Degree project

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The Emotional Rollercoaster of Borderline Personality Disorder: Neural Correlates of Cognitive Reappraisal

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Abstract

Individuals with borderline personality disorder (BPD) experience emotional instability and have a high suicide rate. Treatment for BPD includes psychotherapy and adaptive emotion regulation strategies, which include cognitive reappraisal. Previous systematic reviews indicate that abnormal brain patterns may cause emotional instability in BPD individuals. To further explore this, this review collected articles that examined neural activity using fMRI during cognitive reappraisal in subjects with BPD and healthy controls. We identified four relevant articles through a search of Web of Science and PubMed. The articles included conflicting results in both participant groups regarding increased or decreased activity during cognitive reappraisal applying either reinterpretation or distancing. The affected brain regions were the following: lateral and ventrolateral prefrontal cortex, left middle temporal gyrus, and superior temporal gyri. Three of the articles reported consistent results of activity in the dorsolateral prefrontal cortex during downregulation, two in all participants and one only in the healthy control group. However, no significant group differences were found in this region during cognitive reappraisal. The discussion includes limitations regarding the comparability of the included studies, such as the method of eliciting negative affect, the use of written or verbal instructions, and the cognitive reappraisal strategy applied. Further research is necessary to better understand the involvement of distinct brain regions in cognitive reappraisal and BPD, as well as to establish more standardized research methods. These efforts can offer comprehensive insights into the neural mechanisms underlying cognitive reappraisal in individuals with BPD.

[*Keywords*: Borderline Personality Disorder, Emotion Regulation, Cognitive Reappraisal, fMRI]

The Emotional Rollercoaster of Borderline Personality Disorder: Neural Correlates of Cognitive Reappraisal

Introduction

We all feel stressed, angry, and anxious. However, most of us learn to manage these negative emotions. You can leave the situation, take a few deep breaths, or try to think positively. This is called emotion regulation and develops throughout our lives (Cole, 2014). People with borderline personality disorder (BPD) often lack this ability. Therefore, emotional dysregulation is a major feature of the illness (American Psychiatric Association, 2013)

Emotion Regulation

Emotions guide and influence our behavior in different situations and consist of behavioral, physiological, and subjective experiences (Taschereau-Dumouchel et al., 2022). These aspects collectively determine how one responds to an emotional situation. However, emotion regulation can be used to control one's response (Gross, 2008). The ability to regulate one's emotions is determined by psychological, social, and physical health factors (Goldin et al., 2008).

There are adaptive methods for regulating one's emotions, such as acceptance and cognitive reappraisal, and there are maladaptive strategies such as rumination, suppression, and self-harm (Aldao & Nolen-Hoeksema, 2012). The latter strategies may first reduce negative affect but are not sustainable in the long run. Adaptive emotion regulation strategies are a more sustainable alternative. They alleviate negative affect in the present and provide a durable coping mechanism for the future (Wolff, 2019).

Cognitive Reappraisal

Cognitive reappraisal is one of the most researched and adaptive emotion regulation strategies (Goldin et al., 2008). It is a cognitive-linguistic strategy divided into two methods: reinterpretation and distancing (Powers & LaBar, 2019). Reinterpretation involves interpreting the meaning of the emotional situation in non-emotional terms (Goldin et al., 2014; Gross, 2003). Distancing involves viewing emotional situations as an objective observer from a detached perspective (Koenigsberg et al., 2009)

Borderline Personality Disorder

BPD is described in the DSM-5 as a cluster B personality disorder, characterized by the following: 1) abandonment issues, 2) unstable and intense relationships with extreme idealization and devaluation, 3) unstable sense of self, 4) impulsivity in potentially self-harming areas, 5) suicidality, self-mutilating behaviors, 6) emotional instability, 7) feelings of emptiness, 8) intense anger and the dysregulation of anger, and 9) paranoid ideation or dissociative symptoms (American Psychiatric Association, 2013). Extreme feelings of anger and sadness are commonly elicited when a person with BPD is threatened by abandonment (Paton et al., 2015).

Approximately 1.6% of the population and 20% of psychiatric inpatients have BPD (Chapman et al., 2022), with women accounting for 75% of those diagnosed (American Psychiatric Association, 2013). Suicide occurs in 8-10% and self-mutilation, suicide threats, and suicide attempts are common (American Psychiatric Association, 2013; Paris, 2019). Recurrent suicidality is the most common reason individuals with BPD seek help (American Psychiatric Association (2013). A systematic review by Meuldijk et al. (2017) showed that individuals with BPD seek mental health services more frequently than other psychiatric patients because they often require multiple, urgent, and repeated treatments. The prevalence of BPD in inpatients and outpatients and the potential negative consequences associated with untreated BPD create a financial burden on society.

Treatment

According to several guidelines psychotherapy should be the main treatment for BPD (Paton et al., 2015). Nonetheless, 87% of patients diagnosed with BPD (without a comorbid condition present) are prescribed psychotropic medications such as antidepressants, mood stabilizers, and antipsychotics (Paton et al., 2015).

Repetitive Transcranial Magnetic Stimulation

Sverak et al. (2022) studied the effects of repetitive transcranial magnetic stimulation on the right dorsolateral prefrontal cortex in BPD patients. It demonstrated that less activation of the amygdala and insula leads to a reduction in BPD symptoms, such as better emotion regulation evidenced by a significant reduction in the Difficulties in Emotion Regulation Scale. However, the use of this intervention remains controversial because of the high cost and difficulty in determining the magnitude of placebo effects (Malhi et al., 2021).

Dialectical Behavior Therapy

In dialectical behavior therapy, one learns how to regulate one's emotions. After 12 weeks of dialectical behavior therapy, individuals diagnosed with BPD showed a decrease in amygdala activation and improved emotion regulation, measured by the Difficulties in Emotion Regulation Scale (Goodman et al., 2014). In addition, BPD patients showed an increase in grey matter volume in the superior temporal gyrus, inferior frontal gyrus, and anterior cingulate cortex after a 12-week program of dialectical behavior therapy (Mancke et al., 2018). This finding is consistent with the results of a study by Silvers et al. (2016), which found that left inferior frontal gyrus activation was negatively correlated with the Difficulties in Emotion Regulation Scale in BPD subjects.

BPD and Emotion Regulation

Individuals with BPD, characterized by emotional dysregulation and an inability to use healthy coping mechanisms, often use maladaptive emotion regulation strategies such as rumination, suppression, and self-harm (Aldao & Nolen-Hoeksema, 2012). However, dialectical behavior therapy directed at BPD patients includes practicing adaptive emotion regulation (Empower Your Mind Therapy, 2021). In addition, cognitive reappraisal has shown symptom relief for emotional dysregulation in individuals with BPD, as evidenced by a reduction in the Difficulties in Emotion Regulation Scale (Marco et al., 2021).

Affected Brain Areas

Borderline Personality Disorder

Emotional dysregulation in BPD is thought to be related to abnormal brain connectivity (Schulze et al., 2019). Research has shown that individuals with BPD have increased amygdala activation and hyperactivity in the posterior cingulate cortex and medial and posterior parts of the insula (Schulze et al., 2016). Furthermore, increased activity has been demonstrated bilaterally in both the middle temporal gyrus and the left superior temporal gyrus (Soloff et al., 2008).

In contrast, activation is reduced in the dorsolateral, orbitofrontal, medial, and ventromedial prefrontal cortex, as well as the anterior and dorsal cingulate cortex (Sampedro et al., 2021; Schulze et al., 2016; Wolf et al., 2012). In addition, research has shown that abnormal activation of the amygdala in individuals with BPD leads to decreased habituation of the amygdala to negative stimuli (Sicorello & Schmahl, 2021). Abnormal activation of the amygdala has also been linked to emotional dysregulation (Sampedro et al., 2021).

Emotion Regulation

Regarding cognitive reappraisal, the areas of the dorsolateral, medial, and ventrolateral prefrontal cortex, anterior cingulate cortex, and dorsal anterior cingulate are activated (Goldin et al., 2008; Nam Bae et al., 2006; Ochsner et al., 2012; Piretti et al., 2021; Schulze et al., 2011; Van Zutphen et al., 2018). Further, an enhanced Blood-Oxygen-Level-Dependent signal was detected during cognitive reappraisal in the dorsolateral, medial, and ventrolateral prefrontal cortex in healthy participants (Goldin et al., 2008). Furthermore, a decrease in the amygdala and the lateral left insula has been demonstrated during cognitive reappraisal in healthy participants (Goldin et al., 2008;

Schulze et al., 2011). Additionally, the ventromedial prefrontal cortex, specifically the rostral anterior cingulate and the orbitofrontal cortex, works as inhibitors of the amygdala and their interactions are necessary for emotion regulation (Andrewes & Jenkins, 2019).

Different cognitive reappraisal techniques have also been shown to activate different areas, as observed in participants with mood and anxiety disorders. Reinterpretation shows activation in the left superior temporal gyrus and left ventrolateral prefrontal cortex, while utilizing distancing activates medial, frontal, and parietal areas (Picó-Pérez et al., 2017).

Aim

There is currently a gap in knowledge regarding the neural correlates of emotional dysregulation and cognitive reappraisal in individuals with BPD. More specifically, what brain areas are affected by BPD in ways that influence the use of cognitive reappraisal? Conversely, how does cognitive reappraisal affect brain activity in individuals with BPD? This thesis aims to systematically review studies of neural correlates and subjective experiences during cognitive reappraisal in BPD individuals. This is to optimize cognitive reappraisal for emotional dysregulation in BPD. The research question is how neural activation during cognitive reappraisal differs between individuals with BPD and healthy controls.

