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Emotion Regulation in Social Anxiety Disorder: Exploration and Neuromodulation of Underlying Neural Mechanisms of Cognitive Reappraisal

by

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Thesis for the degree of Doctorate in Clinical Psychology

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ABSTRACT

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Up to 12 percent of the population experience Social Anxiety Disorder (SAD) in their lifetime, significantly impacting on quality of life. National guidance recommends Cognitive Behavioural Therapy (CBT); however, up to 40 percent of individuals experience symptoms post-treatment, with evidence for improved efficacy with a more cognitive approach. Cognitive reappraisal of negative thinking is a cognitive strategy utilised to regulate emotion. However, the neurophysiological mechanisms are not well understood.

Therefore, a systematic review of the literature was completed, in which fourteen research papers were included. Methodologies utilised were varied in terms of imaging methodology, reappraisal task and sample utilised. However, the results support previous research with evidence for altered activation across the prefrontal cortices (PFC; dorso-lateral PFC, dorso-medial PFC, dorsal anterior cingulate cortex), in addition to the inferior parietal lobe and superior temporal gyrus in SAD. This may present the neural mechanisms by which cognitive reappraisal, exerts therapeutic effect in SAD, demonstrating a neural substrate consistent with the Threat Reappraisal Mediation Hypothesis.

Furthermore, recent evidence suggests that transcranial direct current stimulation (tDCS) of the PFC can improve cognitive reappraisal success in healthy adults. Therefore, this study aimed to investigate the selective effects of PFC tDCS on cognitive reappraisal in adults experiencing symptoms of SAD, in comparison to active (cerebellar) and sham control groups. A secondary, exploratory aim was to investigate the effects of cerebellar tDCS on emotion recognition.

Thirty-three healthy students with symptoms of social anxiety received 20-minutes of PFC, cerebellar or sham tDCS whilst completing an autobiographical social situations reappraisal task, before completing an emotion recognition task; within this multi-site, mixed, double-blind design. The main findings were that PFC and cerebellar tDCS improved cognitive reappraisal in the first trial block. Additionally, tDCS improved recognition sensitivity for happy faces and increased reaction times to angry faces. Clinical implications and suggestions for future research are discussed.

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DECLARATION OF AUTHORSHIP

I, ...Gabriella Bethaney Haeems..... [please print name]

declare that this thesis and the work presented in it are my own and has been generated by me as the result of my own original research.

Emotion Regulation in Social Anxiety Disorder: Exploration and Neuromodulation of Underlying Neural Mechanisms of Cognitive Reappraisal

I confirm that:

1. This work was done wholly or mainly while in candidature for a research degree at this University;

2. Where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated;

3. Where I have consulted the published work of others, this is always clearly attributed;

4. Where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work;

5. I have acknowledged all main sources of help;

6. Where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself;

7. None of this work has been published before submission.

Signed:
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1 Chapter 1: The Neurophysiological Mechanisms of Cognitive Reappraisal in Adults with Social Anxiety: A Systematic Review of the Literature

1.1 Introduction

1.1.1 Social Anxiety

Social anxiety disorder (SAD) is defined within the Diagnostic and Statistical Manual (DSM-5) of Mental Disorders (American Psychiatric Association, APA, 2013) as an excessive and enduring (6 months or more) fear of social or performance situations, where the individual is exposed to unfamiliar people or potential social scrutiny, resulting in high levels of distress and/or avoidance impacting on the individuals' daily life. Up to 12 percent of the population experience SAD in their lifetime (Kessler et al., 2005), as the most common anxiety disorder, across ethnic groups (Asnaani, Richey, Dimaite, Hinton & Hofmann, 2010), impacting significantly on employment, relationships and overall quality of life (Wittchen, Fuetsch, Sonntag, Müller & Liebowitz, 2000; Wong, Sarver & Beidel, 2012).

1.1.2 Psychological Models of Social Anxiety

1.1.2.1 *Cognitive Models of Social Anxiety*

The Clark and Wells (1995) model of SAD describes how maladaptive assumptions and beliefs become activated in social situations causing individuals to believe they are in danger of negative social-evaluation. The model describes four consequent maintaining factors which act as barriers to disconfirm maladaptive beliefs; including a shift to self-focused attention and monitoring, the use of safety behaviours, negatively focused evaluations of past and future social interactions in detail and overestimating negative evaluations of self from others. Therefore, Clark and Wells

(1995) place importance on *internal* focused attentional processes in producing and maintaining anxiety, through the detection of internal cues of social threat (Schultz & Heimberg, 2008).

Alternatively, Rapee and Heimberg (1997) suggest that it is the detection of both internal and external cues of social threat, through attentional focus on both the self, but also the environment, that cause and maintain social anxiety (Schultz & Heimberg, 2008). Rapee and Heimberg (1997) describe how individuals with SAD perceive others as a threat of negative evaluation and so become hyper-vigilant for external and internal cues which confirm these beliefs. On exposure to a social situation, an individual's mental representation of the self is activated, encompassing an image of how they think they appear to others, in addition to negative self-beliefs (NSBs) developed from past experiences.

However, Hirsch, Clark and Mathews (2006) argued that cognitive biases in social anxiety do not occur independently, but instead it is the combination of these which cause the development and maintenance of SAD. The combined cognitive biases hypothesis (Hirsch, Clark & Mathews, 2006) identifies two cognitive biases in particular: negative self-imagery of how the self is perceived negatively by others in social situations, and negative interpretation biases of ambiguous social stimuli/situations. The authors suggest that each bias holds mutual impact on the other, as well as memory, influencing attentional focus for threat in future situations.

Consequently, Heimberg, Brozovich and Rapee (2010) updated their cognitive model to include the role of negatively biased imagery, from the observer perspective; impacting on experience of anxiety and consequently impacting behaviour and the mental representation of how others see oneself. The updated

model also recognised the role of 'post-event processing' of actions of self and others after social situations; fear of positive and negative evaluation, leading to future social expectations which the individual feels cannot be maintained; emotion regulation through emotion suppression as a safety behaviour, with beliefs that others will view expression negatively, whilst impacting on the ability to form close relationships with others.

1.1.3 Treatment: Cognitive behavioural Therapy (CBT)

Cognitive behaviour therapy (CBT), is psychological therapy offered to adults with SAD, recommended by the National Institute for Health and Care Excellence (NICE, 2013). CBT incorporates a range of strategies for therapeutic effect, including psychoeducation, exposure, relaxation, social skills training and cognitive restructuring (Heimberg, 2002).

CBT has been widely researched as an effective treatment for SAD in adults (Ponniah & Hollon, 2008) with 60 to 65.8 percent response rates recorded across randomised controlled trials (e.g. Stangier, Schramm, Heidenreich, Berger & Clark, 2011; Leichsenring et al., 2013) with large effect sizes (Mayo-Wilson et al., 2014). However, the mechanisms underlying the effectiveness of CBT is under-researched (Klumpp, Fitzgerald & Phan, 2013). Furthermore, 34 to 40 percent of individuals treated for SAD do not respond with clinically important improvement in symptoms post-treatment (Parker & Waller, 2015; Klumpp, Fitzgerald et al., 2017). Consequently, recent literature has emphasised the importance of identifying key CBT methods of change on which to capitalise treatment efficacy.

Cognitive models emphasise the importance of addressing cognitions when treating anxiety disorders (Clark & Beck, 2011), with cognitive restructuring an

integral part of CBT focusing on challenging negative thinking processes. Throughout CBT for SAD, individuals are trained to become aware of negative thoughts and interpretations around social threat and assess their rationality and truthfulness, to cognitively reappraise negative thinking and generate more balanced alternatives (Heimberg, 2002; Brozovich et al., 2014). Subsequently, the Threat Reappraisal Mediation Hypothesis suggests that the reappraisal of threat cognitions is a key mechanism through which CBT exerts therapeutic effect (Hofmann, 2008; Smits, Julian, Rosenfield & Powers, 2012), with evidence to suggest improved efficacy for a more cognitive-focused therapy in SAD (Clark et al., 2006).

