al., 2011; Rubin-Falcone et al., 2018, 2020) primarily using emotional stimuli extracted from established databases or frequently used monetary reward processing tasks that have shown to elicit reward circuit activation ($n = 4$; Dichter et al., 2009; Hanuka et al., 2022; Queirazza et al., 2019; Straub et al., 2015). The remaining tasks contained statements assessing dysfunctional attitudes (Sankar et al., 2015), self-referential material (Yoshimura et al., 2014), and a future-thinking task (Katayama et al., 2021).

Methodologically, most studies ($n = 8$) calculated group-by-time interactions (followed by post-hoc tests), and $n = 4$ studies calculated *t*-tests to detect longitudinal activity changes. Regression analyses ($n = 3$), correlations ($n = 8$), or both were conducted for the investigation of objective 2. Most a priori ROIs were limbic areas such as the amygdala ($n = 5$) and hippocampus ($n = 2$), components of the striatum (nucleus accumbens (NAcc), putamen, caudate; $n = 3$), and parts of the cingulate ($n = 6$) and prefrontal cortex (PFC; $n = 5$). $n = 9$ studies performed

Table 1
Sample characteristics, study design and MRI assessment of included studies.

Reference	Sample characteristics									Study design and MRI assessment									
	MDD	Diagnosis[e]	Comparison group	Age in years[e] *M* (*SD*)	Sex[e] (m/f)	Clinical interview[e]	Mood scale[e] *M* (*SD*)	Comorbidity[e]	Medication[e]	CBT form	Number of sessions	Pre-post-scan interval in weeks	Therapy response	Field strength scanner (T)	Task domain	Paradigm	Contrasts	Atlas/templates	Whole brain	ROIs
Chuang et al. (2016)	13	Moderate or severe MDD	20 HC	15.56 (1.28)	0/33	K-SADS-PL	SMFQ = 18.15 (4.81)	Possible	Possible	CBT	5–21; *M* = 12.85 (4.49)	243.15 days (49.81)	[a]	3	Affective processing	Affective go/no-go task (happy/sad/neutral words)	Sad/happy vs. sad/neutral; happy/sad vs. happy/neutral	MNI	No	All activated/deactivated regions identified via whole brain analysis using whole sample (left OFC)
Dichter et al. (2009)	12[b]	MDD or dysthymia	15 HC	39.0 (10.4)	6/6	SCID IV	HDRS-17 = 23.8 (2.3); BDI = 27.1 (5.1)	None	None	BAT	8–14; *M* = 11.4 (2.0)	15	9/12	4	Monetary reward processing	Wheel of fortune task	Selection and anticipation: monetary vs. control; feedback: win vs. control, loss vs. control	FSLView v3.0	Yes	–
Dichter et al. (2010)	12[b]	MDD or dysthymia	15 HC	39.0 (10.4)	6/6	SCID IV	HDRS-17 = 23.8 (2.3); BDI = 27.1 (5.1)	None	None	BAT	8–14; *M* = 11.4 (2.0)	15	9/12	4	Affective processing	Forced-choice reaction time target detection task (sad/neutral pictures)	Targets in sad blocks vs. targets in neutral blocks	FSLView v3.0	Yes	
Fu et al. (2008)	16[c]	MDD	16 HC	40.0 (9.4)	3/13	SCID IV	HDRS-17 = 20.9 (1.9); BDI = 38.0 (11.7)	None (Axis 1)	None	CBT	16	16	13/16	1.5	Affective processing	Implicit sad facial affect recognition task	Mean overall activity: baseline vs. facial; load-response: response elicited by linear trend between intensities of sadness at facial trials	Talairach	Yes	Amygdala
Hanuka et al. (2022)	26	Mild or moderate MDD	42 HC; 26 MDD with attention control	30.42 (8.30)	10/16	SCID IV	SHAPS = 29.76 (5.96)	No significant suicidal ideation	None	iCBT	6	10	[a]	3	Monetary reward processing	Monetary incentive delay task	Reward anticipation and reward feedback vs. baseline	MNI	Yes	NAcc, putamen, caudate, sgACC
Katayama et al. (2021)	16	MDD with CBT	15 MDD with talking control	[a]	[a]	SCID IV	HDRS-17 = 20.2 (1.1)	3 patients with anxiety disorders	Possible	CBT	16	16	[a]	3	Other	Future-thinking task	Conditions: distant future; near future; distant past; near past,	MNI	Yes	Frontopolar cortex (distant future)
Klein et al. (2014)	10	CD	10 HC	38.2 (13.2)	4/6	SCID IV	HDRS-17 = 16.6 (2.2); BDI-II = 29.1 (10.2)	No BPS, no suicidal ideation	1 patient (stable)	CBASP	*M* = 15.8 (3.6)	12	6/10	1.5	Affective processing	Implicit and explicit emotional processing task	Implicit/explicit; emotion (fearful, sad, happy, neutral)	Talairach	No	Amygdala, cingulate

(*continued on next page*)

Table 1 (*continued*)

Reference	Sample characteristics									Study design and MRI assessment									
	MDD	Diagnosis[e]	Comparison group	Age in years[e] *M* (*SD*)	Sex[e] (m/f)	Clinical interview[e]	Mood scale[e] *M* (*SD*)	Comorbidity[e]	Medication[e]	CBT form	Number of sessions	Pre-post-scan interval in weeks	Therapy response	Field strength scanner (T)	Task domain	Paradigm	Contrasts	Atlas/templates	Whole brain	ROIs
Queirazza et al. (2019)	25	MDD	–	[a]	[a]	CIS-R	BDI ≥ 14	None	None	cCBT	[a]	6–10 weeks cCBT + 2 months waiting before scan 2	18/7	3	Monetary reward processing	Probabilistic reversal-learning task	Win/loose	MNI	No	Amygdala, striatum
Ritchey et al. (2011)	11	Moderate or severe MDD	14/7 HC (pre/post, post was excluded)	[a]	3/8	SCID IV	[a]	Anxiety disorders	None	CBT	10–35; *M* = 20.7 (7.6)	10–49, *M* = 30.3	[a]	1.5	Affective processing	Emotion evaluation task	Overall: all trials vs. baseline; arousal: negative+positive vs. neutral; valence: negative vs. positive	MNI	No	ROIs with significant differences in activity compared to HC at baseline[f]
Rubin-Falcone et al. (2018)	23[d]	MDD	12 HC	[a]	[a]	SCID IV	[a]	Anxiety and personality disorders possible	None	CBT	14	12	14/23	3 (2 different scanners, as covariate in analyses)	Affective processing	Voluntary emotion regulation task while recalling negative autobiographical memories	Feel vs. analyze	MNI	Yes	Lingual G., sgACC, medial PFC
Rubin-Falcone et al. (2020)	23[d]	MDD	11 HC	[a]	[a]	SCID IV	[a]	Anxiety and personality disorders possible	None	CBT	14	12	14/23	3 (2 different scanners, as covariate in analyses)	Affective processing	Image-based reappraisal task	Look negative > look neutral; distance negative > look negative; look negative > distance negative	MNI	Yes	Emotional reactivity: amygdala, sgACC; emotion regulation: right angular G., right mid-frontal cortex, left temporal cortex, left occipital cortex, left inferior frontal G., sgACC, right frontal cortex
Sankar et al. (2015)	16[c]	MDD	16 HC	40.00 (9.27)	3/13	SCID IV	HDRS-17 = 20.9 (1.9)	None (Axis I)	None	CBT	16	16	13/16	1.5	Other	Dysfunctional attitudes task	Regular attributions vs. control statements; extreme attributions vs. control statements	Talairach	Yes	–
Straub et al. (2015)	10/18[g]	MDD	12 MDD (waiting list)	16.39 (1.58)/16.66 (1.37)	2/8 / 3/15	K-SADS-PL	CDRS = 56.70 (11.28)/	Anxiety disorders (2/5), ADD (1), conduct	None	CBT (group)	5	5	[a]	3	Monetary reward processing	Monetary incentive task	Win vs. loss	MNI	No	sgACC, hippocampus, amygdala, NAcc

(*continued on next page*)

Table 1 (*continued*)

Reference	Sample characteristics									Study design and MRI assessment										
	MDD	Diagnosis[e]	Comparison group	Age in years[e] *M* (*SD*)	Sex[e] (m/f)	Clinical interview[e]	Mood scale[e] *M* (*SD*)	Comorbidity[e]	Medication[e]	CBT form	Number of sessions	Pre-post-scan interval in weeks	Therapy response	Field strength scanner (T)	Task domain	Paradigm	Contrasts	Atlas/ templates	Whole brain	ROIs
Yoshimura et al. (2014)	23	MDD	15 HC	37.3 (7.2)	16/7	SCID IV	56.11 (9.11) HDRS-17 = 11.0 (4.8); BDI = 21.4 (8.5)	disorder (0/1) No significant suicidal ideation	All patients (stable)	CBT (group)	12	~12	[a]	1.5	Other	Self-referential task using emotional trait words	Self-reference vs. control for positive and negative words	MNI	Yes	–

MDD, major depressive disorder; CD, chronic depression; HC, healthy controls; ROI, region of interest; SCID-IV, Structured Clinical Interview for DSM-IV; CIS-R, Clinical Interview Schedule-Revised; K-SADS-PL, Kiddie-Schedule for Affective Disorders and Schizophrenia Present and Lifetime; BDI, Beck Depression Inventory; HDRS, Hamilton Depression Rating Scale; SMFQ, Short Mood and Feelings Questionnaire; SHAPS, Snaith-Hamilton Pleasure Scale; CDRS, Children's Depression Rating Scale – Revised; BPS, Borderline Personality disorder; CBT, cognitive behavioral therapy; iCBT, internet-based CBT; cCBT, computerized CBT; BAT, Behavioral Activation Therapy; CBASP, Cognitive Behavioral Analysis System of Psychotherapy; MNI, Montreal Neurological Institute and Hospital; NAcc, Nucleus Accumbens; sgACC, subgenual anterior cingulate cortex; PFC, prefrontal cortex. Analyzes were conducted in both samples.