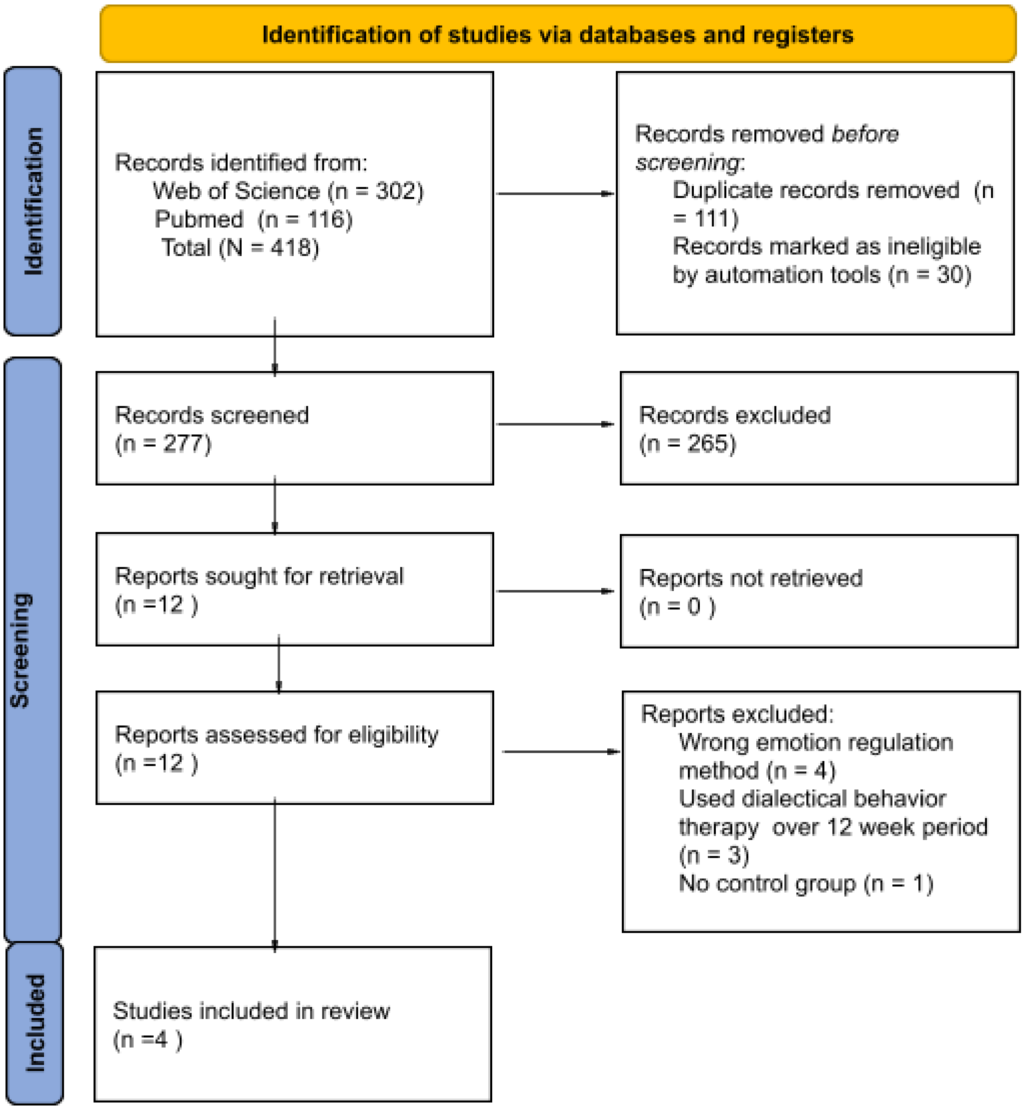
Methods

Search Strategy

Studies were found on Web of Science and PubMed on or before February 27, 2023 (Fig. 2). The following search term was applied: ("ER" OR "affect regulation") AND ("borderline personality disorder" OR BPD OR borderline OR "emotionally unstable personality disorder" OR EUPD OR "emotional intensity disorder" OR EID) AND (neural OR brain OR neuro*).

Fig. 2

PRISMA



Note. Presents the study selection process illustrated in a PRISMA flow chart (Page et al., 2021).

Implemented filters were "English." All results were imported into the online software Rayyan (Ouzzani et al., 2016), and the results were blinded. Duplicates, systematic reviews, and meta-analyzes were removed. During the initial screening, articles were screened to determine whether relevant terms such as BPD, emotion regulation, and cognitive reappraisal were included in the title, abstract, or keywords. The blind mode was then turned off and the results were discussed internally. For the second screening, the blind mode was turned on and the full text of the articles was sought for retrieval, read, checked for suitability, and discussed among the researchers. In case of disagreement, the researchers contacted their supervisor.

Inclusion Criteria

Studies were included if they 1) were published or available in English; 2) were published between 1994 and 2023; 3) mentioned cognitive reappraisal, BPD, and emotion regulation in the title, abstract, or keywords; 4) BPD subjects were compared in terms of neural activation with healthy controls; 5) fMRI was used; 6) full text was available through the University of Skövde; 7) the study was peer-reviewed; 8) the study was empirical; 9) participants were over 18 years of age.

Only articles published between 1994 and 2023 were included because the American Psychiatric Association reformulated the diagnostic criteria for BPD in 1994. Additionally, only studies that reported results on cognitive reappraisal (reinterpretation or distancing) were included. The reason for this is that cognitive reappraisal is well-researched and adaptive (Goldin et al., 2008). In addition, it is appropriate for fMRI studies because it provides a solid foundation for methodology (Ochsner et al., 2012). Cognitive reappraisal is also non-invasive and relatively easy to learn. The studies additionally required a healthy control group, as clinical populations show abnormal neural activity during emotion regulation (Schulze et al., 2016; Schulze et al., 2019). Lastly, fMRI was chosen as the neuroimaging technique because it is noninvasive and has a high spatial resolution. Participants also had to be of age to reduce potential confounding effects of developmental differences and to better generalize the results.

Data Extraction

We compiled studies examining the effect of cognitive reappraisal in BPD using fMRI, focusing on the prefrontal cortex, anterior and dorsal anterior cingulate, insula, and amygdala. In addition, we looked at participants' self-assessments in the included studies.

We tabulated the results of the studies, including information on sample size, study design, brain region(s) examined, and self-assessment measures used.

Results

Search Results

The researchers identified 418 articles (Fig. 2). Using the online software Rayyan (Ouzzani et al., 2016), 111 were identified as duplicates and manually removed. Thirty were automatically flagged as systematic reviews or meta-analyses and manually removed. Of the remaining articles (*n* = 277) 12 were read in full text. Of these, eight were removed because they 1) applied a different emotion regulation method; 2) implemented dialectical behavior therapy and had 12 weeks between scans; 3) lacked a healthy control group. Thus, four articles were included.

Descriptive Statistics

The articles were published between 2009 and 2021 and included 66 participants diagnosed with BPD and 65 healthy controls. Altogether, the total age range for one study (De la Peña-Arteaga et al., 2021) was 21-63 years, the remaining included studies did not report this information. The total mean age range for the BPD group was *m* = 27.21 - 37.68 years old while it ranged between *m* = 24.53 - 35.84 for the healthy control group. The mean sample size of BPD subjects was *m* = 16.5. Two studies (Lang et al., 2012; Schulze et al., 2011) included only female participants (Table 1). In one study, 55.56% (*n* = 10) were female (Koenigsberg et al., 2009) and in another, 52.63% (*n* = 10) were female (De la Peña-Arteaga et al., 2021).

Table 1

An Overview of Characteristics of the Studies

First author	Year	*N*	Emotion stimuli	ER method	Self-assessment
Koenigsberg	2009	BPD: *N* =18 (10 women) HC: *N* = 16	Social pictures from IAPS	Distancing	ALS
Lang	2012	BPD: *N* = 14 (14 women) HC: *N* = 15	Scripts from ANET	Distancing	ERQ
De la Peña-Arteaga	2021	BPD: *N* = 19 (10 women) HC: *N* = 19	IAPS	Distancing or Reinterpreting	DERS, CERQ
Schulze	2011	BPD: *N* = 15 (15 women) HC: *N* = 15	IAPS, supplemented by similar pictures	Reinterpreting	Post-scan ratings

Note. Abbreviations: BPD = borderline personality disorder, ER = emotion regulation, IAPS = International Affective Picture System, ANET = Affective Norms for English Text, HC = healthy controls, ALS = Affective Lability Scale, ERQ = Emotion Regulation Questionnaire, DERS = Difficulties in Emotion Regulation Scale, CERQ = Cognitive Emotion Regulation Questionnaire, post scan ratings on a scale from 1 to 9.

Regarding the emotion regulation strategies applied, two implemented distancing, one reinterpretation, and one both distancing and reinterpretation (Table 1). In three articles (Koenigsberg et al., 2009; Lang et al., 2012; Schulze et al., 2011), the BPD group was free of psychotropic medications for at least two weeks before the experiment. One article (De la Peña-Arteaga et al., 2021) did not report this information. In one article, illnesses with Axis I comorbidity were present (Koenigsberg et al., 2009), whereas, in one article, both Axis I and II were present in the BPD sample (Lang et al., 2012). In two articles (De la Peña-Arteaga et al., 2021; Schulze et al., 2011), the BPD sample was free of current comorbid conditions.