1.2 Cognitive Reappraisal

The term 'cognitive reappraisal' is used to describe an emotion regulation strategy involving the cognitive reinterpretation of an anxiety provoking situation or stimulus, through the active process of developing alternative, less toxic interpretations of the situation to modify an elicited emotional response (John & Gross, 2004). Evidence suggests that habitual use of cognitive reappraisal predicts increased positive well-being and protects against the development of depressive symptoms and emotional disorders (Haga, Kraft & Corby, 2009; Kalisch, 2009; Troy, Wilhelm, Shallcross & Mauss, 2010; Aldao & Nolen-Hoeksema, 2010), in addition to improved inter-personal functioning and experience of positive emotion (Gross & John, 2003).

The Process Model of emotion regulation (John & Gross, 2004) describes the behavioural mechanisms through which cognitive reappraisal exerts therapeutic effect. The model details the temporal aspects of emotional responding and states that emotion regulation can take place at five different time-points of emotion generation; *situation selection, modification, attentional deployment, cognitive change or response modulation* (John & Gross, 2004). The authors described how

emotion regulation at any of the first four time-points denotes an 'antecedent focused' whereas the fifth time-point denotes a 'response focused' emotion regulation strategy. John and Gross (2004) suggest that the cognitive reappraisal of meaning is an antecedent focused strategy, in which the cognitive meaning is reinterpreted, with evidence that it is this change in cognition which exerts emotion regulatory effect (Urry, 2010).

The utilisation of cognitive reappraisal has been shown to be associated with anxiety symptom improvement post-CBT (Smits, Julian, Rosenfield & Powers, 2012), mediate and predict CBT response and symptom reduction in adults with SAD (Moscovitch et al., 2012; Goldin, Ziv et al., 2012). Therefore, there has been a recent surge in research to explore the mechanisms of effect of cognitive reappraisal as an emotion regulation strategy, due to the centrality to CBT treatment.

1.2.1 Neurocognitive mechanisms of Cognitive Reappraisal

Buhle et al (2014) conducted a meta-analysis of 48 neuroimaging studies to reveal the neural mechanism of cognitive reappraisal through which healthy participants downregulate negative affect. Areas consistently identified across research include the dorso-medial prefrontal cortex (dmPFC), dorso-lateral prefrontal cortex (dlPFC), ventro-lateral prefrontal cortex (vlPFC) and posterior parietal lobe; leading to suggestions of pre-frontal cognitive control facilitating reappraisal of stimulus interpretations, impacting on feelings of anxiety and amygdala activity.

In clinical populations, Zilverstand, Parvaz and Goldstein (2017) recently conducted a systematic review to identify the neural mechanisms of cognitive reappraisal across mood disorders, anxiety, schizophrenia, addiction and personality disorders. Utilising a transdiagnostic approach, they found that when down-

regulating negative emotion, participants with clinical disorders show a reduction in activity within the dlPFC and vlPFC. However, individuals with anxiety disorders specifically demonstrated reduced dorsal anterior cingulate cortex (dACC) and inferior/superior parietal cortex activity; with the authors suggesting impaired attentional distribution. This suggests that whilst there are similar mechanisms at work across populations, disorder-specific neural correlates of emotion regulation are also present.

1.2.1.1 *Neurophysiology of Social Anxiety*

Neuroimaging research suggests a general cognitive bias towards threat processing in SAD (Klumpp, Fitzgerald & Phan, 2013), with consistent evidence for hyperactivity within the amygdala and insula cortices in SAD as reported within a meta-analysis of functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) research, conducted by Etkin and Wager (2007). The amygdala is widely associated with emotion processing, particularly threat perception and anxiety (Hahn et al., 2011), as a key component within fear circuitry interlinked and regulated by prefrontal regions (LeDoux, 2000). Evidence from lesion studies demonstrate that amygdala lesioning results in diminished fear responding to threat and consequent disinhibition (Amaral, 2003), due to disrupted prefrontal links. Therefore, amygdala hyperactivity present in SAD could underlie persistent threat processing biases (Akirav & Maroun, 2007).

This is further supported by Freitas-Ferrari et al (2010) who also found increased activity within the amygdala and insular regions in SAD in a recent literature review. Additionally, medial pre-frontal cortex (mPFC), dopamine and gamma-aminobutyric acid neurotransmitter (GABA) abnormalities were also observed in SAD compared to healthy controls; with impaired GABA function linked to amygdala hyperactivity

(Aroniadou-Anderjaska, Qashu & Braga, 2007) and lending support for a dopamine dysregulation model (Mathew, Coplan & Gorman, 2001).

1.2.2 Rationale for this Review

Whilst CBT is the first-line treatment for adults with SAD, up to 40 percent of individuals do not respond to therapy. Evidence suggests that cognitive reappraisal is a key component to treatment response and outcome, exerted through pre-frontal control; but how cognitive reappraisal exerts therapeutic effect in social anxiety in particular, remains unclear (Klumpp, Fitzgerald & Phan, 2013). To the author's knowledge, a review of the neurophysiological mechanisms underlying cognitive reappraisal in social anxiety has not been conducted. Whilst Zilverstand, Parvaz and Goldstein (2017) conducted a literature review across diagnoses, a limited search strategy was employed with minimal terms included for paper identification as a more superficial summation of a narrow search. In addition to this, Zilverstand, Parvaz and Goldstein (2017) reported very few studies on social anxiety, as a result of the narrow scope of the review and a synthesis of cognitive reappraisal neural mechanisms in social anxiety specifically, was absent.

Therefore, in consideration of the limitations of the previous literature reviews conducted within this area, this review primarily aimed to investigate the neurophysiological mechanisms by which cognitive reappraisal exerts therapeutic effect in adults with SAD. This review furthers the work of Zilverstand, Parvaz and Goldstein (2017) through the adoption of more broad inclusion criteria, including a range of participant samples with social anxiety across brain-imaging designs, to ensure a maximum cohort of data is captured within this under-researched area. All available evidence is examined methodically within this systematic literature review,

to reduce the effect of potential bias and ensure reliability of results (Booth, Sutton & Papaioannou, 2016).

A secondary aim of this review is to explore and critique cognitive reappraisal task protocols and identify key moderating and mediating factors for emotion regulation success and neural activity. Finally, this review critically evaluates research methodologies utilised and discusses future research and implications for clinical practice.

1.3 Method

1.3.1 Information Sources and Search terms

Initial scoping of the research area was completed using Delphis (Southampton database) and PsychInfo. The search formulation utilised the Population, intervention, comparison, outcome (PICO) format (Richardson, Wilson, Nishikawa & Hayward, 1995) and search terms and strategy were refined and verified through the adoption of a second reviewer and liaison with the library team confirming reliability and validity. The full literature search was completed in March 2018 across Web of Science, PubMed and PsychInfo databases. An example of the search terms utilised are listed below, which were appropriately adapted for each database:

("social anxiety disorder" OR "social anxiety" OR "social phobia") AND ("cogniti* reapprais*" OR "emotion regulat*" OR "emotion regulat* strateg*" OR "self-regulat*" OR "cognitive therapy" OR "down regulat*" OR "up regulat*" OR "reframe*" OR "cognitive-linguistic strateg*") AND (("tDCS" OR "transcranial direct current stimulation" OR "brain stimulat*") OR ("tms" OR "transcranial magnetic stimulation" OR "brain stimulat*") OR ("fMRI " OR "functional magnetic resonance imaging") or ("brain imag*") OR ("MRI" OR "magnetic resonance imaging") OR ("PET" OR "Positron emission tomography") OR ("EEG" OR "electroencephalogr*" OR "brain wave*") OR (“LPP” OR “late positive potential”)).

1.3.2 Inclusion and Exclusion Criteria

The article inclusion criteria comprised empirical research, utilising an adult sample (18-64) with social anxiety, published within a peer reviewed journal. Eligible studies utilised brain-imaging methodology to explore neural mechanisms of cognitive reappraisal in social anxiety and include a cognitive reappraisal task to evaluate this. There were no restraints of publication date in this search due to the

relative novelty of the methodology required for inclusion and the limited number of papers obtained in initial scoping searches.