[a] Not reported (for final sample).

[b] Overlapping samples of Dichter et al. (2009) and Dichter et al. (2010).

[c] Overlapping samples of Fu et al. (2008) and Sankar et al. (2015).

[d] Overlapping samples of Rubin-Falcone et al. (2018) and Rubin-Falcone et al. (2020).

[e] Patient sample.

[f] Overall activity: ventromedial PFC, superior frontal G., fusiform G., superior parietal lobule, lingual G., cuneus; arousal-related activity: amygdala, caudate, hippocampus, dorsolateral PFC, mid-cingulate G., superior temporal G., paracentral lobule, superior parietal lobule; valence-related activity: anterior temporal lobe/ventrolateral PFC, dorsolateral PFC, insula, dorsal ACC, superior frontal sulcus, medial frontal G., ventrolateral PFC, precentral G., hippocampus, superior temporal G., inferior temporal G., inferior parietal lobule, precuneus, middle occipital G., fusiform G.

[g] Initially $N = 10$ patients, due to ethical reasons, $N = 8$ patients of the waiting group received treatment after the waiting period, extending the complete sample size to $N = 18$.

whole brain analyses. All reported significant results of the studies are summarized in the supplemental material and Table 2 shows the significant differences within patient samples.

3.2. Synthesis of longitudinal brain activity changes

Due to theoretically assumed alterations in brain function among depressive patients (Disner et al., 2011) and the congruent selection of a priori ROIs in the included studies, evidence of longitudinal brain activity changes in limbic, cingulate, striatal, and prefrontal areas among the MDD patients is further synthesized and provided in Table 3, subsequently summarized in the following.

3.2.1. Limbic system

Six out of seven studies that investigated effects in limbic areas such as the amygdala and (para)hippocampus found significant alterations in activity during various tasks, including emotion and reward processing, as well as dysfunctional attitudes. After CBT, reduced activity was primarily observed: during tasks involving the attribution of dysfunctional attitudes (Sankar et al., 2015), affective processing (Fu et al., 2008; Ritchey et al., 2011 (valence: negative and neutral stimuli)) and reward processing (Dichter et al., 2009 (monetary selection); Straub et al., 2015). However, Dichter et al. (2009) also noted increased activity in monetary anticipation following therapy, as did Klein et al. (2014) during affective processing. Ritchey et al. (2011) found no significant changes in the valence contrast in the hippocampus, and Rubin-Falcone et al. (2020) in the amygdala during emotion regulation. Among the two studies examining effects relative to symptom improvement, one observed a negative correlation between amygdalar activity and BDI score change (Queirazza et al., 2019). In contrast, Rubin-Falcone et al. (2020) found no correlation.

3.2.2. Cingulate

Among the nine studies investigating effects within the cingulate, six demonstrated differently directed significant changes: Increased activity in the anterior cingulate cortex (ACC) and decreased activity in the posterior cingulate cortex (PCC) during affective processing (Fu et al., 2008), heightened ventral ACC (vACC) activity following therapy when exposed to positive self-referential stimuli (Yoshimura et al., 2014), as well as decreased activity in response to such negative stimuli (Yoshimura et al., 2014) and dysfunctional attitudes (Sankar et al., 2015), and mixed findings in the ACC for reward stimuli (Straub et al., 2015: decrease; Hanuka et al., 2022: increase for monetary feedback, no significant results for monetary anticipation). Conversely, three studies did not observe significant changes in this area during affective processing (Klein et al., 2014; Ritchey et al., 2011; Rubin-Falcone et al., 2020) and monetary anticipation (Hanuka et al., 2022). Four out of five studies that examined effects related to symptom improvement revealed significant positive associations: Hanuka et al. (2022; monetary reward) and Yoshimura et al. (2014; negative self-referential stimuli) where a greater increase in activity was linked with fewer symptoms, while Straub et al. (2015; monetary reward) and Rubin-Falcone et al. (2018; affective processing) reported greater decreases in activity associated with fewer symptoms. Rubin-Falcone et al. (2020; affective processing) did not find these associations.

3.2.3. (Pre)frontal cortex

Seven out of eight studies investigating differences in (pre)frontal areas found significant activity changes. During affective processing, Chuang et al. (2016) observed decreased activity in the orbitofrontal cortex (OFC) following psychotherapy, Dichter et al. (2010) revealed reduced activity in the OFC, alongside increased activity in the right frontal pole and right inferior frontal gyrus (FG) after BATD, Fu et al. (2008) showed increased activity after CBT in the superior FG, while Ritchey et al. (2011) showed decreased activity in the ventrolateral PFC (vlPFC) following therapy. Katayama et al. (2021) reported decreased frontopolar cortex activity during future thinking after therapy. Yoshimura et al. (2014) revealed increased medial PFC (mPFC) activity during the presentation of positive and decreased BOLD-activity during negative self-referential material after psychotherapy. Dichter et al. (2009) reported diminished activity following psychotherapy during monetary selection in the superior FG and monetary feedback in the OFC, alongside increased activation during monetary anticipation in the FG. Conversely, two studies did not find significant changes in PFC structures during affective processing tasks (ROIs ventromedial PFC, dorsolateral PFC, FG, superior frontal sulcus: Ritchey et al., 2011; ROIs FG, mid-frontal cortex, frontal cortex: Rubin-Falcone et al., 2020). Considering symptom improvement, two out of four studies investigating effects revealed significant results: during affective processing, Rubin-Falcone et al. (2018) revealed a positive association between greater reduction of activity in the mPFC-ROI and medial frontal pole on whole brain level and lower BDI-scores after therapy as well as Rubin-Falcone et al. (2020) in the dorsolateral PFC on whole brain level. Contrary, no associations were found in certain studies (ROI OFC during affective processing: Chuang et al., 2016; ROI frontopolar cortex during future thinking: Katayama et al., 2021; ROIs FG, mid-frontal cortex, frontal cortex during affective processing: Rubin-Falcone et al., 2020).

3.2.4. Striatum

Four out of five studies reported significant effects in the NAcc, caudate, and putamen. There were consistent findings of increased BOLD-activity in response to rewards after CBT (Dichter et al., 2009 (monetary selection and monetary anticipation); Hanuka et al., 2022 (monetary feedback)) and decreased activity in the caudate during future thinking (Katayama et al., 2021) and emotion processing (Ritchey et al., 2011). A contradictory result was significantly decreased activity in the caudate during monetary feedback (Dichter et al., 2009), while Straub et al. (2015) did not observe significant changes in the NAcc-ROI as well as Hanuka et al. (2022) in the ROIs of the putamen and caudate during monetary reward and in the NAcc during monetary anticipation. Among the two studies investigating associations between signal change and symptom improvement, significant changes were observed in one: During monetary anticipation, Hanuka et al. (2022) revealed a significant positive association between NAcc activity increase and symptom decrease, while this association was not evident for the putamen and caudate ROIs or in the study by Queirazza et al. (2019) in the striatum-ROI.

4. Discussion

This review aimed to summarize alterations in brain activity observed in patients diagnosed with MDD or dysthymia pre and post CBT employing task-based fMRI and the association of these neural changes with symptom improvement. The most consistent findings were BOLD-activity changes in structures of cortico-limbic brain loops and the reward system, including limbic areas, striatal structures, and the PFC and cingulate. Especially with regard to the first objective of this review, there is evidence for (1) reduced limbic reactivity in MDD patients after CBT during affective and reward processing and the processing of dysfunctional attitudes, (2) increased activity of striatal structures during reward processing and decreased activity during affective processing and future thinking and (3) altered activity in the cingulate and PFC across different tasks, as it is visualized in Fig. 2. This indicates improved neural emotion processing and regulation abilities in depressed patients after therapy and increased neural reward receptiveness. Thus, the reduction of negative cognitive biases after CBT is also visible on a neural level. Regarding the second objective, the most consistent findings are relationships between the activity change in the subgenual ACC (sgACC) and symptom improvement, as well as between prefrontal areas and symptom improvement during affective processing.

Table 2
Significant results of included studies.