Materials

Three studies (De la Peña-Arteaga et al., 2021; Koenigsberg et al., 2009; Schulze et al., 2011) induced negative affect using the International Affective Picture System (IAPS) (Lang et al., 1997). The IAPS is a database of pictures with standardized ratings for valence and arousal. It is frequently used in studies regarding emotion regulation to better allow experimental control, facilitate comparison of different studies, and promote replications (Lang et al., 2008). As of April 11th, its manual has 4225 citations on Google Scholar. In contrast, Lang et al. (2012) used Affective Norms for English Text (ANET) (Bradley & Lang, 2007). ANET has, as of April 11th, 137 citations on Google Scholar. It consists of 120 short sentences, such as "You are lying in bed on a Sunday morning" (Buechel & Hahn, 2016), with three standardized negative and three neutral scripts.

Both IAPS and ANET have been documented to represent empirically determined responses of subjects related to valence arousal dominance using the Self Assessment Manikin (Buechel & Hahn, 2016).

The arousal and valence of ANET were assigned in a pilot study outside the scanner for the study by Lang et al. (2012). However, no standardized measurements were reported. Each script was rated using a five-point Likert scale, ranging from "not aroused and very pleasant" to "extremely aroused and very disagreeable". Regarding arousal, m = 5.67, *SD* 2.14 (negative scripts), and m = 1.92, *SD* 1.22 (neutral scripts). Regarding valence m = 2.83, *SD* 1.37 (negative scripts), and m = 6.12, *SD* 1.19 (neutral scripts).

Procedure

All of the included studies had a cross-sectional comparative study design and a between-group experimental design. Three studies used IAPS (De la Peña-Arteaga et al., 2021; Koenigsberg et al., 2009; Schulze et al., 2011), while one implemented ANET (Lang et al., 2012). However, one study (Koenigsberg et al., 2009) only used material representing social situations from IAPS, arguing that an important symptom of BPD is the dysregulation of emotions related to negative social experiences. Another study (Schulze et al., 2011) supplemented the IAPS with additional images selected by the researchers.

Two of the studies (Koenigsberg et al., 2009; Lang et al., 2012) instructed participants to apply distancing, while one study (Schulze et al., 2011) instructed participants to use reinterpretation. The study by De la Peña-Artega et al. (2021) had their participants choose between distancing and reinterpretation.

In two studies (Lang et al., 2012; Schulze et al., 2011), participants were asked to either upregulate, downregulate, or maintain their initial emotional response. To signal upregulation the word "enhance" was displayed on the screen, prompting participants to increase their emotional involvement in the stimuli. The word "distancing" was displayed to prompt participants to view the stimuli from a more detached third-person perspective. The prompt "maintain" instructed participants to maintain their emotions.

In another study (De la Peña-Artega et al., 2021), participants were first presented with instructions on the screen and then an image. If the instruction was "observe," the pictures were neutral and participants had to view them passively. If the instruction was "maintain," a negative image was shown and participants had to maintain the negative emotions elicited by the images. If the instruction was "regulate," negative images were presented and participants had to reduce their negative emotions by distancing or reinterpreting them.

In contrast to the other three studies, Koenigsberg et al. (2009), gave verbal instructions. Participants were instructed to either "suppress" or "maintain." In response to the auditory command "suppress," distancing was applied. In response to the command "maintain," participants did not suppress their initial response. In all studies, participants were asked to rate their subjective task experience.

Self-Assessments

Difficulties in Emotion Regulation Scale

This five-point Likert scale range from "almost never" to "almost always" (Gratz & Roemer, 2004). Eleven of the 36 questions are reversibly scored and should be subtracted from the total. A higher score indicates greater problems with emotion regulation (Gratz & Roemer, 2004). The maximum score is 180 and the minimum score is 36.

Emotion Regulation Questionnaire

The Emotion Regulation Questionnaire is a seven-point Likert scale that ranges from "strongly disagree" to "strongly agree" to assess both emotional experience and expression (Gross & John, 2003). There are ten items, six in the cognitive reappraisal group and four in the expressive suppression group. Each group is scored separately with a higher score representing better skills (Gross & John, 2003). The maximum score for the cognitive reappraisal group is 42 and the minimum score is six. The maximum score for the expressive suppression group is 26 and the minimum score is four.

Cognitive Emotion Regulation Questionnaire

This is a five-point Likert scale, ranging from "almost never" to "almost always." Participants are instructed to imagine experiencing challenging events and answer questions to assess emotion regulation skills (Garnefski & Kraaij, 2007). The 36 questions are divided into subscales and represent both adaptive and maladaptive emotion regulation. A higher score represents better emotion regulation skills. The maximum score is 180 and the minimum score is 36.

Affective Lability Scale

The Affective Lability Scale is a 54-item questionnaire that measures labile affect. The items consist of sentences referring to subjective, physiological, and behavioral experiences. Participants rate the sentences on a four-point Likert scale ranging from "Very

Undescriptive" to "Very Descriptive". The maximum score is 216 and the minimum score is 54.

Responses

In all studies, participants self-reported their subjective experiences (Table 1). De la Peña-Arteaga et al. (2021) used the Difficulties in Emotion Regulation Scale and the Cognitive Emotion Regulation Questionnaire. The mean valence ratings of the Cognitive Emotion Regulation Questionnaire sub-scale reappraisal, for the healthy control group, was *m* = 10.37 *(SD* 4.57*),* and for the BPD group *m* = 8.32 *(SD* = 4.74). The mean valence ratings for the sub-scale rumination, for the healthy control group, was *m* = 8.89 *(SD* = 3.16*),* and for the BPD group *m* = 9.74 *(SD* = 2.60*)*. The mean valence ratings for the Difficulties in Emotion Regulation Scale for the healthy controls were *m* = 58.21 *(SD* = 15.10*)* and for the BPD group *m* = 96.95 *(SD* = 33.05*)*. The latter demonstrated a significant positive correlation between scores and connectivity between the right ventrolateral prefrontal cortex and the left inferior temporal gyrus in BPD patients. Koenigsberg et al. (2009) used the Affective Lability Scale and reported *m* = 94.9 (*SD* = 23.7) for the BPD group and *m* = 20.3 (*SD* = 16.0) for the healthy control group.

Lang et al. (2012) applied the Emotion Regulation Questionnaire and Schulze et al. (2011) used "post-scan ratings ... on a scale from 1 to 9" and demonstrated no group differences, without specifying any further. Lang et al. (2012) used the Emotion Regulation Questionnaire and Koenigsberg et al. (2009) used the Affective Lability Scale and showed that both the BPD group and the healthy controls reported less arousal during downregulation. Lang et al. (2012) furthermore presented that all participants reported a higher degree of arousal during upregulation. However, for both up- and downregulation, the BPD group showed a slightly higher level of arousal, compared to the control group (Lang et al., 2012).

Brain Activity during Maintain

Koenigsberg et al. (2009) presented that individuals with BPD had higher activation, at a non-significant level, in the right superior temporal, anterior, posterior cingulate, and left cerebellar cortex during the look condition compared with healthy controls, independent of valence or stimulus. De la Peña-Arteaga et al. (2021) additionally found that BPD patients showed increased activation in the ventrolateral prefrontal cortex and bilateral orbitofrontal cortex, however at an uncorrected level.

Schulze et al. (2011) revealed that BPD subjects showed increased activation in the left amygdala, as well as bilateral middle temporal gyrus, supramarginal gyrus, right inferior gyrus, superior parietal gyrus, left fusiform gyrus during early viewing of negative images. Right thalamus, right posterior cingulate gyrus, thalamus, right inferior temporal gyrus, right superior frontal gyrus, as well as medial frontal gyrus, and inferior frontal gyrus (specifically, the triangular) compared with healthy controls. Additionally, a more sensitive approach showed increased activation in the right amygdala.

In addition, Koenigsberg et al. (2009) presented increased activation in the fusiform gyrus and prefrontal regions in healthy controls.

Brain Activity During Downregulation

For a table of all brain regions mentioned, see Appendix.

Three of the included studies (Koenigsberg et al., 2009; Lang et al., 2012; Schulze et al., 2011) reported increased activation of the left dorsolateral prefrontal cortex during downregulation applying cognitive reappraisal (Table 2). Two of the studies (Koenigsberg et al., 2009; Schulze et al., 2011) reported this increased activity for both the BPD and the healthy control group and one reported it only for the healthy controls (Lang et al., 2012).