1.3.3 Search Strategy

On completion of the full search and identification of relevant studies, a citation search was also undertaken within Web of Science, to ensure inclusion of relevant papers, expanding the breadth of search. In addition to this, a bibliography search was completed, involving the manual extraction of additional relevant articles from the extracted literature. Articles of interest were systematically subjected to title screenings, followed by abstract and full-text screens of eligibility for inclusion within this review (Booth, Sutton & Papaioannou, 2016) (see figure 1).

1.3.1 Data extraction

The primary outcomes for this review were the identification of neural regions involved in cognitive reappraisal. Therefore, relevant data including brain imaging methodology utilised and key neural regions implicated in cognitive reappraisal was collated alongside participant, task and relevant methodological information; including study and sample descriptive characteristics, diagnostic/trait measures of social anxiety, cognitive reappraisal task, strategy and stimuli utilised, measure of cognitive reappraisal success. Relevant data detailing moderating and mediating factors and methodological strengths and limitations were also extracted and considered. Where multiple experiments were reported, only the eligible cognitive reappraisal study was included within this literature review.

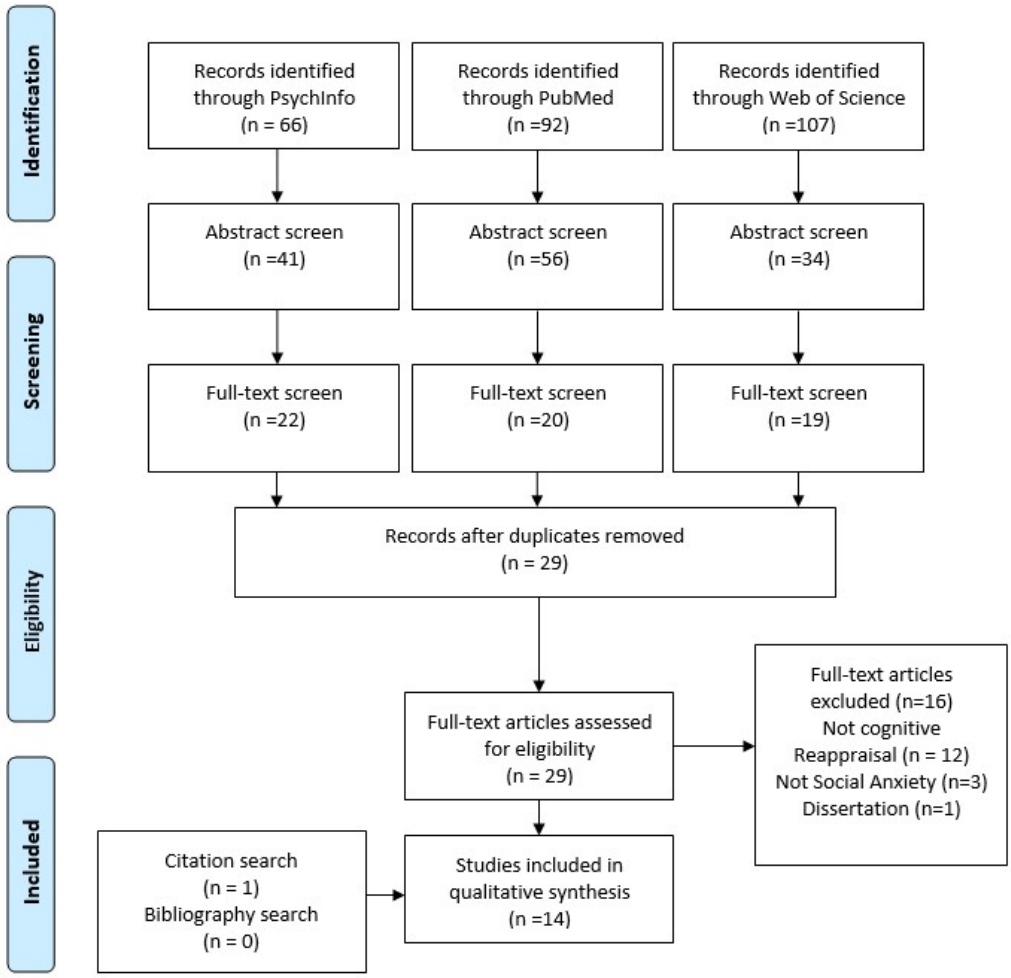

Figure 1. PRISMA flow diagram of systematic literature search and paper selection for inclusion.

1.3.2 Review of literature

A narrative analysis of the obtained studies is presented. This method was employed rather than more quantitative and meta-analysis approaches, to allow for the synthesis of varying results across distinct neuro-imaging methods, including fMRI and Electroencephalogram (EEG) which are not easily combined (Freitas-Ferrari et al., 2010).

1.4 Results

A total of 14 studies were included within this review (see table 1 for a summary of included studies).

1.4.1 Key findings: regions and mechanisms identified

1.4.1.1 *fMRI*

A summary of the brain regions implicated in cognitive reappraisal in SAD, across the included fMRI research is presented in table 2. Areas within the pre-frontal cortex (PFC) are most frequently implicated in cognitive reappraisal, with the dlPFC identified by six fMRI studies (3, 5, 6, 7, 11, 12; see figure 2). Five studies found decreased activity in the dlPFC during cognitive reappraisal in comparison controls (3, 5, 6, 7, 11). Conversely, two studies (6, 12) demonstrated increased activity within dlPFC in SAD. However, differences in reported activity may be a result of the variation in temporal information provided, with (6) demonstrating decreased *early* dlPFC activity but increased *late* dlPFC activity; a pattern which is also demonstrated within the vlPFC (6). This is supported by Bruhl et al (2013; 3) who reported decreased dlPFC activity in anticipation of reappraisal, demonstrating decreased early activity. Kreifelts et al., (2017; 12) concluded that left dlPFC activity mediates the impact of SAD on emotion regulation, presenting reduced dlPFC connectivity in SAD to wider areas such as the temporal voice area (TVA) when reappraising socially threatening stimuli (laughter), demonstrating a widespread variation in dlPFC activation and connectivity. However, evidence from CBT intervention designs demonstrate the utilisation of this neural marker as a mediator of therapeutic response. Klumpp, Roberts et al (2017; 11) found that decreased dlPFC activity predicted CBT response and related to increased changes in social anxiety symptomology. This demonstrates the relationship between dlPFC activity and

Table 1

A summary of studies included within the systematic review, with key findings in brain response

No.	Study	Location	Participants (*N*)	Diagnostic Measure	Age Mean(SD) F/M	Design	Reappraisal Stimuli	Reappraisal Strategy	Key Findings	Methodological Strengths	Methodological Limitations
1	Adolph, Meister & Pause, (2013)	Germany	18 non-socially anxious 18 HSA	SIAS	23.72(4.86) 18F/0M	EEG	Anxious Facial expressions (KDEF)	Up/down/watch	↑Early N170 amplitudes (ERPs) in HSA than LSA when instructed to watch and down regulate emotions in control chemosensory stimuli at left and midline electrodes. LPP varied with emotion regulation instruction in LSA only- ↑LPPs in lateral right electrode sites, when instructed to enhance vs watch in the context of chemosensory stimuli	1. Training and practice 2. Large number of trials 3. Included social desirability measure 4. Up and down regulation as a measure of overall cognitive control	1. All female participants 2. Anxious male faces only, no neutral comparison 3. Risk habituation to trials 4. Emotions elicited by chemosensory stimuli not assessed – i.e. disgust response. 5. Excluded comorbidity
2	Blair et al (2012)	USA	19 gSAD 17 GAD 17 gSAD/ GAD 18 HC	SCID	29.4(8.70) 10F/8M 36.1(11.75) 13F/4M 35.7 (9.54) 12F/5M 33.4(9.65) 10F/8M	fMRI	IAPS	Up/down/view	↑ dACC, superior parietal cortex in downregulate in HC compared to SAD and GAD/SAD.	**1.** Healthy and clinical comparison groups 2. Up and down regulation as a measure of overall cognitive control 3. Training and practice	1. Inadequate power 2. Excluded other comorbidities. 3. Generic stimuli are less ecologically valid 4. No neutral reappraisal stimuli, positive and negative only
3	Bruhl, Herwig, Delsignore, Jäncke & Rufer, (2013)	Switzerland	14 gSAD no cognitive control 14 gSAD cognitive control	M.I.N.I semi-SCID	33.4(12.0) 7F/7M 35.2(9.3) 6F/8M	fMRI	IAPS	Down/react (between groups)	Anticipatory Reappraise: ↓left amygdala, left middle insular cortex, left dlPFC and the bilateral parietotemporal regions Reappraise: ↓left prefrontal, bilateral temporal and parietal areas during the perception of negative in cog group vs basic ↓left thalamic and left parahippocampal gyrus/amygdala due to reappraisal in cognitive control group	1. Between-groups comparisons 2. Positive, negative and neutral stimuli comparisons 3. Included participants on medication 4. Included comorbidity 5. Participants had no experience of CBT 6. Training and practice	1. Significantly different SAD severity scores between groups 2. fMRI methodological issues (e.g., change of the scanner)