Reference	Field of view	Contrast	Effects of CBT		Association with symptom improvement	
			Analyses	Significant results in MDD patients	Analyses	Significant results
Chuang et al. (2016)	ROI	Sad/happy vs. sad/neutral	ANCOVA 2 (group) × 2 (time) (covariate: age)	↓ left orbitofrontal cortex	Partial correlation (covariate: age) pre-post signal changes and SMFQ-improvement, normalized by baseline-SMFQ-score	–
Dichter et al. (2009)	Whole brain	Monetary selection (monetary vs. control)	2 (group) × 2 (time); two-tailed within-group *t*-tests (α = 0.05) in clusters with significant interactions	↑ left putamen, right supramarginal G., left posterior temporal fusiform G. ↓ left amygdala, left superior frontal G., left superior lateral occipital cortex, left occipital pole, left postcentral G., left precentral G., left supramarginal G., right inferior temporal G.	–	
		Monetary anticipation (monetary vs. control)		↑ left caudate, left cingulate G., left frontal G., left hippocampus, right insular cortex, left lingual G., occipital cortex, left parahippocampal G., precentral G., right precuneus, right subcallosal cortex, right temporal fusiform cortex, left temporal pole ↓ right precuneus, left inferior temporal G.		
		Monetary feedback (win vs. control)		↑ right superior occipital cortex, left planum temporale, right posterior temporal fusiform cortex ↓ left caudate, left posterior cingulate G., right paracingulate G., left postcentral G., superior anterior temporal G.		
		Monetary feedback (non-win vs. control)		↑ left angular G., left orbitofrontal cortex, left lingual G., right posterior planum polare ↓ left superior occipital cortex, left precentral G., left anterior supramarginal G.		
Dichter et al. (2010)	Whole brain	Sad - neutral	2 (group) × 2 (time); two-tailed within-group *t*-tests (α = 0.05) in clusters with significant interactions	↑ right frontal pole, right inferior frontal G. (pars triangularis), left precentral G. ↓ right orbitofrontal cortex, left Heschl's G., left occipital pole, right pallidum, left paracingulate G., postcentral G., precentral G., left temporal G., right temporal G., right supramarginal G.	–	
Fu et al. (2008)	ROI whole brain	Mean overall activity (baseline vs. sad faces)	ANOVA 2 (group) × 2 (time)	↓ right amygdala, hippocampus ↑ ACC, superior frontal G., posterior cingulate G., inferior parietal cortex, precuneus	–	
		Linear load response activity (low vs. medium vs. high intensity of sadness)		↓ fusiform and lingual G., left lateral temporal cortex, inferior parietal cortex, posterior cingulate cortex, precuneus		
Hanuka et al. (2022)	ROI	Reward feedback vs. baseline	ANOVA 3 (group) × 2 (time), for significant regions additional 3 (group) × 2 (time) ANOVA for feedback type (reward/neutral)	↑ NAcc and sgACC to reward (not neutral) feedback: ↑ sgACC	Regression of pre-post signal changes on SHAPS-improvement (reward feedback, controlling for neutral feedback)	NAcc and subgenual ACC: ↑ activation pre-post ➔ ↑ SHAPS-improvement
Katayama et al. (2021)	Whole brain	Distant future Near future	Within-group *t*-tests	↓ frontopolar cortex (BA10) ↓ right caudate ↑ right precentral G.	–	
		Distant past		↓ right precuneus (BA7) ↑ insula		
		Near past		↓ left precuneus (BA7)		
	ROI	Distant future		↓ medial frontopolar cortex (BA10)	Correlation pre-post signal changes in BA10 and HDRS-changes	–
Klein et al. (2014)	ROI	Implicit; implicit and explicit	ANOVA 2 (group) × 2 (time)	↑ left amygdala	–	

(*continued on next page*)

Table 2 (*continued*)

Reference	Field of view	Contrast	Effects of CBT		Association with symptom improvement	
			Analyses	Significant results in MDD patients	Analyses	Significant results
Queirazza et al. (2019)	ROI	Parameter estimates responder > non-responder	–		Correlation pre-post signal changes in the right striatum and right amygdala and symptom change	Right amygdala: $r = -0.60$ ($p = .001$)
Ritchey et al. (2011)	ROI	Arousal (emotional vs. neutral)	Within-group *t*-tests	Negative and neutral: ↓, positive: ↑ right amygdala, right caudate, left hippocampus (larger differences post vs. pre)	–	
		Valence (negative vs. positive)		↓ left anterior temporal lobe/ ventrolateral PFC		
Rubin-Falcone et al. (2018)	Whole brain	Feel vs. analyze	–		Regression of post-BDI and -HDRS (covariate: pre-BDI/-HDRS) on pre-post signal changes (F-tests)	↑ deactivation pre-post in lingual G./cerebellum, left precentral G./putamen, left medial frontal pole/sgACC, left supramarginal G. ➔ ↑ BDI-improvement ↑ deactivation pre-post in lingual G. ➔ ↑ HDRS-improvement
	ROI				correlation pre-post signal changes and post-BDI (covariate: baseline-BDI)	medial PFC: $r = -0.44$ ($p = .034$)
Rubin-Falcone et al. (2020)	Whole brain	Emotional reactivity (negative > neutral)	Within-group *t*-tests	–	Regression of pre-post signal changes on post-BDI and - HDRS (covariate: pre-BDI/pre-HDRS)	–
		Emotion regulation activity (regulate negative > look negative), emotion		–		↑ deactivation pre-post in right dorsolateral PFC, precuneus, lateral occipital cortex ➔ ↑ BDI-improvement
	ROI	Regulation deactivation (inverse)	Between-groups *t*-tests	–	Correlation pre-post signal changes and post-BDI/HDRS D (covariate: pre-BDI/-HDRS)	–
Sankar et al. (2015)	Whole brain	Extreme attributions vs. control sentences	ANOVA 2 (group) × 2 (time)	↓ left parahippocampal G. (BA37), right posterior cingulate G. (BA30)	Correlation pre-post signal changes in left precentral G. and HDRS-improvement	$r = 0.74$ ($pcorr = 0.004$)
Straub et al. (2015)	ROI	Win-loss	Within-group *t*-tests one-tailed between-groups *t*-tests in areas with significant win-loss-differences	↓ amygdala, hippocampus, subgenual ACC ↓ left amygdala, left hippocampus, right subgenual ACC	Correlation pre-post signal changes in subgenual ACC and BDI- and CDRS-R-improvement	BDI: left: $r = 0.57$ ($p = .01$); right: $r = 0.54$ ($p = .02$)
Yoshimura et al. (2014)	Whole brain	Self-reference vs. control	ANOVA 2 (group) × 2 (time) × 2 (valence) (covariate: sex)	For self/positive condition ↑, for self/negative condition ↓ left ventral ACC, left superior temporal cortex, left medial PFC	Correlation pre-post signal changes and rumination-improvement	Ventral ACC-changes in self/ negative condition: $r = 0.49$ ($p < .05$); $r2 = 0.24$ ($p < .05$)

↑, activity-increase after CBT; ↓, activity-decrease after CBT; G., gyrus; ROI, region of interest; BDI, Beck Depression Inventory; HDRS, Hamilton Depression Rating Scale; SMFQ, Short Mood and Feelings Questionnaire; SHAPS, Snaith-Hamilton Pleasure Scale; CDRS, Children's Depression Rating Scale – Revised; NAcc, Nucleus Accumbens; ACC, anterior cingulate cortex; PFC, prefrontal cortex.

4.1. Discussion of longitudinal brain activity changes

4.1.1. Limbic system

With six out of seven studies revealing effects, the amygdala-hippocampus-complex could clearly be identified as a core region where longitudinal changes after CBT occur. According to the cognitive neurobiological model of depression from Disner et al. (2011), increased amygdala activity is a key component of the neurobiological architecture of negative cognitive biases and, additionally, hippocampal overactivity is assumed to be involved in biased memory and rumination. Given this hyperactivity during depressive state, theoretically, an activity reduction would be expected after successful therapy, normalizing the neuronal patterns.

In line with this, most studies reported decreased amygdala activity after therapy during different tasks, including affective processing (Fu et al., 2008; Ritchey et al., 2011), monetary reward (Dichter et al., 2009; Straub et al., 2015) and dysfunctional attitudes (Sankar et al., 2015). Moreover, Queirazza et al. (2019) could also show an association between amygdala-activity-change and symptom improvement, showing that patients with greater activity decrease had a greater symptom improvement during monetary reward. The only contrary results were found by Klein et al. (2014) and Rubin-Falcone et al. (2020), which might be explained due to methodological issues (e.g., no baseline differences between patients and HCs). For the hippocampus, also predominantly decreased activity after therapy occurred during affective processing (Fu et al., 2008; Ritchey et al., 2011) and monetary reward (Straub et al., 2015), as well as for the parahippocampal gyrus during the presentation of dysfunctional attitudes (Sankar et al., 2015). However, Dichter et al. (2009) revealed contrarily increased activity during monetary anticipation.