Table 2

A Comparison of the Neural Activation Patterns in BPD and Healthy Controls during Down Regulation of Negative Images Compared to Maintain

Brain areas	Koenigsberg et al. 2009	Lang et al. 2012	Peña-Arteaga et al. 2021	Schulze et al. 2011
	Distancing	Distancing	Reinterpreting & Distancing	Reinterpreting
Left dorsolateral prefrontal cortex	HC: ↑ BPD: ↑	HC: ↑ BPD: -	HC: - BPD: -	HC: ↑ BPD: ↑
Left middle temporal gyrus	HC: - BPD: -	HC: ↑ BPD: ↑	HC: - BPD: -	HC: - BPD: ↓
Left inferior parietal gyrus	HC: - BPD: -	HC: ↑ BPD: -	HC: - BPD: -	HC: - BPD: ↑
Left precuneus	HC: - BPD: -	HC: ↑ BPD: -	HC: - BPD: -	HC: - BPD: ↓
Left middle occipital gyrus	HC: ↑ BPD: -	HC: - BPD: -	HC: - BPD: -	HC: - BPD: ↑
Right parahippocampal gyrus	HC: ↑ BPD: ↑	HC: ↑ BPD: -	HC: - BPD: -	HC: - BPD: -
Superior temporal gyri	HC: ↑ BPD: ↑	HC: - BPD: ↑	HC: - BPD: -	HC: - BPD:↓
Left supramarginal gyrus	HC: - BPD: -	HC: ↑ BPD: -	HC: - BPD: -	HC: ↑ BPD: ↑
Lateral and ventrolateral prefrontal cortex	HC: ↑ BPD: ↑	HC: - BPD: -	HC: - BPD: ↓	HC: - BPD: -

Note. A table consisting of brain areas mentioned by two or more articles. The arrows represent whether the area increased (↑) or decreased (↓) in activation during cognitive reappraisal in between-group comparisons. Abbreviations; BPD = borderline personality disorder, HC = healthy controls.

The left supramarginal gyrus showed increased activity in healthy controls and subjects with BPD (Lang et al., 2012; Schulze et al., 2011). The left inferior temporal gyrus was also reported to be increased in individuals with BPD (Schulze et al., 2011). In another article (Lang et al., 2012), an increase in the same area was reported, however only in healthy controls. The right parahippocampal gyrus also showed increased activity, both in BPD and in healthy control subjects, as demonstrated by Koenigsberg et al. (2009). Another study (Lang et al., 2012) additionally confirmed increased activity, but only in healthy controls. Furthermore, two studies reported increased left middle occipital gyrus activity, in one study (Schulze et al., 2011) activation in the BPD group, and in the other (Koenigsberg et al., 2009), only in healthy controls. Moreover, decreased activity in the left precuneus was found in the BPD group (Schulze et al., 2011), in contrast to healthy controls who showed increased activation (Lang et al., 2012).

Increased activation of the left middle temporal gyrus was demonstrated by Lang et al. (2012), whereas the superior temporal gyri demonstrated increased activation by two articles (Koenigsberg et al., 2009; Lang et al., 2012). However, Schulze et al. (2011) reported decreased activation in these two areas. Similarly, the lateral and ventrolateral prefrontal cortex was reported to increase in all participants (Koenigsberg et al., 2009). In contrast, De la Peña-Artega et al. (2021) reported that the BPD group had decreased activity in both the lateral and ventrolateral prefrontal cortex.

Brain Activity during Upregulation

Lang et al. (2012) reported that healthy control subjects showed increased activation in the left amygdala, left dorsomedial and left dorsolateral prefrontal cortex, and the posterior cingulate gyrus during upregulation. In contrast, Schulze et al. (2011), reported that both groups showed increased activation in the left orbitofrontal cortex, anterior cingulate cortex, and bilateral insula. Along with a cluster comprising the supplementary motor area and amygdala. Additionally, BPD participants showed deactivation in the left medial prefrontal cortex, anterior cingulate cortex, and right precuneus (Lang et al., 2012). Together with decreased activation in the right pallidum, left orbitofrontal cortex, middle frontal gyrus, right superior temporal gyrus, left precuneus, and left middle temporal gyrus (Schulze et al., 2011). Furthermore, increased activation was found in the left inferior parietal gyrus, left inferior temporal gyrus, left middle occipital gyrus, and left postcentral gyrus (Schulze et al., 2011).

Additional late activations were observed in the right anterior cingulate cortex and the left middle temporal gyrus in healthy controls, whereas BPD subjects showed activation in the left middle temporal cortex (Lang et al., 2012).

Brain Activity Concerning Socially Depicted Images

Two studies (Koenigsberg et al., 2009; Schulze et al., 2011) reported different patterns of brain activity when participants were presented with stimuli related to social situations. One study (Koenigsberg et al., 2009) reported that BPD patients showed greater neural activation in the left superior temporal gyri, posterior cingulate, anterior cingulate, and cerebellum compared to healthy subjects. Another study (Schulze et al., 2011) found greater activation in the insula and amygdala in participants with BPD compared to healthy controls when reacting to socially depicted images.

Discussion

This thesis aimed to conduct a systematic review to examine the difference in the neural correlates between individuals with BPD and healthy controls during cognitive reappraisal. Four articles were included for data extraction and synthesis. This section discusses the results, methodology, limitations, and future directions. A table of brain regions mentioned in two or more articles is provided in Table 2, and a table of all brain regions mentioned is provided in Appendix.

Neural Correlates of Cognitive Reappraisal

Below, we deliberate the findings in more detail. Based on the data extraction and findings, parts of the prefrontal, anterior cingulate, orbitofrontal cortex, and amygdala are discussed.

Amygdala and Orbitofrontal Prefrontal Cortex

One study (Koenigsberg et al., 2009) reported that healthy controls showed decreased amygdala activity during distancing. Whereas individuals with BPD exhibited increased activity. The amygdala plays a significant role in modulating sympathetic autonomic responses associated with flight, fight, or freeze, and BPD individuals generally have hyperactivity in this region (Schulze et al., 2016).

Along with the decreased amygdala activity reported by Koenigsberg et al. (2009), one can further expect increased activity levels of the orbitofrontal and ventromedial prefrontal cortex, as these regions function as amygdala inhibitors (Andrewes & Jenkins, 2019). Unfortunately, ventromedial and orbitofrontal cortex activity was not reported (Koenigsberg et al., 2009). Schulze et al. (2011), however, demonstrated increased bilateral activity in the orbitofrontal cortex in both participant groups, which may imply appropriate regulation of the amygdala. However, this cannot be concluded since Schulze et al. (2011) did not disclose any information regarding amygdala activity.

Dorsolateral Prefrontal Cortex

Three studies (Koenigsberg et al., 2009; Lang et al., 2012; Schulze et al., 2011) found increased activity in the dorsolateral prefrontal cortex during the downregulation phase, compared to the maintain phase. Two of the studies (Koenigsberg et al., 2009; Schulze et al., 2011) found this increased activity in individuals with BPD, while Lang et al. (2012) only reported it in healthy controls. As the dorsolateral prefrontal cortex is involved in emotion regulation (Piretti et al., 2021), the increased activity suggests that the participants applied appropriate emotion regulation.

According to Schulze et al. (2016), individuals with BPD generally have lower activity in the dorsolateral prefrontal cortex. However, two articles (Koenigsberg et al., 2009; Schulze et al., 2011) found no significant differences between healthy controls and individuals with BPD. This could be the effect of successfully implemented emotion regulation, increasing the activity of the dorsolateral prefrontal cortex in BPD subjects to a level equivalent to healthy controls. In addition to this, the experimental design required participants to remember multiple instructions. Given that the dorsolateral prefrontal cortex is involved in working and short-term memory (Brunoni & Vanderhasselt, 2014; Hertrich et al., 2021), this may explain the reported activity.

Dorsal Anterior Cingulate Cortex

Koenigsberg et al. (2009) demonstrated that during distancing compared to maintain, activity in the dorsal anterior cingulate cortex increased in healthy controls and decreased in BPD subjects. The dorsal anterior cingulate cortex is involved in evaluating and controlling the emotional aspects of stimuli. Moreover, the dorsal anterior cingulate cortex is involved when integrating information needed to actualize the meaning of a stimulus (Piretti et al., 2021). Considering the results of Koenigsberg et al. (2009), it can therefore be assumed that healthy controls integrated a new meaning of the situation, whereas BPD subjects did not.

Contradictory Results

Lateral and Ventrolateral Prefrontal Cortex

Koenigsberg et al. (2009) reported that during distancing compared to maintain, the lateral and ventrolateral prefrontal cortex activity increased for both participant groups. In contrast, De la Peña-Arteaga et al. (2021), whose participants choose between distancing and reinterpretation, showed decreased activity in these areas in the BPD group during cognitive reappraisal, when compared to a healthy control group.

Considering that Koenigsberg et al. (2009) applied distancing, one could expect activation in the inferior parietal gyrus, similar to Lang et al. (2012). Nonetheless, Koenigsberg et al. (2009) did not report any activity in the parietal areas. One reason for this is that they used only socially presented images, and the ventrolateral prefrontal cortex shows a significant role in processing emotions of social exclusion (He et al., 2018). In this regard, the findings of Koenigsberg et al. (2009) may represent successful emotion regulation when viewing stimuli that represent social interactions. Furthermore, Koenigsberg et al. (2009) instructed their participants verbally, and the lateral prefrontal cortex has been mapped with fMRI to show activation in trials with verbal instructions (Hartstra et al., 2011).

The decrease in the ventrolateral prefrontal cortex reported by De la Peña-Arteaga et al. (2021), may be attributed to unsuccessful emotion regulation in the BPD group. Additionally, the BPD group possibly had severe symptoms, further leading to a decrease in activity in the ventrolateral prefrontal cortex when compared to healthy controls.

Left Middle Temporal Gyrus and Superior Temporal Gyri

Regarding activation of the left middle temporal gyrus and superior temporal gyri, the findings of four included studies (Koenigsberg et al., 2009; Lang et al., 2012; Schulze et al., 2011) are contradictory (Table 2). Lang et al. (2012) found an increase in the left middle temporal gyrus in all participants, whereas Schulze et al. (2011) found a decrease in the BPD subjects when compared to maintain. The left middle temporal gyrus is involved in language processing (Cabeza & Nyberg, 2000), explaining why Lang et al. (2012), who applied scripts from ANET, reported activation.