4	Gaebler, Daniels, Lamke, Fydrich & Walter (2014)	Germany	21 SAD 23 healthy controls	SCID	30.5(7.17) 5F/16M 30.0(7.99) 5F/18M	fMRI	IAPS	Up/down	NO SIG DIFFERENCES BETWEEN GROUPS.	1. Healthy control group 2. Included participants on medication 3. Included comorbidity 4. Up and down regulation as a measure of overall cognitive control 5. Negative and neutral stimuli comparison 6. Training and practice	1. No additional measures of comorbidity 2. Utilised less ecologically valid generic stimuli
5	Goldin, Manber, Hakimi, Canli & Gross (2009)	USA	15 with SAD 17 healthy matched	ADIS	31.6(9.7) 9F/6M 32.1(9.3) 9F/8M	fMRI	Harsh faces and violent scenes and neutral scenes	Down/look	HC ↑dlPFC, dACC, medial cuneus, posterior cingulate, bilateral dorsal parietal and bilateral fusiform, superior temporal gyrus in HC than SAD in downregulate faces condition vs look. ALL dmPFC and right superior frontal gyrus, left inferior frontal gyrus, left supramarginal gyrus, and bilateral posterior superior temporal gyrus. ↑dmPFC during cognitive regulation was associated with significant reduction in negative emotion ratings.	1. Healthy control group 2. Included comorbidities 3. Negative and neutral stimuli comparison 4. Training and practice	1. Neutral comparison did not match harsh face stimuli 2. Excluded participants on medication
6	Goldin, Manber-Ball, Werner, Heimberg & Gross, (2009)	USA	27 patients with gSAD 27 healthy controls	ADIS	32.1(9.2) 12F/15M 32.2(9.5) 12F/15M	fMRI	autobiographical social situations and NSB	Down/react	↑late dlPFC, vlPFC, bilateral insular cortex, inferior parietal lobule, precuneus compared to HC in reappraisal REDUCED ↑early dACC, mPFC, dmPFC, bilateral dlPFC and vlPFC, left inferior frontal gyrus and medial precuneus, bilateral inferior parietal lobule compared to HC	1. Healthy control group 2. Included comorbidities 3. Included participants on medication 4. Idiosyncratic reappraisal stimuli 5. No experience of CBT 6. Negative and neutral stimuli comparison 7. Training and practice	1. No measure of social desirability

									FCA = more PFC cognitive control regions inversely related to amygdala activation in controls: three regions in the left dlPFC, two regions in the right lPFC and attention regulation regions (inferior parietal lobule)		
7	Goldin et al (2013)	USA	31 gSAD CBT 29 gSAD wait-list	ADIS	33.4(7.6) 11F/20M 33.6 (10.4) 9F/20M	fMRI CBT	autobiographical social situations and NSB	Down (CBT)	↑early dmPFC, ↑left dlPFC in CBT vs waitlist. FCA=CBT produced greater inverse connectivity between the dmPFC and left amygdala and the right hippocampus and positive connectivity in the medial PFC and 2 dlPFC regions.	1. Idiosyncratic reappraisal stimuli 2. CBT intervention compared to waitlist controls 3. Included participants on medication 4. Included comorbidities 5. No experience of CBT 6. Negative and neutral stimuli comparison 7. Randomised Control trial	1. No healthy control group 2. Reported dropout due to lying about symptoms 3. Unable to conclude if effects are a result of cognitive reappraisal specifically, as one part of wider CBT treatment
8	Goldin et al (2014)	USA	31 gSAD CBT 28 gSAD WL	ADIS	33.7(7.9) 15F/16M 33.3(10.1) 13F/15M	fMRI CBT	Video clips of actors delivering social criticism or shame	Down/watch	CBT↑ and WL↓ pre-post: right SFG and right MOG CBT↓ and WL↑ pre-post left posterior STG	1. Included social desirability measure 2. CBT intervention compared to waitlist controls 3. Included comorbidities 4. No experience of CBT 5. More generalisable and SAD relevant video stimuli	1. No healthy control group 2. No neutral stimuli comparison 3. Excluded participants on medication 4. Risk of habituation to trials 5. Unable to conclude if effects are a result of cognitive reappraisal specifically, as one part of wider CBT treatment
9	Kivity & Huppert (2018)	Israel	49 gSAD 35 healthy controls	DSM-IV-TR	28.29(7.12) 22F/27M 28.49(6.28) 15F/20M	EEG	Shame-arousing and neutral pictures	Down/ View/ Suppress	NO SIGNIFICANT DIFFERENCES BETWEEN GROUPS ON LPP = No impairments in lab-based reappraisal	1. Healthy control group 2. Included suppression comparison group 3. Included participants on medication	1. Standardised Lab generated stimuli – less ecological validity

										4. Included comorbidities 5. Negative and neutral stimuli comparison	
10	Klumpp, Fitzgerald et al (2017)	USA	38 gSAD	SCID-IV	25.2(5.9) 23F/15M	fMRI CBT	IAPS unpleasant and neutral	Down/ Maintain/ Look	Amygdala positively correlated with rACC and dACC in reappraise vs Maintain. ↓rACC baseline activation in reappraise differentiated CBT responders from non-responders.	1. No current therapy 2. CBT intervention repeated measures design 3. Included participants on medication 4. Included comorbidities 5. Neutral and negative stimuli comparison	1. No healthy or waitlist control groups 2. Generic stimuli are less ecologically valid 3. Modest power and sample size 4. Unable to conclude if effects are a result of cognitive reappraisal specifically, as one part of wider CBT treatment
11	Klumpp, Roberts et al (2017)	USA	34 SAD	SCID-IV	25.0(4.7) 22F/12M	fMRI CBT	IAPS unpleasant and neutral	Down (CBT) /look	↓dlPFC predicted responder status to CBT and related to increased symptom change	1. No current therapy 2. CBT intervention repeated measures design 3. Included comorbidities 4. Neutral and negative stimuli	1. No healthy or waitlist control group 2. Excluded participants on medication 3. Generic stimuli are less ecologically valid 4. Unable to conclude if effects are a result of cognitive reappraisal specifically, as one part of wider CBT treatment 5. Modest sample size
12	Kreifelts et al (2017)	Germany	12 SAD 14 HC	SCID	23.3(3.4) 6F/6M 25.3(2.1) 7F/7M	fMRI	Videos of laughing faces	Down/React	↑left dlPFC during reappraise in SAD compared to HC ↓dlPFC connectivity to TVA in reappraisal compared to HC	1. Healthy control group 2. Included comorbidities 3. More generalisable SAD relevant stimuli 4. Positive, negative and neutral comparison stimuli	1. Rated laughter as including/excluding rather than affect measure 2. Small sample size
13	Yuan, Zhou & Hu (2014)	China	15 HSA 13 LSA	PRCA-24	20.47(1.85) 15F/0M 20.00(2.58) 13F/0M	EEG	Neutral and threatening photographs of faces from NimStim	Down/Look	↓SPN than the LSA group when viewing the reappraisal cue word ↓ P2-N2 for reappraisal vs look in LSA not HSA	1. LSA control group 2. Neutral and negative stimuli	1. Artificial lab environment 2. Small sample size 3. No details of inclusion/exclusion criteria reported