Taken together, the functional adjustment of the amygdala-hippocampus-complex could be identified as a potential neurobiological mechanism of CBT. These findings are in line with the implications of other reviews (Chalah and Ayache, 2018; Franklin et al., 2016). The results suggest reduced limbic reactivity after CBT not only for affective processing but also for stimuli like dysfunctional attitudes or rewards.

Table 3
Qualitative synthesis of results in limbic, cingulate, prefrontal and striatal areas.

Investigated brain region	Effects of psychotherapy								Association with symptom improvement							
	N	Significant results	Direction	Domain	Analysis	Nonsignificant results	Domain	Analysis	*N*	Significant results	Direction	Domain	Analysis	Nonsignificant results	Domain	Analysis
Limbic system	6/7	Dichter et al. (2009)	↓	Monetary reward (selection)	Whole brain amygdala	Ritchey et al. (2011)	Affective processing (valence)	ROI hippocampus	1/2	Queirazza et al. (2019)	↓ → ↓	Monetary reward	ROI amygdala	Rubin-Falcone et al. (2020)	Affective processing	ROI amygdala
		Dichter et al. (2009)	↑	Monetary reward (anticipation)	Whole brain hippocampus, parahippocampal G.	Rubin-Falcone et al. (2020)	Affective processing	ROI amygdala								
		Fu et al. (2008)	↓	Affective processing	ROI amygdala, hippocampus											
		Klein et al. (2014)	↑	Affective processing	ROI amygdala											
		Ritchey et al. (2011)	↓	Affective processing (arousal: negative/neutral)	ROI amygdala, hippocampus											
		Sankar et al. (2015)	↓	Other (dysfunctional attitudes)	Whole brain parahippocampal G.											
		Straub et al. (2015)	↓	Monetary reward	ROI amygdala, hippocampus											
Cingulate	6/9	Dichter et al. (2009)	↑	Monetary reward (anticipation)	Whole brain cingulate G.	Hanuka et al. (2022)	Monetary reward (anticipation)	ROI subgenual ACC	4/5	Hanuka et al. (2022)	↑ → ↓	Monetary reward	ROI subgenual ACC	Rubin-Falcone et al. (2018)	Affective processing	ROI subgenual ACC
		Dichter et al. (2009)	↓	Monetary reward (anticipation)	Whole brain posterior cingulate G., paracingulate G.	Klein et al. (2014)	Affective processing	ROI cingulate		Rubin-Falcone et al. (2018)	↓ → ↓	Affective processing	Whole brain subgenual ACC	Rubin-Falcone et al. (2020)	Affective processing	ROI subgenual ACC
		Fu et al. (2008)	↑	Affective processing	Whole brain ACC, posterior cingulate G.	Ritchey et al. (2011)	Affective processing	ROI dorsal ACC, mid-cingulate G.		Straub et al. (2015)	↓ → ↓	Monetary reward	ROI subgenual ACC			
		Fu et al. (2008)	↓	Affective processing	Whole brain posterior cingulate cortex	Rubin-Falcone et al. (2020)	Affective processing	ROI subgenual ACC		Yoshimura et al. (2014)	↓ → ↓	Other (self-referential)	Whole brain ventral ACC			
		Hanuka et al. (2022)	↑	Monetary reward (feedback)	ROI sgACC											
		Sankar et al. (2015)	↓	Other (dysfunctional attitudes)	Whole brain posterior cingulate G.											
		Straub et al. (2015)	↓	Monetary reward	ROI subgenual ACC											
		Yoshimura et al. (2014)	↑	Other (positive self-referential)	Whole brain ventral ACC											
		Yoshimura et al. (2014)	↓	Other (negative self-referential)	Whole brain ventral ACC											

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Table 3 (*continued*)

Investigated brain region	Effects of psychotherapy								Association with symptom improvement							
	N	Significant results	Direction	Domain	Analysis	Nonsignificant results	Domain	Analysis	*N*	Significant results	Direction	Domain	Analysis	Nonsignificant results	Domain	Analysis
PFC	7/8	Chuang et al. (2016)	↓	Affective processing	ROI OFC	Ritchey et al. (2011)	Affective processing	ROI ventromedial PFC, dorsolateral PFC, frontal G., superior frontal sulcus	2/4	Rubin-Falcone et al. (2018)	↓ → ↓	Affective processing	ROI medial PFC, whole brain medial frontal pole	Chuang et al. (2016)	Affective processing	ROI OFC
		Dichter et al. (2009)	↑	Monetary reward (anticipation)	Whole brain frontal G.	Rubin-Falcone et al. (2020)	Affective processing	ROI frontal G., mid-frontal cortex, frontal cortex		Rubin-Falcone et al. (2020)	↓ → ↓	Affective processing	Whole brain dorsolateral PFC	Katayama et al. (2021)	Other (future thinking)	ROI frontopolar cortex
		Dichter et al. (2009)	↓	Monetary reward (selection)	Whole brain superior frontal G.									Rubin-Falcone et al. (2020)	Affective processing	ROI frontal G., mid-frontal/ frontal cortex
		Dichter et al. (2009)	↑	Monetary reward (feedback non-win)	Whole brain OFC											
		Dichter et al. (2010)	↓	Affective processing	Whole brain OFC, right frontal pole											
		Dichter et al. (2010)	↑	Affective processing	Whole brain right inferior frontal G.											
		Fu et al. (2008)	↑	Affective processing	Whole brain superior frontal G.											
		Katayama et al. (2021)	↓	Other (future thinking)	ROI frontopolar cortex, whole brain frontopolar cortex											
		Ritchey et al. (2011)	↓	Affective processing	ROI ventrolateral PFC											
		Yoshimura et al. (2014)	↓	Other (negative self-referential)	Whole brain medial PFC											
		Yoshimura et al. (2014)	↑	Other (positive self-referential)	Whole brain medial PFC											
Striatum	4/5	Dichter et al. (2009)	↑	Monetary reward (selection)	Whole brain putamen	Hanuka et al. (2022)	Monetary reward (anticipation)	ROI NAcc	1/2	Hanuka et al. (2022)	↑ → ↓	Monetary reward (anticipation)	ROI NAcc	Hanuka et al. (2022)	Monetary reward	ROI putamen, caudate
		Dichter et al. (2009)	↑	Monetary reward (anticipation)	Whole brain caudate	Hanuka et al. (2022)	Monetary reward	ROI putamen, caudate						Queirazza et al. (2019)		ROI striatum
		Dichter et al. (2009)	↓	Monetary reward (feedback)	Whole brain caudate	Straub et al. (2015)	Monetary reward	ROI NAcc								
		Hanuka et al. (2022)	↑	Monetary reward (feedback)	ROI NAcc											

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Table 3 (*continued*)

Investigated brain region	Effects of psychotherapy						Association with symptom improvement					
	N Significant results	Direction	Domain	Analysis	Nonsignificant results	Domain	Analysis	*N* Significant results	Direction	Domain	Nonsignificant results	Domain	Analysis
	Katayama et al. (2021)	↓	Other (future thinking)	Whole brain caudate									
	Ritchey et al. (2011)	↓	Affective processing	ROI caudate									

N, number of studies reporting significant results/number of studies investigating effect; ↑, activity-increase after CBT; ↓, activity-decrease after CBT; ↓ → ↓, greater activity-decrease associated with greater symptom-score-decrease; ↑ → ↓, greater activity-increase associated with greater symptom-score-decrease; ROI, region of interest; G., gyrus; OFC, orbitofrontal cortex; ACC, anterior cingulate cortex; PFC, prefrontal cortex; NAcc, nucleus accumbens. Nonsignificant whole brain analyses not shown in this table due to visual reasons.

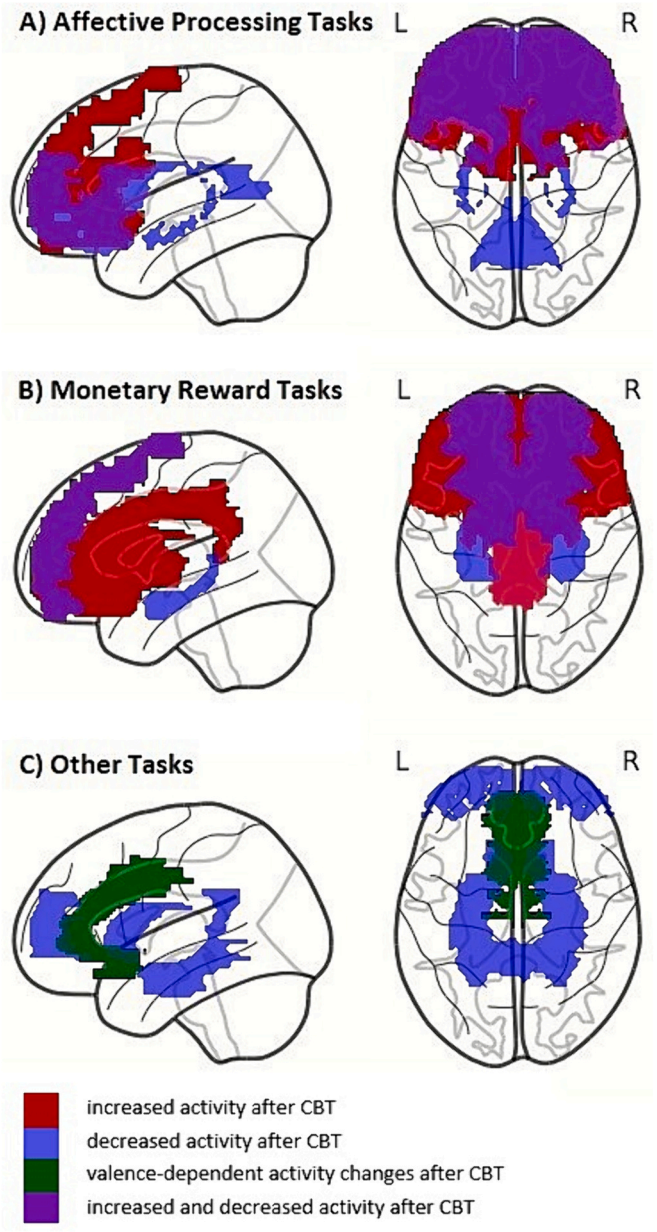

Fig. 2. Regions with revealed activity changes pre to post CBT depending on fMRI task domain.