Similarly, the superior temporal gyrus is involved in language comprehension and interpretation of auditory input (Yi et al., 2019). This explains why Koenigsberg et al. (2009), who used verbal instructions, and Lang et al. (2012), who used scripts, reported activation.

Summary

Healthy controls and BPD subjects showed opposite activation in two brain areas (Koenigsberg et al., 2009): the dorsal anterior cingulate cortex and the amygdala. The former showed increased activity in healthy controls but decreased activity in BPD participants, whereas the latter showed the opposite pattern. These results are consistent with previous studies reporting hyperactivity in the amygdala (Schulze et al., 2016) and decreased activity in the dorsal anterior cingulate cortex in BPD subjects (Wolf et al., 2012).

Limitations

Limitations of Reviewed Studies

Instructions

It is remarkable how similar distancing and reinterpretation are described in the different studies. Schulze et al. (2011) describe reinterpretation as " imagining that the situation was not real or that they were a detached observer" p. 565, while two studies explain distancing as experiencing the stimuli as a detached and objective observer (Koenigsberg et al., 2009; Lang et al., 2012.)

Reinterpretation increases activation in the temporal, lateral prefrontal, orbitofrontal, inferior frontal, and superior frontal cortex (Dörfel et al., 2014; Ochsner et al., 2004), along with the left superior temporal gyrus (Picó-Pérez et al., 2017). Distancing, on the other hand, activates the cingulate gyrus, the inferior and bilateral superior parietal cortex, and the angular gyrus (Dörfel et al., 2014; Ochsner et al., 2004).

Schulze et al. (2011) showed increased activation in the left inferior parietal gyrus, an area involved in distancing (Dörfel et al., 2014), in the BPD group compared to healthy controls. In contrast, Koenigsberg et al. (2009) found increased activation in the dorsolateral, lateral, and ventrolateral prefrontal cortex, as well as the left superior temporal gyrus in all participants. Areas associated with reinterpretation (Dörfel et al., 2014; Picó-Pérez et al., 2017).

The activation presented in these two articles is a possible consequence of unclear and similar instructions for two separate strategies. In studies where both strategies are implemented without specifying which strategy leads to which outcome, a problem with uncertain results could arise. Therefore, in future studies, a clear description of the emotion regulation strategy used should be conveyed both in the article and to the participants.

Sample Size and Gender Inclusion

A commonality among all studies, nonetheless a limitation, was the sample size. All articles have a sample size of 14-19 BPD subjects (Table 1). BPD is a complex mood disorder that presents in varying ways and severity among diagnosed individuals. In addition, it has been suggested that subtypes of BPD may activate different neurobiological substrates in relation to the individual's predominant symptom (Bassir Nia et al., 2018). Thus, a small sample size means that the results are less generalizable and may be influenced by subtypes of BPD.

In addition, two articles (Lang et al., 2012; Schulze et al., 2011) had only female participants, while De la Peña-Arteaga et al. (2021) and Koenigsberg et al. (2009) had eight and nine in the clinical group, respectively. Gender differences in emotion regulation are still unclear, with several studies providing conflicting results (Whittle et al., 2011). However, male BPD patients have reduced gray matter volume in the anterior cingulate cortex and increased gray matter volume in the putamen (Mancke et al., 2018). Therefore, it can be argued that studies that exclude male subjects provide a more reliable result. At the same time, it is less generalizable to the clinical population.

Limitations of the Present Systematic Review

One limitation was the low quantity of articles. This may limit the reliability and make it difficult to conclude. The low amount of included studies is a consequence of the narrow inclusion criteria. However, the criteria were formulated to avoid comparing studies not relevant to each other and to specifically examine reinterpretation and distancing regarding neural correlates and BPD. To avoid a low quantity of studies, future replications should conduct a broader literature search. The current review does, additionally, not mention inter-rater reliability. This is a consequence of insufficient documentation during the screening phases. The lack of inter-rater reliability could lead to inconsistent inclusion of articles by the two investigators. However, with careful inclusion criteria and a supervisor, this was avoided. Finally, conducting a systematic review takes more time than a normal research paper (Wee & Banister, 2016). Therefore, the time limit of approximately four months may have expedited the work.

Eliciting Negative Affect; IAPS and ANET

The IAPS has been cited to a greater extent than ANET and is more commonly used in emotion research. In addition, using text instead of pictures risks activating areas involved in language processing, such as the left middle temporal gyrus and superior temporal gyri, demonstrated by two articles (Koenigsberg et al., 2009; Lang et al., 2012). With this in mind, IAPS is recommended to minimize variance in replication studies. However, regardless of the medium used, it is important to be aware of the brain areas affected.

BPD and Social Imagery

Koenigsberg et al. (2009) only used socially presented images, whereas Schulze et al. (2011) included both socially and non-socially presented images. Nevertheless, Schulze et al. still found evidence supporting BPD subjects' sensitivity to socially presented images. The two articles showed higher activation in BPD subjects compared to healthy controls when viewing social motifs during maintain. Schulze et al. (2011) in the amygdala and insula and Koenigsberg et al. (2009) in the right superior temporal, anterior, and posterior cingulate, as well as the left cerebellar.

Koenigsberg et al. (2009) stated that activation of primary visual processing regions could demonstrate that BPD individuals have increased identification of emotional faces. Further discussed by Mauchnik and Schmahl (2010), the activation of the superior temporal gyrus, might indicate that BPD individuals have more reflexive and automatic response networks. In contrast, healthy controls rely more on higher-level conscious cortical processing using the dorsolateral prefrontal cortex. Complementing this, Vestergaard et al. (2020) concluded that female BPD patients have preconscious attention to fearful faces, compared to happy expressions, in contrast to healthy controls. In addition, BPD subjects classify faces as angry more often (Vestergaard et al., 2020), possibly supporting Mauchnik and Schmahl (2010). However, the activation of the superior temporal gyrus could be a consequence of the implementation of verbal instructions (Yi et al., 2019) and participants applying reinterpretation instead of distancing (Picó-Pérez et al., 2017).

Schulze et al. (2011) reported increased activity in the amygdala and insula. They showed that activity in the aforementioned regions increased in response to both neutral and negative social stimuli (Schulze et al., 2011). This could be a consequence of the procedure, where BPD participants expected negative stimuli because the majority of the pictures had negative valence. In terms of brain areas, the anticipation of negative stimuli is comparable to actual confrontation, with the amygdala being activated both when experiencing negative stimulus and when anticipating it (Scherpiet et al., 2014). The fact that BPD individuals often misinterpret faces as angry and have a predisposition for vigilance toward fearful faces (Vestergaard et al., 2020), as well as anticipation of negative stimuli, may account for the results from Schulze et al. (2011).

These findings could explain BPD subjects' sensitivity to social interactions. Reflexively, faces are experienced as angry, with implicit awareness of fearful faces (Vestergaard et al., 2020), leading to anticipation of these faces and consequently activating areas such as the amygdala (Scherpiet et al., 2014).

Societal Impact

Through the use of negative language and sexism, research on BPD may further stigmatize diagnosed individuals (Masland et al., 2022). According to Masland et al. (2022), BPD patients experience less sympathy and more hostility, with labels such as "manipulative", "difficult", and "dangerous" from both the public and mental health clinicians. Researchers may perpetuate this stigma by using pejorative language, such as describing BPD patients' fear of abandonment as manipulative and their self-harm as attention-seeking (Masland et al., 2022). However, the included articles avoid portraying stereotypes, with one article (Schulze et al., 2011) showing empathy by writing, "We aimed to validate patients' difficulties" p. 564. In addition, the research articles promote language that dismantles the dangerous precedent that BPD individuals are, e.g. attention-seeking.

Further research aiming to demonstrate difficulties with BPD, is Ntshingila et al. (2016) who interviewed eight diagnosed women. One participant stated "Then I started cutting because I was so confused 'cause I was so angry. I was so emotional" p. 117. Therefore, to develop more effective interventions and tools for BPD patients, the subjective view must be given greater consideration. As stated by Taschereau-Dumouchel et al. (2022): "...subjective distress is a core feature of the definition of an emotional disorder (e.g., in the DSM-5). From this perspective, self-report is the most direct measure of the patient's problem and treatment efficacy." p. 1326. Nevertheless, the included articles offered limited insight into subjective experiences.

While all studies implemented validated questionnaires, the Difficulties in Emotion Regulation Scale has been cited the most, with 4599 citations as of May 8th. However, the questionnaires rate different aspect of emotion regulation, and future studies need to be aware of which questionnaire best fit their research question.

Current Research

Dialectical behavior therapy and mentalization-based therapy is currently the most effective treatment for BPD, showing positive impacts on severity, psychosocial functioning, self-harm, suicide-related outcomes, specific diagnostic criteria, and depression. However, the quality and certainty of evidence supporting these treatments are low (Chanen et al., 2020; Stoffers-Winterling et al., 2022).

Additionally, emotional dysregulation is a common feature of several mental illnesses. Current research is examining how the use of cognitive reappraisal can aid other disorders such as obsessive-compulsive disorder (Picó-Pérez et al., 2022), ADHD (Liu et al., 2022), depression (Toleson et al., 2023), and adolescents with a family history of harmful alcohol usage (Kirk-Provencher et al., 2023).