							Emotional Face Stimuli database				4. Standardised Lab generated stimuli
14	Ziv, Goldin, Jazaieri, Hahn & Gross (2013)	USA	27 SAD 27 HC	ADIS-IV-L	31.1(7.6) 12F/15M 32.6(9.5) 13F/14M	fMRI	Harsh faces Video clips NSB	Down/React	Faces: ↑late left IFG, dACC, ↑early and late left LOFC in HC Videos: ↑early bilateral fusiform gyrus, ↑left lingual gyrus, ↑late left putamen, ↑early and late right cerebellum in HC Autobiographical:↑late STG in HC; ↓late dmPFC in SAD	1. Healthy control group 2. Utilised range of stimuli for comparison 3. Positive, negative and neutral stimuli comparison 4. No experience of CBT 5. No current therapy 6. Included comorbidities	1. Excluded medication

Note. ↑=increase; ↓=decrease; SAD=Social Anxiety Disorder; gSAD=generalised Social Anxiety Disorder; HSA = High social anxiety; LSA = low social anxiety; HC=Healthy controls; F=Female; M=Male; SCID=Structured Clinical Interview for DSM-IV; ADIS-IV-L= Anxiety Disorders Interview Schedule for DSM-IV-TR Lifetime version; PRCA-24 = Personal Report of Communication Apprehension; M.I.N.I= The Mini-International Neuropsychiatric Interview; EEG=electroencephalogram; fMRI=Functional magnetic resonance imaging; CBT=Cognitive Behavioural Therapy; KDEF= Karolinska Directed Emotional Faces set; IAPS=International Affective Picture System; NSB=Negative Self Beliefs; ERP= Event-related Potential; LPP =Late Positive Potential; dACC=Dorsal Anterior Cingulate Cortex; dlPFC= Dorsolateral Prefrontal Cortex; dmPFC=Dorsomedial Prefrontal Cortex; vlPFC= Ventrolateral Prefrontal Cortex; mPFC=Medial Prefrontal Cortex; PFC=Prefrontal Cortex; FCA = Functional Connectivity Analysis; lPFC=lateral Prefrontal Cortex; SFG=Superior Frontal Gyrus; MOG= Middle Occipital Gyrus; STG= Superior Temporal Gyrus; rACC= rostral Anterior Cingulate Cortex; TVA=Temporal Voice Area; SPN = stimuli-preceding negativity; IFG = Inferior Frontal Gyrus; LOFC=lateral orbitofrontal cortex.

effective cognitive reappraisal as an emotion regulation strategy in SAD. Other prefrontal areas have been found to present with a different pattern of activation. Three studies have found decreased early (6, 7) and late (14) activity within dmPFC in SAD in comparison to controls; with a similar pattern presented for the wider mPFC (3, 6), lateral orbitofrontal cortex (LOFC; 14) and Inferior Frontal Gyrus (IFG; 6, 8, 14). However, the beneficial effects of CBT on dmPFC activation were presented by Goldin et al (2013; 7), demonstrating increases in early dmPFC activity post-CBT, in comparison to individuals with SAD on the waitlist; with increases in dmPFC activity associated with successful emotion regulation across all groups (5) and uniquely for SAD, across differing cognitive reappraisal tasks (14). The results of four studies (2, 5, 5, 14) consistently presented with decreased activation within the dACC in SAD compared with controls, during both early (6) and late (14) activity; as an area which has been widely documented in reappraisal (Messina, Bianco, Sambin & Viviani, 2015). Additionally, decreased activation in the rostral Anterior Cingulate Cortex (rACC) differentiated CBT responders from non-responders, suggesting a role in the mediation of wider lateral and medial PFC (10). However, Klumpp, Fitzgerald et al, (2017; 10) also found that amygdala activity positively correlated with rACC and dACC during cognitive reappraisal, in comparison to maintain trials, leading to suggestions that individuals with SAD were not effective in regulating amygdala activity.

Evidence is also presented for the involvement of regions within the parietal cortex, including the superior parietal lobe implicated in three studies (2, 5, 8), demonstrating reduced activity in comparison to controls. Additionally, the superior temporal gyrus (STG) was presented across three studies, with differing levels of activity; with one study presenting increased activity (8) and two studies

demonstrating decreased activity in comparison to controls (5, 14), with decreases in late activation specifically (14). The importance of temporal features is again presented in Ziv et al (2013; 14) who uniquely found activation across the right cerebellum, however on conduction of temporal analyses, concluded that this was more a result of reactivity to video stimuli than cognitive reappraisal.

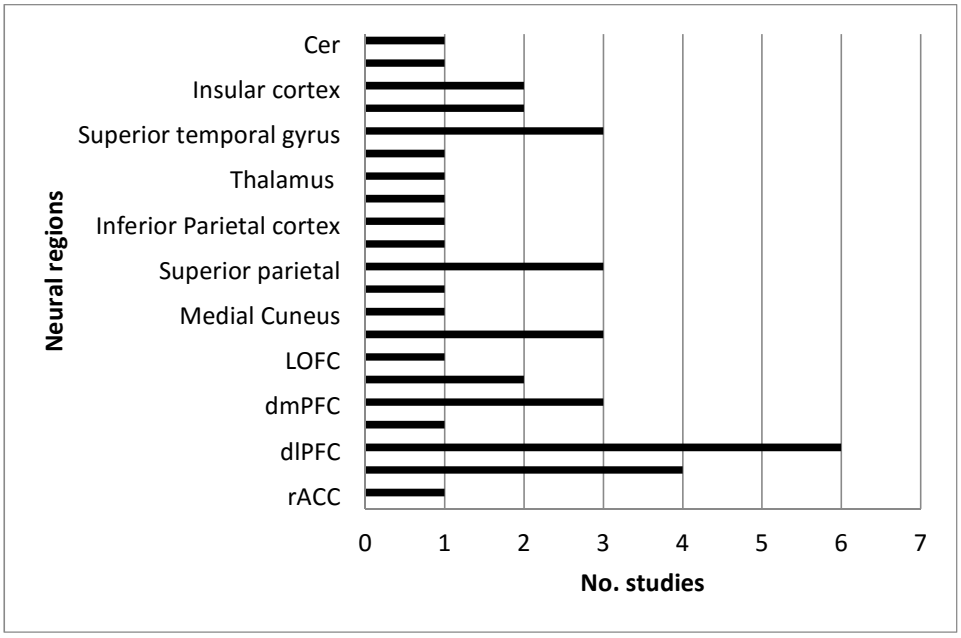

Figure 2. A bar chart showing the number of fMRI studies implicating differing neural regions in cognitive reappraisal in SAD. Cer=Cerebellum; LOFC=lateral orbitofrontal cortex; dlPFC= Dorsolateral Prefrontal Cortex; dmPFC=Dorsomedial Prefrontal Cortex; rACC= rostral Anterior Cingulate Cortex.

1.4.1.2 *EEG*

Adolph et al (2013; 1) reported larger early N170 amplitudes at left and midline electrodes, and whilst there were no significant differences between groups in late positive potential (LPP) (1, 9) larger LPPs were observed in right lateral electrode sites, in the high social anxiety (HSA) group in comparison to the low social anxiety (LSA) group during watch and cognitive reappraisal, demonstrating enhanced early structural encoding and elaborative processing of fearful faces in HSA (1).