This could reflect a diminished negative bias and improvements in emotion perception, it's appraisal, and processing. Partially, these alterations also seem associated with the (clinical) symptom improvement.

4.1.2. Cingulate

Evidence regarding cingulate cortex activity presents a mixed picture: six out of nine studies that investigated cingulate activity reported significant changes. Their direction was dependent on the task and location (ACC vs. PCC). During affective processing, heightened activity in the ACC occurred, whereas activity was decreased in the PCC (Fu et al., 2008), and an association between greater activity decreases and greater symptom improvement was revealed (Rubin-Falcone et al., 2018). The latter finding suggests a normalization of elevated ACC activity observed in MDD patients (Disner et al., 2011; Pilmeyer et al., 2022), contrasting Fu et al.'s (2008) result. During the processing of dysfunctional attitudes, activity decreases in the PCC were evident (Sankar et al., 2015), supporting the assumption that increased PCC

activity in MDD patients reflects ruminative thinking (Lin et al., 2021). Consequently, findings (Fu et al., 2008; Sankar et al., 2015) indicate that CBT might reduce ruminative thinking with observable neural correlates.

A meta-analysis by Groenewold et al. (2013) revealed heightened ACC activity toward negative stimuli and diminished activity toward positive stimuli in MDD patients. The results of Yoshimura et al. (2014), showing increased vACC activity after therapy during positive self-referential stimuli processing and decreased activity during negative stimuli processing, could be interpreted as a normalization of these patterns following CBT and a diminished negative bias resulting in more neural response to positive stimuli, better emotion regulation abilities and less rumination about negative stimuli, consistent with symptom reduction associations with activity changes in this region (Yoshimura et al., 2014).

In response to reward processing tasks, a pattern of activity increases in sgACC (Hanuka et al., 2022) and cingulate (Dichter et al., 2009) was observed, which is linked to improved symptomatology (Hanuka et al., 2022). The sgACC's involvement in reward circuits suggests enhancements in reward responsiveness post-CBT. Straub et al. (2015) reported decreased ACC activity differences between win and loss tasks following CBT, additionally linked to symptom-scale reduction, potentially indicating reduced loss aversion given ACC's involvement in error avoidance (Magno et al., 2009).

However, null results were reported in some studies (Klein et al., 2014; Ritchey et al., 2011; Rubin-Falcone et al., 2020), possibly due to methodological limitations (e.g., response rate, sample size, see limitations section). On the other hand, these inconsistencies may also reflect the multifunctional roles of the cingulate cortex (e.g., reward and emotion processing and regulation, self-referential processing, episodic memory, action-outcome learning processes) as discussed in the literature (Disner et al., 2011; Northoff and Bermpohl, 2004; Ochsner and Gross, 2005; Phillips et al., 2003; Rayner et al., 2016).

In summary, evidence suggests that CBT induces differential changes in task-induced activity within cingulate regions implicated in various impaired brain processes in MDD patients. Particularly, CBT modulates neural processing of self-referential, emotional, and reward-related stimuli, potentially reducing the negative bias toward more balanced regulation processes. Importantly, the sgACC emerges as the region with the most evidence regarding the second objective of this review: greater activity changes in this area seem to be related to greater symptom improvement in all except one study. Although some reviews and meta-analyses (Franklin et al., 2016; Sankar et al., 2018) revealed ACC activity changes as the most consistently reported neurobiological effects of psychotherapy, given the present results, however, this can only partly be agreed on.

4.1.3. (Pre)frontal cortex

Seven out of eight studies investigating differences in (pre)frontal regions found significant BOLD signal response changes following CBT. Key regions of MDD-associated dysregulations, such as negative bias, blunted reward sensitivity, and heightened rumination/self-referential negative thinking, are located within the prefrontal cortex (Disner et al., 2011; Ng et al., 2019; Northoff et al., 2006; Northoff and Bermpohl, 2004; Phillips et al., 2003).

Among studies investigating changes in affective processing after CBT, three noted significantly decreased BOLD signal response to negative stimuli (OFC: Dichter et al., 2010; frontal pole: Dichter et al., 2010; vlPFC: Ritchey et al., 2011). These results align with the assumption that decreased activity to negative stimuli might reflect neurobiological correlates of reduced negative bias in depressive patients following CBT (Phillips et al., 2003; Zhang et al., 2024). Contrarily, one study found decreased activity in response to positive affective stimuli in the right OFC post-CBT (Chuang et al., 2016), aligning with meta-analytic evidence of increased OFC activity toward positive stimuli in MDD patients (Groenewold et al., 2013). Accordingly, uncertainties persist regarding the role of the OFC in depressed patients, although CBT appears to modulate these activity patterns. Increased activity following CBT was observed in the superior FG (Fu et al., 2008), supporting a therapy-induced normalization of a hypoactive dorsal system and increased cognitive control according to neurobiological models of MDD (Disner et al., 2011; Phillips et al., 2003). Contradictory to Phillips et al.'s (2003) model, Dichter et al. (2010) revealed activity increases in the (ventral) inferior FG, and Rubin-Falcone et al. (2018, 2020) linked greater activity decreases in the mPFC, dlPFC and medial frontal pole with greater symptom improvement. This is in contrast to the assumption of DeRubeis et al. (2008) that CBT might increase neuronal cognitive control. Additionally, there were also null results in prefrontal areas during affective processing regarding objective 1 (Ritchey et al., 2011; Rubin-Falcone et al., 2020), possibly due to methodological issues and also regarding objective 2 (Chuang et al., 2016; Rubin-Falcone et al., 2020).

Prefrontal areas are also involved in reward processing: For example, dysfunctions in the OFC in MDD patients are broadly discussed (for review, see Zhang et al., 2024). Thus, theoretical assumptions would predict increased activity after successful CBT, contrasting the results of Dichter et al. (2009). However, the authors additionally revealed activity increases in the FG during monetary anticipation, potentially signifying the normalization of previously decreased activity observed in depressive episodes (Smoski et al., 2009).

The frontopolar cortex has been associated with pessimistic future thinking and increased activation in MDD patients (Katayama et al., 2019). Thus, Katayama et al.'s (2019) result of decreased frontopolar cortex activity following CBT is in line with this, indicating normalization of this activity pattern. During self-referential processing, mPFC activity is shown (Northoff et al., 2006), and greater activity is associated with heightened negative affectivity (Lemogne et al., 2011). Therefore, Yoshimura et al.'s (2014) finding of decreased mPFC activity toward negative self-referential material and increases toward positive self-referential stimuli post-therapy might be interpreted as reductions in this negativity, reflecting improved cognitive-emotional processing with diminished negative bias and a more balanced cognitive style after CBT, correcting the aspect of the negative view on the self of Beck's (1967) cognitive triad. However, frontopolar activity changes were not linked to symptom improvement.

Inconsistencies in results examining task-induced BOLD signal responses following CBT in MDD patients especially in the PFC arise from methodological and sample differences but also from the large heterogeneity of the PFC and its involvement in a multitude of functions. Furthermore, the distinction to other areas, such as the cingulate, can be challenging in some cases. Despite this, the assumption of DeRubeis et al. (2008) that CBT increases cognitive control and, therefore, PFC activity appears too simplistic in light of the current results. Rather than solely increasing cognitive control, successful CBT outcomes may also involve reduced ruminative thinking and subsequently decreased brain activity. The heterogeneous results speak against a generalized view of frontal areas and underscore that a more differentiated perspective is necessary in this context. One neural mechanism of CBT appears to be the alteration in frontal cortical activity, but there are inconsistent findings regarding the direction of the change in activity, as it is depicted in Fig. 2, which is in line with the findings of similar previous reviews (Chalah and Ayache, 2018; Franklin et al., 2016). With regard to symptom-improvement-related changes in activity, there is some evidence during affective processing, although findings remain inconsistent.