Future Research and Replication

Despite the fact that BPD has moderate to high heritability, researchers have limited knowledge about its underlying genetic makeup (Bassir Nia et al., 2018). To advance the development of pharmaceuticals, it is crucial to investigate the etiology of BPD. Motivating this research, a recent article has discovered a specific gene leading to anxiety, with the possibility of creating novel drug targets (Mucha et al., 2023).

Additionally, individuals with BPD receive major stigmatization, with labels such as manipulative and dangerous (Masland et al., 2022). The diagnosis, of which 77% affects women, additionally intersects with sexism and negatory language aimed at women. Future research, therefore, needs to be aware of their language and avoid sex- and gender-related research design and language.

Furthermore, current research is already looking into negativity bias, specifically in touch (Löffler et al., 2022) and faces (Vestergaard et al., 2020). However, more research in this area can help improve treatment options concerning psychotherapy, e.g. providing BPD individuals with the necessary support regarding navigating this negativity bias.

Ultimately, to avoid the “generalizability crisis”, Yarkoni (2022) suggests researchers should, among other precautions, in detail convey information on factors like research site, experimenter, effects of stimuli, and more, treat multiple design factors as a varying effect (to state which conditions are necessary for the hypothesis) and increase generalizability by implementing variance in study designs.

For replication, we recommend increasing the sample size in BPD (focusing on female participants), clearly defining the technique of cognitive reappraisal, applying IAPS, and considering which self-assessment is most appropriate for the research question. Furthermore, we propose the dorsolateral prefrontal cortex as a region of interest because of its reportedly decreased activity in BPD (Schulze et al., 2016), yet no significant differences were found in the included studies. Finally, the brain regions associated with the negativity bias observed in BPD require further research.

Conclusion

Individuals with BPD have a suicide rate almost 50 times higher than the general population (Ntshingila et al., 2016) and despite therapy being the primary treatment, 87% of BPD patients receive psychotropic medication (Paton et al., 2015). Learning adaptive emotion regulation for these individuals is crucial, and cognitive reappraisal is a specifically adaptive intervention. This is because it is relatively easy to learn and can be incorporated into everyday life. Nonetheless, the abnormal neural correlates of BPD concerning cognitive reappraisal are elusive, with only four included studies published around 12 years ago. Future research needs replicable methodology, with a focus on the subjective experience of the intervention cognitive reappraisal, to alleviate symptoms of emotional dysregulation.

Word count: 7400

References

Aldao, A., & Nolen-Hoeksema, S. (2012). When are adaptive strategies most predictive of psychopathology?. *Journal of abnormal psychology*, *121*(1), 276. https://doi.org/10.1037/a0023598

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). American Psychiatric Publishing. https://doi.org/10.1176/appi.books.9780890425596

Andrewes, D. G., & Jenkins, L. M. (2019). The role of the amygdala and the ventromedial prefrontal cortex in emotional regulation: implications for post-traumatic stress disorder. *Neuropsychology review*, *29*, 220-243. https://doi.org/10.1007/s11065-019-09398-4

Bassir Nia, A., Eveleth, M. C., Gabbay, J. M., Hassan, Y. J., Zhang, B., & Perez-Rodriguez, M. M. (2018). Past, present, and future of genetic research in borderline personality disorder. *Current Opinion in Psychology*, *21*, 60-68. https://doi.org/10.1016/j.copsyc.2017.09.002

Bradley, M. M., & Lang, P. J. (2007). Affective Norms for English Text (ANET): Affective ratings of text and instruction manual. *Techical Report. D-1, University of Florida, Gainesville, FL.*

Brunoni, A. R., & Vanderhasselt, M. A. (2014). Working memory improvement with non-invasive brain stimulation of the dorsolateral prefrontal cortex: a systematic review and meta-analysis. *Brain and cognition*, *86*, 1-9. https://doi.org/10.1016/j.bandc.2014.01.008

Buechel, S., & Hahn, U. (2016). Emotion analysis as a regression problem–dimensional models and their implications on emotion representation and metrical evaluation. *ECAI 2016* (pp. 1114-1122). IOS Press.

Cabeza, R., & Nyberg, L. (2000). Imaging cognition II: An empirical review of 275 PET and fMRI studies. *Journal of cognitive neuroscience*, *12*(1), 1-47. https://doi.org/10.1162/08989290051137585

Chanen, A. M., Nicol, K., Betts, J. K., & Thompson, K. N. (2020). Diagnosis and treatment of borderline personality disorder in young people. *Current Psychiatry Reports*, *22*, 1-8. https://doi.org/10.1007/s11920-020-01144-5

Chapman, J., Jamil, R. T., & Fleisher, C. (2022). Borderline Personality Disorder. In *StatPearls*. StatPearls Publishing.

Cole, P. M. (2014). Moving ahead in the study of the development of emotion regulation. *International Journal of Behavioral Development*, *38*(2), 203–207. https://doi.org/10.1177/0165025414522170

De la Peña-Arteaga, V., Berruga-Sánchez, M., Steward, T., Martínez-Zalacaín, I., Goldberg, X., Wainsztein, A., & Soriano-Mas, C. (2021). An fMRI study of cognitive reappraisal in major depressive disorder and borderline personality disorder. *European Psychiatry*, *64*(1), e56. https://doi.org/10.1192/j.eurpsy.2021.2231[Opens in a new window]

Dörfel, D., Lamke, J., Hummel, F., Wagner, U., Erk, S., & Walter, H. (2014). Common and differential neural networks of emotion regulation by Detachment, Reinterpretation, Distraction, and Expressive Suppression: A comparative fMRI investigation. *NeuroImage*, *101*, 298-309. https://doi.org/10.1016/j.neuroimage.2014.06.051

Empower Your Mind Therapy. (2021). Emotional regulation skills in DBT therapy. Retrieved February 23, 2023, from https://eymtherapy.com/blog/emotional-regulation-skills-dbt-therapy/

Garnefski, N., & Kraaij, V. (2007). The cognitive emotion regulation questionnaire. European Journal of Psychological Assessment, 23(3), 141-149. https://doi.org/10.1027/1015-5759.23.3.141

Goodman, M., Carpenter, D., Tang, C. Y., Goldstein, K. E., Avedon, J., Fernandez, N., Mascitelli, K. A., Blair, N. J., New, A. S., Triebwasser, J., Siever, L. J., & Hazlett, E. A. (2014). Dialectical behavior therapy alters emotion regulation and amygdala activity in patients with borderline personality disorder. *Journal of psychiatric research*, *57*, 108. https://doi.org/10.1016/j.jpsychires.2014.06.020

Goldin, P. R., Jazaieri, H., & Gross, J. J. (2014). Emotion Regulation in Social Anxiety Disorder. Social Anxiety (Third Edition), 511-529. https://doi.org/10.1016/B978-0-12-394427-6.00017-0

Goldin, A. R.countae, K., Ramel. W., & Gross, J.J. (2008). The Neural Bases of Emotion Regulation: Reappraisal and Suppression of Negative Emotion. *Biological Psychiatry, 63*(6), 577-586. https://doi.org/10.1016/j.biopsych.2007.05.031

Gratz, K. L. & Roemer, L. (2004). Multidimensional assessment of emotion regulation and dysregulation: Development, factor structure, and initial validation of the Difficulties in Emotion Regulation Scale. Journal of Psychopathology and Behavioral Assessment, 26, 41-54. https://doi.org/10.1023/B:JOBA.0000007455.08539.94

Gross, J. J. (2008). *Handbook of emotions*. (2nd ed.). Guilford Press.

Gross, J. J. (2003). Emotion regulation: Affective, cognitive, and social consequences. *Psychophysiology, 39*. 281-291. https://doi.org/10.1017/S0048577201393198

Gross, J.J., & John, O.P. (2003). Individual differences in two emotion regulation processes: Implications for affect, relationships, and well-being. Journal of Personality and Social Psychology, 85, 348-362. https://doi.org/10.1037/0022-3514.85.2.348

Hartstra, E., Kühn, S., Verguts, T., & Brass, M. (2011). The implementation of verbal instructions: An fMRI study. *Human Brain Mapping*, *32*(11), 1811-1824. https://doi.org/10.1002/hbm.21152

Hertrich, I., Dietrich, S., Blum, C., & Ackermann, H. (2021). The role of the dorsolateral prefrontal cortex for speech and language processing. *Frontiers in human neuroscience*, *15*, 645209. https://doi.org/10.3389/fnhum.2021.645209

He, Z., Lin, Y., Xia, L., Liu, Z., Zhang, D., & Elliott, R. (2018). Critical role of the right VLPFC in emotional regulation of social exclusion: a tDCS study. *Social cognitive and affective neuroscience*, *13*(4), 357-366. https://doi.org/10.1093/scan/nsy026

Kirk-Provencher, K. T., Penner, A. E., McRae, K., & Gowin, J. L. (2023). Emotion regulation in young adults with family history of harmful alcohol use: A fMRI study. *Drug and Alcohol Dependence*, *243*, 109752. https://doi.org/10.1016/j.drugalcdep.2022.109752

Koenigsberg, H. W., Fan, J., Ochsner, K., Liu, X., Guise, K. G., Pizzarello, S., Dorantes, C., Guerreri, S., Tecuta, L., Goodman, M., New, A., & Siever, L. J. (2009). Neural Correlates of the Use of Psychological Distancing to Regulate Responses to Negative Social Cues: A Study of Patients with Borderline Personality Disorder. *Biological psychiatry*, *66*(9), 854. https://doi.org/10.1016/j.biopsych.2009.06.010

Lang, S., Kotchoubey, B., Frick, C., Spitzer, C., Grabe, H. J., & Barnow, S. (2012). Cognitive reappraisal in trauma-exposed women with borderline personality disorder. *Neuroimage*, *59*(2), 1727-1734.