Table 2

Brain regions implicated in cognitive reappraisal in SAD across fMRI studies in comparison to controls, by assigned study number

	Frontal lobes								Occipital lobe		Parietal Lobes			Temporal lobes						
No.	rACC	dACC	dlPFC	vlPFC	dmPFC	mPFC	LOFC	IFG	Medial Cuneus	Lingual gyrus	Superior Parietal	Precuneus	Inferior Parietal	PC	Thalamus	Para-hippocampal gyrus/amygdala	STG	Fusiform Gyrus	Insular cortex	Putamen	Cer
2	-	↓	-	-	-	-	-	-	-	-	↓	-	-	-	-	-	-	-	-	-	-
3	-	-	↓	-	-	↓	-	-	-	-	-	-	-	-	↓	↓	-	-	↓	-	-
5	-	↓	↓	-	-	-	-	-	↓	-	↓	-	-	↓	-	-	↓	↓	-	-	-
6	-	↓E	↑ L ↓E	↑L ↓E	↓E	↓E	-	↓E	-	-	-	↑L ↓E	↑L ↓E	-	-	-	-	-	↑L	-	-
7	-	-	↓	-	↓ E	-	--	-	-	-	-	-	-	-	-	-	-	-	-	-	-
8	-	-	-	-	-	-	-	↓	-	-	↓	-	-	-	-	-	↑	-	-	-	-
10	↓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
11	-	-	↓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
12	-	-	↑	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
14		↓ L			↓L		↓ L ↓E	↓ L		↓							↓L	↓E		↓L	↓L ↓E

Note. For this purposes of this, CBT waitlist controls were included as social anxiety groups, with CBT groups utilised as 'controls' with improved symptomology. ↑ = increase relative to controls; ↓ = decrease relative to controls; L= Late activation; E=Early activation; rACC = rostral anterior cingulated cortex; dACC= dorsal anterior cingulated cortex; dlPFC = dorsolateral prefrontal cortex; vlPFC= ventrolateral prefrontal cortex; dmPFC = dorsomedial prefrontal cortex; mPFC= medial prefrontal cortex; LOFC = lateral orbitofrontal cortex; IFG= Inferior frontal gyrus; PC = Posterior Cingulate; STG = Superior Temporal Gyrus; Cer=Cerebellum.

Additionally, reduced stimuli-preceding negativity (SPN) was observed in HSA in comparison to LSA, when viewing the reappraisal cue word although conversely, reduced P2-N2 amplitudes were observed for LSA but not for HSA during reappraisal in comparison to look condition (13).

However, it is of note, that two of the three EEG studies utilised participants with high levels of social anxiety, as opposed to a diagnosis of SAD.

1.4.1.3 *Consensus*

The balance of evidence abstracted across studies included within this literature review present a consensus of PFC involvement and activation in cognitive reappraisal in SAD, in addition to the inferior parietal lobe and STG; regions which have been widely implicated in the top down cognitive control of amygdala activity in healthy controls (Goldin, Manber-Ball et al, 2009) with evidence presented here suggesting altered activation and connectivity with other regions, impacting on emotion regulation success. Evidence is present for connectedness between this top-down regulation system and amygdala activity; however, some studies suggest this connection may be impaired, impacting on effective regulation of amygdala activity and downregulation of anxiety.

However, whilst some studies present with aligning conclusions, there may be methodological caveats to consider including limited imaging protocols which prevent extraction of temporal information, sample sizes, use of control groups, limited cognitive reappraisal protocols. Therefore, extracted study details will be discussed and critiqued to provide a wider context in which the findings exist which may provide caution when interpreting results. A summary of methodological

strengths and weaknesses for each individual study is presented in table 1 (see pages 28 to 31).

1.4.2 Descriptive Characteristics of Studies

All identified studies were completed within the last decade, with the earliest eligible study published in 2009 (5, 6) and the most recent published in 2018 (9); demonstrating the novelty of this research area. All papers identified were published in English, with the majority conducted in the United States of America (n=8; 2, 5, 6, 7, 8, 10, 11, 14) with similar studies across Germany (n=3; 1, 4, 12), Switzerland (n=1; 3), Israel (n=1; 9) and China (n=1; 13).

1.4.2.1 *Design and Participants*

The most common research design utilised an fMRI methodology (n=11; 2, 3, 4, 5, 6, 7, 8, 10, 11, 12, 14) with the remaining studies using EEG (n=3; 1, 9, 13). The majority employed a mixed design (n=11; 1, 2, 4, 5, 6, 7, 8, 9, 12, 13, 14) to compare the effects of cognitive reappraisal task instruction (e.g. reappraise or react; within groups variable), between groups of participants (between groups variable). Of these eleven studies, nine utilised a clinical sample of individuals with diagnosed SAD (2, 4, 5, 6, 7, 8, 9, 12, 14). Seven of these studies utilised a healthy control group (2, 4, 5, 6, 9, 12, 14) with one study recruiting additional clinical samples for comparison (GAD and comorbid SAD/GAD; 2); adopting both healthy and clinical control groups. On the other hand, two studies compared CBT with waitlist controls to evaluate the impact of CBT on cognitive reappraisal and related neural mechanisms (7, 8), thereby omitting a healthy control group for comparison. Alternatively, two studies compared volunteers (13) or students (1) without a clinical diagnosis but with high levels of social anxiety (HSA) with participants with low social anxiety (LSA). Two studies utilised a repeated measures design to evaluate the predictive effects of

cognitive reappraisal related neural activity on CBT treatment response (10, 11), in which all participants had a diagnosis of SAD. One study (3) utilised a between groups design where participants with SAD with high or low cognitive control, completed different reappraisal task conditions.

Studies utilised a total sample size of 28 to 84 participants, with a mean (M) sample size of 46.29 and standard deviation (SD) of 17.80; with a total female to male ratio of 324:305. In terms of the socially anxious experimental groups, sample size ranged from 12 to 49 (M=24.53; SD=10.55) with female to male ratio of 199:168. The mean age of participant groups ranged from 20.0 to 36.1 years.

Some studies recruited samples free from psychotropic medication (n=6; 1, 2, 5, 8, 11, 14) with four studies (3, 4, 9, 10) reporting inclusion. Just one study reported excluding participants with mental health diagnoses (1), with the majority including comorbidity (n=11; 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14) including affective and anxiety disorders (n=4; 3, 4, 9, 12); anxiety disorders alone (n=4; 5, 6, 7, 8) or axis-I disorders only (n=3; 10, 11, 14). Studies included other notable inclusion criteria of right-handedness (n=6; 3, 5, 7, 8, 12, 14), no experience of CBT (n=5; 3, 6, 7, 8, 14) or no current therapy (n=4; 8, 10, 11, 14).

Therefore, studies included within this review present with a range of design and sample differences, and consequently varying levels of validity, reliability and statistical power. Whilst most studies utilised healthy control groups, a small number omitted this option, impacting on internal validity that of observed effects are not a result of confounding variables (Malay & Chung, 2012). Additionally, the adoption of waitlist control groups may pose some ethical concerns around delaying treatment whilst participating in research (Barker & Pistrang, 2015). Additionally,

the problem of power in neuro-imaging research has been widely documented (Button et al., 2013) impacting on reproducibility and reliability of significant findings. However, the majority of studies have included comorbidity to an extent, increasing the ecological validity of results across the wider SAD population, routinely presenting with high levels of comorbidity to services (52-65%; Chartier, Walker & Stein, 2003; Ohayon & Schatzberg, 2010).

1.4.3 Measures of Social Anxiety

1.4.3.1 *Diagnostic*

Twelve studies diagnosed SAD using the DSM-IV criteria (APA, 2000), with most methods adopting the Structural Clinical interview for DSM-IV (SCID; First, Spitzer, Gibbon & Williams, 1997; n=6; 2, 3, 4, 10, 11, 12), followed by the Anxiety Disorders Interview Schedule (ADIS-IV; Brown, Di Nardo, & Barlow, 1994; n=5; 5, 6, 7, 8, 14), with Kivity and Huppert (2018) utilising the Mini-International Neuropsychiatric Interview for DSM-IV (M.I.N.I., Sheehan et al., 1998; 9). Therefore, all studies utilising patients with SAD, adopted DSM-IV criteria and appropriate interview forms to ensure sample validity. The ADIS-IV has been reported as a reliable measure of emotional disorders (Brown, Di Nardo, Lehman & Campbell, 2001), with evidence of reliability in internal consistency reported for the SCID (Maffei et al., 1997) and validity for the M.I.N.I (Sheehan et al., 1998). Other studies utilised the Social Interaction Anxiety Scale (SIAS, Stangier, Heidenreich, Berardi, Golbs & Hoyer, 1999; n=1; 1) which has been demonstrated to be a valid measure of social anxiety (Brown et al., 1997); and the Personal Report of Communication Apprehension (PRCA-24, McCroskey, 1982; n=1; 13) which has been demonstrated to be psychometrically valid and reliable, although predominantly used as measure of communication (Leary, 2013).