4.1.4. Striatum

Four out of five studies reported significant effects in the NAcc, caudate, and putamen, indicating that CBT also alters brain function in striatal areas. There were findings of increased activity in response to rewards after CBT (Dichter et al., 2009; Hanuka et al., 2022), with an association between these changes and reduced scores in an anhedonia scale (Hanuka et al., 2022). Evidence suggests hypoactivity during

reward processing in striatal areas in MDD patients compared to HC (meta-analysis: Ng et al., 2019), and the improvement of these impairments through CBT is now supported by imaging studies. The increased reactivity to rewards might reflect a diminished negative bias and reduced anhedonia after CBT (Der-Avakian and Markou, 2012; Keller et al., 2013; Takamura et al., 2017). In contrast to that, there are also null results (Straub et al., 2015; Hanuka et al., 2022; Queirazza et al., 2019) and Dichter et al. (2009) reported an unexpected decrease in caudate activity during monetary feedback, attributing it partially due to methodological issues with the paradigm (see Section 4.2).

Moreover, findings in striatal regions extend beyond reward processing tasks. In line with the cognitive neurobiological model of depression (Disner et al., 2011), Ritchey et al. (2011) revealed decreased activity after CBT toward negative and neutral emotional stimuli and increased activity toward positive stimuli in the caudate. This aligns with Disner et al.'s (2011) model of negatively biased memory and rumination, suggesting normalization of striatal neural response following CBT. Similarly, Katayama et al.'s (2021) result of decreased caudate activity during future thinking post-CBT could be interpreted in this context, directly referring to the future component of the cognitive triad (Beck, 1967).

In sum, there is evidence for enhanced neural responsiveness to rewards after CBT in MDD patients, a novel finding considering that current reviews on similar topics primarily report changes during affective processing (Chalah and Ayache, 2018; Franklin et al., 2016). Notably, caudate activity decreased post-therapy during future thinking and affective processing as a potential neural mechanism of CBT, reflecting a diminished negative bias and, therefore, correlates of effective therapy. The second objective was only investigated during reward processing, with one study revealing neural activity alterations associated with a symptom scale and one study not finding these associations, making conclusions hard to draw.

4.2. Limitations

Nevertheless, there are some methodological issues within the included studies and also in the review technique that warrant mention: First, most studies did not establish a randomized controlled trial design and investigate a waiting group due to ethical considerations. Consequently, it is not possible to conclude that observed effects were solely due to CBT, and the potential for regression-to-the-mean effects should be acknowledged. Notably, co-therapy with antidepressants might be a confounding factor, considering that the studies did not control for medication load, although only four studies incorporated medication, with stability observed in two of these studies throughout the intervention period. Additionally, variations in treatment durations, frequencies, and scan intervals were observed among the studies, and psychotherapy is a rather long intervention that bears challenges controlling for concurrent changes in patients' lives that could influence outcomes. Also, because a HC group was not necessary, conclusions about normalization are challenging. However, the majority of studies ($N = 11$) had a HC group and conducted group-by-time-interactions with additional post-hoc-tests. Consequently, in some instances, there is suggestive evidence of a convergence of activity patterns toward those of HC following CBT.

Second, the sample sizes in all studies were rather small, and especially given the many potentially confounding factors, this raises questions about the appropriateness of employing whole brain analyses.

Third, although all studies used CBT or sub-forms, for example, BAT focuses more on behavioral activation (Sturmey, 2009), whereas CBASP prioritizes enhancing empathy and interpersonal aspects (McCullough, 2003), it could be argued that these interventions might use distinct mechanisms of action. Additionally, learning processes and their internalization take time, suggesting that the intervals between pre- and post-scan sessions, often just a few weeks, may be insufficient to detect effects.

Fourth, there were many differences between the assessed tasks (e.g., used stimuli, their valence, and evaluated contrasts) in the studies. This variation clearly allows for the investigation of different effects, even under the assumption that psychotherapy fundamentally alters brain function and information processing. Although most of the tasks are well-established and the stimuli within categories are at least similar, the question remains as to how comparable they truly are. This review attempted to categorize the tasks into clusters; however, this categorization is not clear-cut, and cross-study comparisons remain challenging.

Fifth, only few studies investigated the association of activity changes and symptom improvement, thereby posing challenges in addressing the second objective of this review. Further research is necessary, especially investigating distinct symptoms rather than general MDD symptom scales to disentangle the role of neural changes and clinical symptoms. Considering the heterogeneous nature of MDD with its diverse symptom profiles (Fried and Nesse, 2015) and evidence indicating clinical phenotypes are linked to different structural brain alterations (Yu et al., 2021), this might be a promising approach.

In sum, despite the aim of reducing heterogeneity, substantial differences persist across the studies in terms of task content, statistical evaluation (limits for cluster sizes, corrections, whole brain vs. ROI approach), and interventions. Thus, in our view, it is not yet possible to summarize the results in a meta-analysis. Above all, agreement on research standards and the employment of standardized tasks, scan- and intervention-intervals, and analysis of the results, for example, would be an important starting point toward enhancing comprehension of the neuronal mechanisms underlying CBT.

5. Conclusion

Taken together, the results suggest that CBT may modulate brain function in individuals with MDD, thereby partially normalizing neural processing, particularly negative biases. The results, for the most part, are in line with the findings of related reviews (Chalah and Ayache, 2018; Franklin et al., 2016). In particular, evidence suggests reduced limbic activity during task-based fMRI, increased striatal activity in response to reward tasks, decreased striatal activity in response to affective processing and future thinking tasks, and altered activity in the cingulum and PFC during different tasks. Especially in the sgACC, these changes are also associated with symptom reduction.

However, the results also provide mixed evidence for the dual-process models: reduced limbic activity does not necessarily seem to be accompanied by increased prefrontal cortical control. Yet, it remains open if contrary results are due to methodological issues like the comparison of different fMRI tasks, clinically visible differences in the symptom patterns of patients with MDD (Fried and Nesse, 2015), or a combination of both. In order to investigate this, future research should focus on standardizing methods and transdiagnostic research on the symptom level. In summary, while greater standardization in research methodologies is necessary, findings underscore the efficacy of CBT as a treatment modality for MDD through neurobiological insights.

Funding source

The funding sources were involved in the study design, in the analysis and interpretation of data, and in the writing of the report.

CRediT authorship contribution statement

Philine König: Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Conceptualization. **Esther Zwiky:** Writing – review & editing, Validation, Methodology, Formal analysis. **Antonia Küttner:** Writing – review & editing, Validation, Methodology, Formal analysis. **Marie Uhlig:** Writing – review & editing, Visualization,

Validation, Methodology, Formal analysis, Conceptualization. **Ronny Redlich:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

None.

Acknowledgements

The study was supported by grants from the German Research Foundation (DFG grant RE4458/1-1 to R.R.), the Federal Ministry of Education and Research (BMBF), and the Ministry of Saxony-Anhalt within the initial phase of the German Center for Mental Health (DZPG; BMBF grant 01EE2305C to R.R.), involved study design, in the collection, analysis and interpretation of data, and in the writing of the report.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2024.09.084.

References

American Psychiatric Association, 2013. Diagnostic and Statistical Manual of Mental Disorders. American Psychiatric Association. https://doi.org/10.1176/appi.books.9780890425596.

American Psychological Association, 2019. Clinical practice guideline for the treatment of depression across three age cohorts. Retrieved from. https://www.apa.org/depression-guideline.

Angold, A., Costello, E.J., Messer, S.C., Pickles, A., 1995. Development of a short questionnaire for use in epidemiological studies of depression in children and adolescents. Int. J. Methods Psychiatr. Res. 5 (4), 237–249.

Barsaglini, A., Sartori, G., Benetti, S., Pettersson-Yeo, W., Mechelli, A., 2014. The effects of psychotherapy on brain function: a systematic and critical review. Prog. Neurobiol. 114, 1–14. https://doi.org/10.1016/j.pneurobio.2013.10.006.

Beck, A.T., 1967. Depression: Clinical, Experimental, and Theoretical Aspects. Harper & Row.

Beck, A.T., 2008. The evolution of the cognitive model of depression and its neurobiological correlates. Am. J. Psychiatry 165 (8), 969–977. https://doi.org/10.1176/appi.ajp.2008.08050721.

Beck, A.T., Steer, R., 1978. Manual for the Beck Depression Inventory. Psychological Corporation.

Beck, A.T., Steer, R.A., Brown, G.K., 1996. Manual for the Beck Depression Inventory-2. Psychological Corporation.

Bora, E., Harrison, B.J., Davey, C.G., Yücel, M., Pantelis, C., 2012. Meta-analysis of volumetric abnormalities in cortico-striatal-pallidal-thalamic circuits in major depressive disorder. Psychol. Med. 42 (4), 671–681. https://doi.org/10.1017/S0033291711001668.

Borsini, A., Wallis, A.S.J., Zunszain, P., Pariante, C.M., Kempton, M.J., 2020. Characterizing anhedonia: a systematic review of neuroimaging across the subtypes of reward processing deficits in depression. Cogn. Affect. Behav. Ne. 20 (4), 816–841. https://doi.org/10.3758/s13415-020-00804-6.