Lang, P.J., Bradley, M.M., & Cuthbert, B.N. (2008). International affective picture system (IAPS): Affective ratings of pictures and instruction manual. Technical Report A-8. University of Florida, Gainesville, FL.

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1997). International affective picture system (IAPS): Technical manual and affective ratings. *NIMH Center for the Study of Emotion and Attention*, *1*(39-58), 3.

Lehner, T., & Miller, B. L. (Eds.). (2016). *Genomics, circuits, and pathways in clinical neuropsychiatry*. Academic Press.

Liu, Q., Chen, W., Preece, D. A., Xu, D., Li, H., Liu, N., Fu, G., Wang, Y., Qian, Q., Gross, J. J., & Liu, L. (2022). Emotion dysregulation in adults with ADHD: The role of cognitive reappraisal and expressive suppression. *Journal of Affective Disorders*, *319*, 267-276. https://doi.org/10.1016/j.jad.2022.09.058

Löffler, A., Kleindienst, N., Neukel, C. *et al.* Pleasant touch perception in borderline personality disorder and its relationship with disturbed body representation. *bord personal disord emot dysregul* 9, 3 (2022). https://doi.org/10.1186/s40479-021-00176-4

Malhi, G. S., Bell, E., & Mannie, Z. (2021). What are the real costs of rTMS? *Australian & New Zealand Journal of Psychiatry*. https://doi.org/10.1177/00048674211023969

Mancke, F., Schmitt, R., Winter, D., Niedtfeld, I., Herpertz, S. C., & Schmahl, C. (2018). Assessing the marks of change: how psychotherapy alters the brain structure in women with borderline personality disorder. *Journal of Psychiatry and Neuroscience*, *43*(3), 171-181. https://doi.org/10.1503/jpn.170132

Marco, J. H., Fernandez‐Felipe, I., Fonseca, S., Garcia‐Palacios, A., Baños, R., & Guillen, V. (2021). Confirmatory factor analysis and psychometric properties of the Emotion Regulation Questionnaire in participants with personality disorders. *Clinical Psychology & Psychotherapy*, *28*(6), 1598-1606. https://doi.org/10.1002/cpp.2605

Masland, S. R., Victor, S. E., Peters, J. R., Fitzpatrick, S., Dixon-Gordon, K. L., Bettis, A. H., Navarre, K. M., & Rizvi, S. L. (2022). Destigmatizing Borderline Personality Disorder: A Call to Action for Psychological Science. *Perspectives on Psychological Science*. https://doi.org/10.1177/17456916221100464

Mauchnik, J., Schmahl, C. The Latest Neuroimaging Findings in Borderline Personality Disorder. *Curr Psychiatry Rep* 12, 46–55 (2010). https://doi.org/10.1007/s11920-009-0089-7

Meuldijk, D., McCarthy, A., Bourke, M. E., & S. Grenyer, B. F. (2017). The value of psychological treatment for borderline personality disorder: Systematic review and cost offset analysis of economic evaluations. *PLOS ONE*, *12*(3), e0171592. https://doi.org/10.1371/journal.pone.0171592

Mucha, M., Skrzypiec, A. E., Kolenchery, J. B., Brambilla, V., Patel, S., Kudla, L., Murrall, K., Skene, N., Klejman, A., Przewlocki, R., Mosienko, V., & Pawlak, R. (2023). MiR-483-5p offsets functional and behavioural effects of stress in male mice through synapse-targeted repression of Pgap2 in the basolateral amygdala. *Nature Communications*, *14*(1), 1-14. https://doi.org/10.1038/s41467-023-37688-2

Ntshingila, N., Poggenpoel, M., Myburgh, C. P. H., & Temane, A. (2016). Experiences of women living with borderline personality disorder. *health sa gesondheid*, *21*, 110-119. https://doi.org/10.4102/hsag.v21i0.1017

Nam Bae, J., McFall, J. R., Krishnan, R. R., Payne, M. E., Steffens, D. C., & Taylor, W. D. (2006). Dorsolateral prefrontal cortex and anterior cingulate cortex white matter alterations in late-life depression. *Biological Psychiatry, 60*(12), 1356-1363. https://doi.org/10.1016/j.biopsych.2006.03.052

Ochsner, K. N., Silvers, J. A., & Buhle, J. T. (2012). Functional imaging studies of emotion regulation: A synthetic review and evolving model of the cognitive control of emotion. *Annals of the New York Academy of Sciences*, *1251*, E1. https://doi.org/10.1111/j.1749-6632.2012.06751.x

Ochsner, K. N., Ray, R. D., Cooper, J. C., Robertson, E. R., Chopra, S., Gabrieli, J. D., & Gross, J. J. (2004). For better or for worse: neural systems supporting the cognitive down-and up-regulation of negative emotion. *Neuroimage*, *23*(2), 483-499. https://doi.org/10.1016/j.neuroimage.2004.06.030

Ouzzani, M., Hammady, H., Fedorowicz, Z., and Elmagarmid, A. Rayyan — a web and mobile app for systematic reviews. Systematic Reviews. (2016). 5:210, DOI: 10.1186/s13643-016-0384-4.

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Aki, 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. *PLOS Medicine, 18*(3), Article e1003583. https://doi.org/10.1371/journal.pmed.1003583

Paris, J. (2019). Suicidality in borderline personality disorder. *Medicina*, *55*(6), 223. https://doi.org/10.3390/medicina55060223

Paton, C., Crawford, M. J., Bhatti, S. F., Patel, M. X., & Barnes, T. R. (2015). The use of psychotropic medication in patients with emotionally unstable personality disorder under the care of UK mental health services. *The Journal of clinical psychiatry*, *76*(4), 16358. https://doi.org/10.4088/JCP.14m09228

Picó-Pérez, M., Radua, J., Steward, T., Menchón, J. M., & Soriano-Mas, C. (2017). Emotion regulation in mood and anxiety disorders: A meta-analysis of fMRI cognitive reappraisal studies. *Progress in NeuroPsychopharmacology & Biological Psychiatry, 79,* 96-104. https://doi.org/10.1016/j.pnpbp.2017.06.001

Piretti, L., Pappaianni, E., Gobbo, S., Rumiati, R. I., Job, R., & Grecucci, A. (2021). Dissociating the role of dACC and dlPFC for emotion appraisal and mood regulation using cathodal tDCS. *Cognitive, Affective, & Behavioral Neuroscience*, 1-12. https://doi.org/10.3758/s13415-021-00952-3

Powers, J. P., & LaBar, K. S. (2019). Regulating Emotion Through Distancing:A Taxonomy, Neurocognitive Model, and Supporting Meta-Analysis. *Neuroscience and biobehavioral reviews*, *96*, 155. https://doi.org/10.1016/j.neubiorev.2018.04.023

Picó-Pérez, M., Barbosa, R., Couto, B., Castro, I., Magalhães, R., Sousa, N., Ferreira, S., & Morgado, P. (2022). Altered frontoparietal connectivity in patients with obsessive-compulsive disorder during an fMRI cognitive reappraisal task. *Psychiatry Research*, *317*, 114874. https://doi.org/10.1016/j.psychres.2022.114874

Sampedro, F., Farrés, C. C. I., Soler, J., Elices, M., Schmidt, C., Corripio, I., & Pascual, J. C. (2021). Structural brain abnormalities in borderline personality disorder correlate with clinical severity and predict psychotherapy response. *Brain imaging and behavior*, *15*, 2502-2512.https://doi.org/10.1007/s11682-021-00451-6

Scherpiet, S., Brühl, A. B., Opialla, S., Roth, L., Jäncke, L., & Herwig, U. (2014). Altered emotion processing circuits during the anticipation of emotional stimuli in women with borderline personality disorder. *European archives of psychiatry and clinical neuroscience*, *264*, 45-60.