Studies utilising clinical patients with SAD, also adopted the use of an additional measures of severity of social anxiety, in conjunction with diagnostic measures, in order to further explore the mediation effects of SAD symptomology. The Liebowitz Social Anxiety Scale (LSAS, Liebowitz, 1987; Fresco et al., 2001) was utilised by twelve of the included studies (2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14), with additional measures including the Social Phobia Inventory (SPIN**;** 9), with good internal consistency, validity and test-retest reliability (Connor et al., 2000); the Social Phobia Scale and the Social Interaction Anxiety Scale as reliable measures (SPS and SIAS; Mattick & Clarke, 1998; 3) and the Brief fear of negative evaluation scale (BFNE; Leary, 1983; 5, 6). However, subtests of the BFNE have been shown to hold limited validity and recommendations have been made to adopt alternative cut-off points when assessing for social phobia (Weeks et al., 2005). Although this measure was used in conjunction with other more reliable diagnostic measures.

Four studies utilised both the state and trait measures of the State-trait anxiety inventory (STAI, Spielberger, Gorsuch & Lushene, 1970; 1, 3, 11, 12) with a further three studies solely adopting the trait measure (2, 5, 6); with one study adopting the Beck Anxiety Inventory, with good discrimination validity (BAI, Beck, Epstein, Brown& Steer, 1988; 2). To gain an understanding of the disabling impact of symptomology across domains, Goldin, et al (2013; 7) employed the Sheehan Disability Scale (Sheehan, 1983), providing more generalisable outcomes for the CBT interventions under investigation.

1.4.3.2 *Comorbidity*

When considering the role of comorbidity, Bruhl et al (2013; 3) adopted the use of the M.I.N.I (Sheehan et al., 1998) to gain an overall understanding of their sample's mental health, in addition to a diagnostic measure of SAD, whereas Kivity and

Huppert (2018) adopted sole use of the M.I.N.I. for diagnostic purposes. Most studies utilised a measure of depression, allowing for the exploration of comorbid effect on emotional reactivity and cognitive reappraisal success; with the Beck Depression Inventory (BDI, Beck, Ward, Mendelson, Mock & Erbaugh, 1961; n=7; 3, 4, 5, 6, 9, 11, 12) used most often across this sample, in addition to the Hamilton depression rating scale (HAM-D; Hamilton, 1960; 10, 11), with some studies employing unique depression measures; the Self rating depression scale (SDS; 3), the Inventory of Depressive Symptomology (IDS; 2) and the Depressions Skala (Von Zerssen & Koeller, 1976; 1). Two studies utilised an additional measure of mood (Positive and Negative Affect Schedule; PANAS; Watson, Clark & Tellegen, 1988; 5, 6).

Two studies employed a measure of empathy (Interpersonal Reactivity Index; Paulus, 2009; 1, 4), with (12) uniquely measuring understanding and ability to describe emotions (Toronto Alexithymia Scale, TAS; Franz et al., 2001; 4). Some studies utilised measures of intelligence and cognition, including the "Mehrfachwahl-Wortschatz-Intelligenz Test" (MWT-B; Lehrl, 2005; 12) and the Trail Making Test (TMT; Reitan, 1995; 4). Additionally, some studies adopted measures of attentional control including the Attentional Control Scale (Derryberry and Reed, 2002; 10) and the functional and dysfunctional forms of self-focused attention (DFS; Hoyer, 2000; 4).

As previously discussed, most studies have made an attempt to include comorbidity within their sample and the array of measures used across methodologies, predominantly measures of anxiety and depression, present appropriate effort to measure and manage effects. However, most effective determination of comorbidity incorporates a variety of measures and sources,

including self-report, practitioner assessments and records to ensure the most reliable and valid measurement (Lash et al., 2007).

1.4.4 Cognitive Reappraisal Task

1.4.4.1 *Cognitive reappraisal strategy*

In terms of reappraisal strategy, nine studies (1, 2, 3, 8, 9, 10, 11, 13, 14) utilised a combination of self and/or situation focused cognitive reappraisal, as defined by Ochsner et al (2004); with three studies adopting self-focused reappraisal to regulate emotional responses to stimuli (4, 5, 12), defined as actively increasing a sense of objective distance by viewing the stimulus from the third person perspective; and two studies using situation-focused reappraisal techniques (6, 7), which involves the process of actively reinterpreting distressing outcomes of the presented stimulus. Ochsner et al (2004) found distinct neural correlates for self and situation-focused cognitive reappraisal techniques, suggesting an association between self and medial PFC regions and situations and lateral PFC regions in healthy participants. However, the evidence presented here suggests an opposing pattern in SAD, with studies utilising situation focused (6, 7) demonstrating altered neural responding across both lateral and medial areas, with self-focused procedures (4, 5, 12) presenting no difference in activation across medial PFC regions (see tables 1 and 2). However, the majority of studies utilised a combination of self and situational focused, which may explain more generalised PFC involvement.

All studies included a down-regulation of negative emotion condition within their reappraisal task, compared with a neutral/view condition to examine the efficacy of cognitive reappraisal as an emotion regulation strategy. This is a strength of included research, allowing for the differentiation between neural correlates of passively watching negative stimuli and completing cognitive reappraisal. However,

it is possible that participants may utilise alternative emotion regulation techniques in place of cognitive reappraisal. To address this, Kivity et al (2018; 9) utilised an additional task condition of emotion suppression to provide an alternative emotion regulation strategy comparison and allowing for the identification of unique neural mechanisms involved in cognitive reappraisal. However, this was incorporated by just one study. Although, three further studies also employed an additional task condition of up-regulation of negative emotion to investigate overall cognitive control (1, 2, 4). Importantly, all methodologies included comprehensive training and practice in cognitive reappraisal to ensure that participants were proficient in the skill before completing the task.

All included studies have employed at least one comparison task condition to ensure that obtained neural mechanisms are unique to cognitive reappraisal. Although one study (Bruhl et al., 2013; 3) compared watch and down-regulate conditions between participant groups, with all other studies completing within group comparisons. However, the use of between groups comparisons does not control for individual differences in emotion regulation and neural responding and so would present as a less robust methodology.

1.4.4.2 *Task Stimuli*

All studies included negative/unpleasant cognitive reappraisal stimuli; with just one study using negative stimuli alone (1) and eleven studies adopting additional neutral stimuli (3, 4, 5, 6, 7, 9, 10,11, 12, 13, 14). Positive stimuli were also included alongside negative and neutral in three (3,12, 14). However, not all studies utilised neutral stimuli for comparison, with two studies comparing positive and negative stimuli only (2, 8), to avoid confusion between stimuli groups (Blair et al., 2012; 2).

There was variability in the format of the reappraisal stimuli utilised across studies, with six (2, 3, 4, 9, 10, 11) employing pictures from the International Affective Picture System (IAPS; Lang, Bradley & Cuthbert, 2008), three used pictures of faces (1, 5, 13) and two presented videos (8, 12). Alternatively, two studies developed idiosyncratic cognitive reappraisal task trials, utilising participant's own autobiographical situations and NSBs (6, 7) to which, each participant is asked to regulate their emotional response. One study (14) compared faces, videos and autobiographical stimuli across their cognitive reappraisal task.

Whilst IAPS images were utilised most frequently across studies, Klumpp, Roberts et al (2017) suggest that IAPS present with low generalisability, depicting neutral and negative scenes which may not activate social threat to the same extent as faces, videos or personal NSBs. This impacts on the ecological validity of the most commonly utilised cognitive reappraisal stimuli. However, the adoption of idiographic NSBs presented within a context of autobiographical situations, demonstrates a novel alternative, which draws on therapeutic targets as a method of eliciting and assessing cognitive reappraisal ability; as reliable and ecologically valid stimuli.

1.4.4.3 *Measure of cognitive reappraisal success*

When measuring the effects of cognitive reappraisal as an emotion regulation strategy, all studies relied on self-report rating scales. Eight studies commonly used a 5-point likert scale (2, 5, 6, 7, 8, 10, 11, 14) to allow participants to rate their experience of negative emotion (1=not at all to 5=very much). Similarly, Yuan, Zhou and Hu (2014; 13) utilised a 6-point scale (6 = strongly negative; 1 = not negative at all) and Gaebler et al (2014; 4) a 7-point scale (1 = weak, 7 = strong) to rate intensity of emotional response. Other studies (14.3%) asked participants to rate the emotional

valence of the stimuli (3) on a 9-point scale (very negative 1, to very positive 9) or judge whether the stimuli was socially excluding (12) on a 4-point scale. The more formalised Self-assessment manikin (SAM) (Bradley & Lang, 1994) was used by two procedures (1, 9) which allows ratings of current emotion state across domains of valence (rated from -4 to 4), arousal (rated from 1 to 9) and dominance (rated from 1 to 9). In addition to this, nine protocols (1, 2, 3, 4, 5, 6, 9, 10, 11) utilised the Emotion Regulation Questionnaire (ERQ, Gross & John, 2003) as a baseline measure of emotion regulation strategy use.