Chalah, M.A., Ayache, S.S., 2018. Disentangling the neural basis of cognitive behavioral therapy in psychiatric disorders: a focus on depression. Brain Sci. 8 (8), 150. https://doi.org/10.3390/brainsci8080150.

Chuang, J.Y., Whitaker, K.J., Murray, G.K., Elliott, R., Hagan, C.C., Graham, J.M.E., Ooi, C., Tait, R., Holt, R.J., Van Nieuwenhuizen, A.O., Reynolds, S., Wilkinson, P.O., Bullmore, E.T., Lennox, B.R., Sahakian, B.J., Goodyer, I., Suckling, J., 2016. Aberrant brain responses to emotionally valent words is normalised after cognitive behavioural therapy in female depressed adolescents. J. Affect. Disord. 189, 54–61. https://doi.org/10.1016/j.jad.2015.09.008.

Der-Avakian, A., Markou, A., 2012. The neurobiology of anhedonia and other reward-related deficits. Trends Neurosci. 35 (1), 68–77. https://doi.org/10.1016/j.tins.2011.11.005.

DeRubeis, R.J., Siegle, G.J., Hollon, S.D., 2008. Cognitive therapy versus medication for depression: treatment outcomes and neural mechanisms. Nat. Rev. Neurosci. 9 (10), 788–796. https://doi.org/10.1038/nrn2345.

Deussing, J.M., 2006. Animal models of depression. Drug Discov. Today Dis. Model. 3 (4), 375–383. https://doi.org/10.1016/j.ddmod.2006.11.003.

Dichter, G.S., Felder, J.N., Petty, C., Bizzell, J., Ernst, M., Smoski, M.J., 2009. The effects of psychotherapy on neural responses to rewards in major depression. Biol. Psychiatry 66 (9), 886–897. https://doi.org/10.1016/j.biopsych.2009.06.021.

Dichter, G.S., Felder, J.N., Smoski, M.J., 2010. The effects of Brief Behavioral Activation Therapy for Depression on cognitive control in affective contexts: an fMRI investigation. J. Affect. Disord. 126 (1–2), 236–244. https://doi.org/10.1016/j.jad.2010.03.022.

Disner, S.G., Beevers, C.G., Haigh, E.A.P., Beck, A.T., 2011. Neural mechanisms of the cognitive model of depression. Nat. Rev. Neurosci. 12 (8), 467–477. https://doi.org/10.1038/nrn3027.

First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 1996. Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version (SCID-CV). American Psychiatric Press.

Franklin, G., Carson, A.J., Welch, K.A., 2016. Cognitive behavioural therapy for depression: systematic review of imaging studies. Acta Neuropsychiatr. 28 (2), 61–74. https://doi.org/10.1017/neu.2015.41.

Fried, E.I., Nesse, R.M., 2015. Depression is not a consistent syndrome: an investigation of unique symptom patterns in the STAR*D study. J. Affect. Disord. 172, 96–102. https://doi.org/10.1016/j.jad.2014.10.010.

Fu, C.H.Y., Williams, S.C.R., Cleare, A.J., Scott, J., Mitterschiffthaler, M.T., Walsh, N.D., Donaldson, C., Suckling, J., Andrew, C., Steiner, H., Murray, R.M., 2008. Neural responses to sad facial expressions in major depression following cognitive behavioral therapy. Biol. Psychiatry 64 (6), 505–512. https://doi.org/10.1016/j.biopsych.2008.04.033.

GBD 2019 Mental Disorders Collaborators, 2022. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Psychiatry 9 (2), 137–150. https://doi.org/10.1016/S2215-0366(21)00395-3.

Gelenberg, A.J., Freeman, M.P., Markowitz, J.D., Rosenbaum, J.F., Thase, M.E., Trivedi, M.H., Van Rhoads, R.S., 2010. Practice Guideline for the Treatment of Patients With Major Depressive Disorder, 3rd ed. American Psychiatric Association.

Groenewold, N.A., Opmeer, E.M., de Jonge, P., Aleman, A., Costafreda, S.G., 2013. Emotional valence modulates brain functional abnormalities in depression: evidence from a meta-analysis of fMRI studies. Neurosci. Biobehav. Rev. 37 (2), 152–163. https://doi.org/10.1016/j.neubiorev.2012.11.015.

Hamilton, M.A., 1960. A rating scale for depression. J. Neurol. Neurosur. Ps. 23, 56–62.

Hanuka, S., Olson, E.A., Admon, R., Webb, C.A., Killgore, W.D.S., Rauch, S.L., Rosso, I. M., Pizzagalli, D.A., 2022. Reduced anhedonia following internet-based cognitive-behavioral therapy for depression is mediated by enhanced reward circuit activation. Psychol. Med. 1–10. https://doi.org/10.1017/s0033291722001106.

Hollon, S.D., Beck, A.T., 1979. Cognitive therapy of depression. In: Cognitive-behavioral Interventions: Theory, Research, and Procedures. Academic Press.

Joormann, J., Quinn, M.E., 2014. Cognitive processes and emotion regulation in depression. Depress. Anxiety 31 (4), 308–315. https://doi.org/10.1002/da.22264.

Kalsi, N., Altavilla, D., Tambelli, R., Aceto, P., Trentini, C., Di Giorgio, C., Lai, C., 2017. Neural correlates of outcome of the psychotherapy compared to antidepressant therapy in anxiety and depression disorders: a meta-analysis. Front. Psychol. 8, 927. https://doi.org/10.3389/fpsyg.2017.00927.

Kandel, E.R., 1998. A new intellectual framework for psychiatry. Am. J. Psychiatry 155 (4), 457–469. https://doi.org/10.1176/ajp.155.4.457.

Katayama, N., Nakagawa, A., Umeda, S., Terasawa, Y., Kurata, C., Tabuchi, H., Kikuchi, T., Mimura, M., 2019. Frontopolar cortex activation associated with pessimistic future-thinking in adults with major depressive disorder. NeuroImage: Clinical 23, 101877. https://doi.org/10.1016/j.nicl.2019.101877.

Katayama, N., Nakagawa, A., Umeda, S., Terasawa, Y., Abe, T., Kurata, C., Sasaki, Y., Mitsuda, D., Kikuchi, T., Tabuchi, H., Mimura, M., 2021. Cognitive behavioral therapy effects on frontopolar cortex function during future thinking in major depressive disorder: a randomized clinical trial. J. Affect. Disord. 644–655. https://doi.org/10.1016/j.jad.2021.11.034.

Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., Williamson, D., Ryan, N., 1997. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. J. Am. Acad. Child Psy. 36 (7), 980–988. https://doi.org/10.1097/00004583-199707000-00021.

Keller, J., Young, C.B., Kelley, E., Prater, K., Levitin, D.J., Menon, V., 2013. Trait anhedonia is associated with reduced reactivity and connectivity of mesolimbic and paralimbic reward pathways. J. Psychiatr. Res. 47 (10), 1319–1328. https://doi.org/10.1016/j.jpsychires.2013.05.015.

Klein, J.P., Becker, B., Hurlemann, R., Scheibe, C., Colla, M., Heuser, I., 2014. Effect of specific psychotherapy for chronic depression on neural responses to emotional faces. J. Affect. Disord. 166, 93–97. https://doi.org/10.1016/j.jad.2014.04.055.

Krause, F.C., Linardatos, E., Fresco, D.M., Moore, M.T., 2021. Facial emotion recognition in major depressive disorder: a meta-analytic review. J. Affect. Disord. 293, 320–328. https://doi.org/10.1016/j.jad.2021.06.053.

Lemogne, C., Gorwood, P., Bergouignan, L., Pélissolo, A., Lehéricy, S., Fossati, P., 2011. Negative affectivity, self-referential processing and the cortical midline structures. SCAN 6 (4), 426–433. https://doi.org/10.1093/scan/nsq049.

Lewis, G., Pelosi, A.J., Araya, R., Dunn, G., 1992. Measuring psychiatric disorder in the community: a standardized assessment for use by lay interviewers. Psychol. Med. 22 (2), 465–486. https://doi.org/10.1017/S0033291700030415.

Lin, I.-M., Yu, H.-E., Yeh, Y.-C., Huang, M.-F., Wu, K.-T., Ke, C.-L.K., Lin, P.-Y., Yen, C.-F., 2021. Prefrontal lobe and posterior cingulate cortex activations in patients with major depressive disorder by using standardized weighted low-resolution electromagnetic tomography. J. Pers. Med. 11 (11), 1054. https://doi.org/10.3390/jpm11111054.

Magno, E., Simões-Franklin, C., Robertson, I.H., Garavan, H., 2009. The role of the dorsal anterior cingulate in evaluating behavior for achieving gains and avoiding losses. J. Cogn. Neurosci. 21 (12), 2328–2342. https://doi.org/10.1162/jocn.2008.21169.