Schulze L., Schulze A., Renneberg B., Schmahl C., & Niedtfeld I. (2019). Neural Correlates of Affective Disturbances: A Comparative Meta-analysis of Negative Affect Processing in Borderline Personality Disorder, Major Depressive Disorder, and Posttraumatic Stress Disorder. *Biological Psychiatry, 4*(3), 220-232. https://doi.org/10.1016/j.bpsc.2018.11.004

Schulze L., Schmahl C., & Niedtfeld I. (2016). Neural Correlates of Disturbed Emotion Processing in Borderline Personality Disorder: A Multimodal Meta-Analysis. *Biological Psychiatry, 79*(2), 97-106. http://dx.doi.org/10.1016/j.biopsych.2015.03.027

Schulze, L., Domes, G., Krüger, A., Berger, C., Fleischer, M., Prehn, K., Schmahl, C., Grossmann, A., Hauenstein, K., & Herpertz, S. C. (2011). Neuronal Correlates of Cognitive Reappraisal in Borderline Patients with Affective Instability. Biological Psychiatry, 69(6), 564-573. https://doi.org/10.1016/j.biopsych.2010.10.025

Scopus. (2022). *What is Field-weighted Citation Impact (FWCI)?* Retrieved April 11, 2023, from https://service.elsevier.com/app/answers/detail/a_id/14894/supporthub/scopus/~/what-is-field-weighted-citation-impact-%28fwci%29%3F/

Sicorello, M., & Schmahl, C. (2021). Emotion dysregulation in borderline personality disorder: A fronto–limbic imbalance? Current Opinion in Psychology, 37, 114-120. https://doi.org/10.1016/j.copsyc.2020.12.002

Silvers, J. A., Hubbard, A. D., Biggs, E., Shu, J., Fertuck, E., Chaudhury, S., Grunebaum, M. F., Weber, J., Kober, H., Chesin, M., Brodsky, B. S., Koenigsberg, H., Ochsner, K. N., & Stanley, B. (2016). Affective lability and difficulties with regulation are differentially associated with amygdala and prefrontal response in women with Borderline Personality Disorder. *Psychiatry research,* 254, 74-82. https://doi.org/10.1016/j.pscychresns.2016.06.009

Soloff, P., Nutche, J., Goradia, D., & Diwadkar, V. (2008). Structural brain abnormalities in borderline personality disorder: A voxel-based morphometry study. *Psychiatry Research, 164*(3), 223. https://doi.org/10.1016/j.pscychresns.2008.02.003

SPM Software - Statistical Parametric Mapping. (n.d.). Wellcome Centre for Human Neuroimaging © 2023. https://www.fil.ion.ucl.ac.uk/spm/software/

Stoffers-Winterling, J. M., Storebø, O. J., Kongerslev, M. T., Faltinsen, E., Todorovac, A., Sedoc Jørgensen, M., Sales, C. P., Edemann Callesen, H., Pereira Ribeiro, J., Völlm, B. A., Lieb, K., & Simonsen, E. (2022). Psychotherapies for borderline personality disorder: a focused systematic review and meta-analysis. *The British journal of psychiatry : the journal of mental science, 221*(3), 538–552. https://doi.org/10.1192/bjp.2021.204

Sverak T., Linhartova P., Gajdos M., Kuhn M., Latalova A., Lamos M., Ustohal L. & Kasparek T. (2022). Brain Connectivity and Symptom Changes After Transcranial Magnetic Stimulation in Patients With Borderline Personality Disorder. *Fronteirs in Psychiatry, 12*(770353). https://doi.org/10.3389/fpsyt.2021.770353

Taschereau-Dumouchel, V., Michel, M., Lau, H., Hofmann, S. G., & LeDoux, J. E. (2022). Putting the "mental" back in "mental disorders": a perspective from research on fear and anxiety. *Molecular Psychiatry*, *27*(3), 1322-1330. https://doi.org/10.1038/s41380-021-01395-5

Toleson, S., Jimmy, J., Smith, R., Kreutzer, K., Brian, C., & Gorka, S. (2023). 318. Prefrontal Cortex Engagement During Cognitive Reappraisal Impacts the Link Between Depression and Suicidal Ideation in High-Risk Adults. *Biological Psychiatry*, *93*(9), 222-223. https://doi.org/10.1016/j.biopsych.2023.02.558

Yi, H. G., Leonard, M. K., & Chang, E. F. (2019). The Encoding of Speech Sounds in the Superior Temporal Gyrus. *Neuron*, *102*(6), 1096-1110. https://doi.org/10.1016/j.neuron.2019.04.023

Yarkoni, T. (2022). The generalizability crisis. *Behavioral and Brain Sciences, 45*, E1. doi:10.1017/S0140525X20001685

Wee, B. V., & Banister, D. (2016). How to write a literature review paper?. *Transport reviews*, *36*(2), 278-288. https://doi.org/10.1080/01441647.2015.1065456

Van Zutphen, L., Siep, N., Jacob, G. A., Domes, G., Sprenger, A., Willenborg, B., Goebel, R., & Arntz, A. (2018). Always on guard: emotion regulation in women with borderline personality disorder compared to nonpatient controls and patients with cluster-C personality disorder. *Journal of Psychiatry and Neuroscience*, *43*(1), 37-47. https://doi.org/10.1503/jpn.170008

Vestergaard, M., Kongerslev, M. T., Thomsen, M. S., Mathiesen, B. B., Harmer, C. J., Simonsen, E., & Miskowiak, K. W. (2020). Women with borderline personality disorder show reduced identification of emotional facial expressions and a heightened negativity bias. *Journal of Personality Disorders*, *34*(5), 677-698. https://doi.org/10.1521/pedi_2019_33_409

Whittle, S., Yücel, M., Yap, M. B., & Allen, N. B. (2011). Sex differences in the neural correlates of emotion: evidence from neuroimaging. *Biological psychology*, *87*(3), 319-333. https://doi.org/10.1016/j.biopsycho.2011.05.003

Wolff, J. (2019). Emotion Dysregulation and Non-Suicidal Self-Injury: A Systematic Review and Meta-Analysis. *Eur Psychiatry, 59*, 25-36. https://doi.org/10.1016/j.eurpsy.2019.03.004

Wolf, R. C., Thomann, P. A., Sambataro, F., Vasic, N., Schmid, M., & Wolf, N. D. (2012). *European Archives of Psychiatry and Clinical Neuroscience, 262*, 677-685. https://doi.org/10.1007/s00406-012-0303-1

Appendix

Brain areas mentioned in the included studies, together with their functions in relation to emotions and emotion regulation

Brain areas	Koenigsberg et al. 2009 Distancing	Lang et al. 2012 Distancing	Peña-Arteaga et al. 2021 Reinterpreting & Distancing	Schulze et al. 2011 Reinterpreting
Left dorsolateral prefrontal cortex	HC: ↑ BPD: ↑	HC: ↑ BPD: N/A	HC: N/A BPD: N/A	HC: ↑ BPD: ↑
Left middle temporal gyrus	HC: N/A BPD: N/A	HC: ↑ BPD: ↑	HC: N/A BPD: N/A	HC: N/A BPD: ↓
Left inferior parietal gyrus	HC: N/A BPD: N/A	HC: ↑ BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: ↑
Left precuneus	HC: N/A BPD: N/A	HC: ↑ BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: ↓
Left middle occipital gyrus	HC: ↑ BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: ↑
Right parahippocampal gyrus	HC: ↑ BPD: ↑	HC: ↑ BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Superior temporal gyri	HC: N/A BPD: N/A	HC: N/A BPD: ↑	HC: N/A BPD: N/A	HC: N/A BPD:↓
Left supramarginal gyrus	HC: N/A BPD: N/A	HC: ↑ BPD: N/A	HC: N/A BPD: N/A	HC: ↑ BPD: ↑

Brain areas	Koenigsberg et al. 2009 Distancing	Lang et al. 2012 Distancing	Peña-Arteaga et al. 2021 Reinterpreting & Distancing	Schulze et al. 2011 Reinterpreting
Dorsolateral prefrontal cortex	HC: ↑ BPD: ↑	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Right middle temporal gyrus	HC: N/A BPD: N/A	HC: N/A BPD: ↑	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Left inferior frontal gyrus	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: ↑ BPD: ↑
Amygdala	HC: ↓ BPD: ↑	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Right amygdala	HC: N/A BPD:↑	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Left putamen	HC: N/A BPD: N/A	HC: ↑ BPD:↑	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Right insula	HC: ↑ BPD: ↑	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Right pallidum	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: ↓
Left postcentral gyrus	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: ↑

Brain areas	Koenigsberg et al. 2009	Lang et al. 2012	Peña-Arteaga et al. 2021	Schulze et al. 2011
	Distancing	Distancing	Reinterpreting & Distancing	Reinterpreting
Regions bordering the intraparietal sulci bilaterally	HC: ↑ BPD: ↑	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Right posterior cingulate cortex extending to precuneus	HC: ↑ BPD: ↑	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Left superior temporal gyrus	HC: ↑ BPD: ↑	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Right superior temporal gyrus	HC: N/A BPD: N/A	HC: N/A BPD: ↑	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Right superior frontal gyrus	HC: N/A BPD: ↑	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Dorsal anterior cingulate	HC: ↑ BPD: ↓	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Intraparietal sulci bilaterally	HC: ↑ BPD: ↓	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Middle frontal gyrus	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: ↑ BPD: ↑
Left inferior temporal gyrus	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD:↑

Brain areas	Koenigsberg et al. 2009 Distancing	Lang et al. 2012 Distancing	Peña-Arteaga et al. 2021 Reinterpreting & Distancing	Schulze et al. 2011 Reinterpreting
Superior temporal sulcus	HC: N/A BPD: ↑	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Left superior parietal lobe	HC: N/A BPD: N/A	HC: ↑ BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Right thalamus	HC: N/A BPD: N/A	HC: ↑ BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A
Bilateral orbitofrontal cortex	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: ↑ BPD:↑
Medial prefrontal cortex	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: ↑ BPD:↑
Supplementary motor area	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: ↑ BPD:↑
Left precentral	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: N/A BPD: N/A	HC: ↑ BPD:↑

Note. A chart providing information about the brain areas mentioned in the included studies. The studies mentioned in the chart include Koenigsberg et al. (2009), Lang et al. (2012), De la Peña-Arteaga et al. (2021), and Schulze et al. (2011). The chart outlines the functions of different brain areas in healthy controls and individuals with borderline personality disorder (BPD) and indicates whether these functions are increased, decreased, or not applicable for each group. Abbreviations; BPD = borderline personality disorder, HC = healthy controls.