Mayberg, H.S., 2003. Modulating dysfunctional limbic-cortical circuits in depression: towards development of brain-based algorithms for diagnosis and optimised treatment. Br. Med. Bull. 65 (1), 193–207. https://doi.org/10.1093/bmb/65.1.193.

McCullough, J.P., 2003. Treatment for chronic depression using Cognitive Behavioral Analysis System of Psychotherapy (CBASP). J. Clin. Psychol. 59 (8), 833–846. https://doi.org/10.1002/jclp.10176.
National Institute for Health and Care Excellence, 2022. Depression in Adults: Treatment and Management. National Institute for Health and Care Excellence (NICE).
Ng, T.H., Alloy, L.B., Smith, D.V., 2019. Meta-analysis of reward processing in major depre- ssive disorder reveals distinct abnormalities within the reward circuit. Transl. Psychiatry 9 (1), 293. https://doi.org/10.1038/s41398-019-0644-x.
Northoff, G., Bermpohl, F., 2004. Cortical midline structures and the self. Trends Cogn. Sci. 8 (3), 102–107. https://doi.org/10.1016/j.tics.2004.01.004.
Northoff, G., Heinzel, A., de Greck, M., Bermpohl, F., Dobrowolny, H., Panksepp, J., 2006. Self-referential processing in our brain—a meta-analysis of imaging studies on the self. NeuroImage 31 (1), 440–457. https://doi.org/10.1016/j.neuroimage.2005.12.002.
Ochsner, K., Gross, J., 2005. The cognitive control of emotion. Trends Cogn. Sci. 9 (5), 242–249. https://doi.org/10.1016/j.tics.2005.03.010.
Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., Shamseer, L., Tetzlaff, J.M., Akl, E.A., Brennan, S.E., Chou, R., Glanville, J., Grimshaw, J.M., Hróbjartsson, A., Lalu, M.M., Li, T., Loder, E.W., Mayo-Wilson, E., McDonald, S., Moher, D., 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Syst. Rev. 10 (1), 89. https://doi.org/10.1186/s13643-021-01626-4.
Phillips, M.L., Drevets, W.C., Rauch, S.L., Lane, R., 2003. Neurobiology of emotion perception II: implications for major psychiatric disorders. Biol. Psychiatry 54 (5), 515–528. https://doi.org/10.1016/S0006-3223(03)00171-9.
Pilmeyer, J., Huijbers, W., Lamerichs, R., Jansen, J.F.A., Breeuwer, M., Zinger, S., 2022. Functional MRI in major depressive disorder: a review of findings, limitations, and future prospects. J. Neuroimaging 32 (4), 582–595. https://doi.org/10.1111/jon.13011.
Poznanski, E.O., Mokros, H.B., 1996. Children's Depression Rating Scale-Revised Manual. Western Psychological Services.
Queirazza, F., Fouragnan, E., Douglas Steele, J., Cavanagh, J., Philiastides, M.G., 2019. Neural correlates of weighted reward prediction error during reinforcement learning classify response to cognitive behavioral therapy in depression. Sci. Adv. 5 (7), 4962. https://doi.org/10.1126/sciadv.aav4962.
Quidé, Y., Witteveen, A.B., El-Hage, W., Veltman, D.J., Olff, M., 2012. Differences between effects of psychological versus pharmacological treatments on functional and morphological brain alterations in anxiety disorders and major depressive disorder: a systematic review. Neurosci. Biobehav. Rev. 36 (1), 626–644. https://doi.org/10.1016/j.neubiorev.2011.09.004.
Rayner, G., Jackson, G., Wilson, S., 2016. Cognition-related brain networks underpin the symptoms of unipolar depression: evidence from a systematic review. Neurosci. Biobehav. Rev. 61, 53–65. https://doi.org/10.1016/j.neubiorev.2015.09.022.
Ritchey, M., Dolcos, F., Eddington, K.M., Strauman, T.J., Cabeza, R., 2011. Neural correlates of emotional processing in depression: changes with cognitive behavioral therapy and predictors of treatment response. J. Psychiatr. Res. 45 (5), 577–587. https://doi.org/10.1016/j.jpsychires.2010.09.007.
Rubin-Falcone, H., Weber, J., Kishon, R., Ochsner, K., Delaparte, L., Doré, B., Zanderigo, F., Oquendo, M.A., Mann, J.J., Miller, J.M., 2018. Longitudinal effects of cognitive behavioral therapy for depression on the neural correlates of emotion regulation. Psychiatry Res. Neuroimaging 271, 82–90. https://doi.org/10.1016/j.pscychresns.2017.11.002.
Rubin-Falcone, H., Weber, J., Kishon, R., Ochsner, K., Delaparte, L., Doré, B., Raman, S., Denny, B.T., Oquendo, M.A., Mann, J.J., Miller, J.M., 2020. Neural predictors and effects of cognitive behavioral therapy for depression: the role of emotional reactivity and regulation. Psychol. Med. 50 (1), 146–160. https://doi.org/10.1017/S0033291718004154.
Sankar, A., Scott, J., Paszkiewicz, A., Giampietro, V.P., Steiner, H., Fu, C.H.Y., 2015. Neural effects of cognitive-behavioural therapy on dysfunctional attitudes in depression. Psychol. Med. 45 (7), 1425–1433. https://doi.org/10.1017/S0033291714002529.
Sankar, A., Melin, A., Lorenzetti, V., Horton, P., Costafreda, S.G., Fu, C.H.Y., 2018. A systematic review and meta-analysis of the neural correlates of psychological therapies in major depression. Psychiatry Res. Neuroimaging 279, 31–39. https://doi.org/10.1016/j.pscychresns.2018.07.002.
Smoski, M.J., Felder, J., Bizzell, J., Green, S.R., Ernst, M., Lynch, T.R., Dichter, G.S., 2009. fMRI of alterations in reward selection, anticipation, and feedback in major depressive disorder. J. Affect. Disord. 118 (1–3), 69–78. https://doi.org/10.1016/j.jad.2009.01.034.
Snaith, R. P., Hamilton, M., Morley, S., Humayan, A., Hargreaves, D., & Trigwell, P. (1995). A scale for the assessment of hedonic tone the Snaith–Hamilton Pleasure Scale. Br. J. Psychiatry, 167(1), 99–103. doi:https://doi.org/10.1192/bjp.167.1.99.
Straub, J., Plener, P.L., Sproeber, N., Sprenger, L., Koelch, M.G., Groen, G., Abler, B., 2015. Neural correlates of successful psychotherapy of depression in adolescents. J. Affect. Disord. 183, 239–246. https://doi.org/10.1016/j.jad.2015.05.020.
Sturmey, P., 2009. Behavioral activation is an evidence-based treatment for depression. Behav. Modif. 33 (6), 818–829. https://doi.org/10.1177/0145445509350094.
Takamura, M., Okamoto, Y., Okada, G., Toki, S., Yamamoto, T., Ichikawa, N., Mori, A., Minagawa, H., Takaishi, Y., Fujii, Y., Kaichi, Y., Akiyama, Y., Awai, K., Yamawaki, S., 2017. Patients with major depressive disorder exhibit reduced reward size coding in the striatum. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 79, 317–323. https://doi.org/10.1016/j.pnpbp.2017.07.006.
Villalobos, D., Pacios, J., Vázquez, C., 2021. Cognitive control, cognitive biases and emotion regulation in depression: a new proposal for an integrative interplay model. Front. Psychol. 12, 628416. https://doi.org/10.3389/fpsyg.2021.628416.
Villringer, A., Dirnagl, U., 1995. Coupling of brain activity and cerebral blood flow: basis of functional neuroimaging. J. Cereb. Blood Flow Metab. 7 (3), 240–276.
Willner, P., Scheel-Krüger, J., Belzung, C., 2013. The neurobiology of depression and antidepre ssant action. Neurosci. Biobehav. Rev. 37 (10), 2331–2371. https://doi.org/10.1016/j.neubiorev.2012.12.007.
Yoshimura, S., Okamoto, Y., Onoda, K., Matsunaga, M., Okada, G., Kunisato, Y., Yoshino, A., Ueda, K., Suzuki, S., ichi, & Yamawaki, S., 2014. Cognitive behavioral therapy for depression changes medial prefrontal and ventral anterior cingulate cortex activity associated with self-referential processing. SCAN 9 (4), 487–493. https://doi.org/10.1093/scan/nst009.
Yu, M., Cullen, N., Linn, K.A., Oathes, D.J., Seok, D., Cook, P.A., Duprat, R., Aselcioglu, I., Moore, T.M., Davatzikos, C., Oquendo, M.A., Weissman, M.M., Shinohara, R.T., Sheline, Y.I., 2021. Structural brain measures linked to clinical phenotypes in major depression replicate across clinical centres. Mol. Psychiatry 26 (7), 2764–2775. https://doi.org/10.1038/s41380-021-01039-8.
Zhang, B., Rolls, E.T., Wang, X., Xie, C., Cheng, W., Feng, J., 2024. Roles of the medial and lateral orbitofrontal cortex in major depression and its treatment. Mol. Psychiatry 1–15. https://doi.org/10.1038/s41380-023-02380-w.