All studies utilised self-report ratings to assess for cognitive reappraisal success. Whilst this mode of measurement provides direct reports from participants, scores are at risk of bias due to social desirability (Reiss & Judd, 2014). This may particularly be present within a SAD cohort, as described by Schlenka and Leary (1982) in their model for social anxiety, suggesting motivation to present the self positively and consequently receive positive social evaluations from researchers. This was exemplified by one study (7) who reported participant drop-out due to researcher revelation of deception around reported symptoms. However, two studies aimed to combat this effect through the adoption of measures of social desirability to assess validity of self-reported measures. Goldin et al (2014; 8) adopted the use of the Marlowe-Crown Social Desirability Scale (MCSDS; Crowne & Marlowe, 1960) and found no relationship between negative ratings, use of strategies or reported success and the MCSDS. Adolph, Meister and Pause, (2013; 1) used the Lie scale of the Eysenck Personality Inventory, (Eggert & Ratschinski, 1983) and reported low levels of social desirability within their sample of participants. Whilst these measures themselves are in fact self-reported, the quantification of this variable may support controlling for confounding effects, improving response reliability.

1.4.5 Cognitive reappraisal outcomes

Over half of the studies included within this literature review reported effective participant cognitive reappraisal (n=8; 1, 2, 6, 9, 10, 11, 12, 14), demonstrated by reduced negative responding report when instructed to reappraise, in comparison to other instructions (i.e. watch/neutral). It is of note, that three studies reported reduced cognitive reappraisal efficacy within the HSA participants, indicating a negative correlation with symptom severity (1, 2, 6). Additionally, Ziv et al (2013; 14) reported larger reductions in distress in healthy controls for criticism video and NSB stimuli; whereas two studies (9, 12) demonstrated increased reappraisal-related reductions in distress in individuals with SAD compared to healthy controls.

On the other hand, six studies reported no differences between passively viewing and reappraise conditions across participants (3, 4, 5, 7, 8, 13). However, two studies (7, 8) showed evidence for post-CBT reappraisal-related reductions in negative experience in participants with SAD, with no change in wait-list controls.

Therefore, the present studies present variable effectiveness of cognitive reappraisal across participants, despite training and practice trials employed by all. However, details of training are variable, and assessment of adequate learning is not consistent. This provides a further criticism for research findings, presenting neural mechanisms of cognitive reappraisal in the absence of evidence of construct completion. However, CBT research demonstrates that more thorough training delivered within the context of therapy provides effective cognitive reappraisal.

1.4.6 Moderating and mediating factors

1.4.6.1 *Symptom Severity*

There was evidence to suggest associations between increased SAD symptom severity (as measured using the LSAS) and less reappraisal related neural activity within the dmPFC (9, 11), a region strongly implicated in emotion regulation, as previously discussed. Additionally, one study (6) demonstrated an impact on the temporal aspects of responding, with greater early reappraisal related activity in right inferior frontal gyrus, left thalamus, and left inferior parietal lobule associated with symptom severity. However, this relationship was not consistent across studies. Two studies (5, 11) reported no relationship between symptom severity and neural activity, with Goldin, Manber et al (2009; 5) reporting that a correlation was only present when passively responding to negative stimuli (harsh faces). These findings again, demonstrate the importance of temporal information gathering when exploring neural activation in order to differentiate between activity corresponding with perception of stimuli and emotion regulation.

1.4.6.2 *Cognitive Behavioural Therapy*

Five studies compared individuals with SAD before and after CBT, in comparison to wait list controls (n=5; 7, 8, 10, 11,14); with a subset identifying CBT-related reductions in distress and SAD symptomology (7, 8, 10), in addition to altered reappraisal-related activation when reacting to and reappraising stimuli, post-treatment (7, 8). Furthermore, one study (11) presented evidence for a predictive effect between pre-CBT dlPFC activation in individuals with SAD and treatment response, suggesting a mechanism by which CBT exerts therapeutic effect, presenting a target for treatment.

1.4.6.3 *Task Stimuli*

The impact of differing task stimuli on neural responding was directly assessed by Ziv et al (2013; 14), demonstrating evidence for deficient emotion regulation in SAD in comparison to controls during the cognitive reappraisal of NSBs in the context of autobiographical social situations, as highly emotive and personal social anxiety stimuli. This presents evidence for the moderation of differential brain responses as a consequence of the specific stimuli utilised within research protocols, with the cerebellum identified with differences in activity between groups in a video reappraisal task only (14), which may be explained by the moving stimuli.

This is supported by Britton, Taylor, Sudheimer and Liberzon (2006) who found that participants exhibited additional neural activation in STG, insula and ACC when responding to pictures of expressive faces in comparison to IAPS images. Therefore, this emphasises the importance for research within this area to identify neural mechanisms corresponding with cognitive reappraisal as an emotion regulation strategy, as opposed to reactivity to inconsistent stimuli.

1.4.6.4 *Cognitive reappraisal Self-efficacy*

One study (6) demonstrated an association between self-reported reappraisal self-efficacy and increased early dACC activation in controls, but not in individuals with SAD.

1.4.6.5 *Depression*

Studies also demonstrated the effects of comorbid depression on emotion responding and regulation (9) presenting evidence for impact on emotional responding to personal task stimuli in addition to reduced reappraisal efficacy; although depression was also found to predict enhanced emotion suppression efficacy in individuals with SAD.

1.4.6.6 *Chemosensory stimuli*

Evidence has been presented for the role of chemosensory stimuli in the cognitive reappraisal of threatening faces (Adolph, Meister & Pause, 2013; 1), with larger LPP amplitudes present in right lateral regions in HSA than LSA, during down-regulation, in the context of anxiety chemosensory stimuli, suggesting enhanced elaborative processing of threatening faces in the context of chemosensory anxiety signals in HSA.

1.5 Discussion

This review provided a summary of key neural mechanisms involved in cognitive reappraisal in SAD. Evidence abstracted across fMRI studies included within this literature review presents a consensus of PFC involvement (dlPFC, dmPFC, dACC) in cognitive reappraisal in SAD, in addition to the inferior parietal lobe and STG. Three studies utilised EEG demonstrating larger early N170 amplitudes at left and midline electrodes in addition to lesser reductions in P2-N2 amplitudes during cognitive reappraisal in SAD, presenting further evidence of alterations in activity. Most of the included research utilised participants with a diagnosis of SAD, including comorbidity in presentation to varying extents. Additionally, characteristics of cognitive reappraisal investigation is also presented, with all studies utilising self-reported measures of reappraisal success in response to a variety of threat and neutral stimuli; with the majority of studies incorporating a combination of both self- and situation- focused reappraisal strategy. Identified moderation and mediating factors are presented, with evidence for the role of SAD symptom severity on reappraisal related neural activity and the mediating effect of CBT on altering activity pre- to post-treatment.

The findings are consistent with previous research including that of Buhle et al (2014), lending support for models of top-down control of emotional reactivity in addition to presenting evidence for deficient reappraisal-related activity during cognitive reappraisal in SAD.

Prefrontal regions of dlPFC, dmPFC, dACC have been widely implicated across review studies (Messina, Bianco, Sambin & Viviani, 2015; Buhle et al., 2014) with evidence for a dACC role in the employment of dlPFC and dmPFC for top-

down emotion regulation (Kerns et al., 2004); leading to suggestions that reduced early and late activation within the dACC in addition to reduced activation within the dlPFC and dmPFC, as presented here, may demonstrate the neural mechanisms of impaired emotion regulation in SAD (Goldin, Manber-Ball et al., 2009). This is further supported by evidence for an association between increased SAD symptomology and reduced activation within the dmPFC (11), which may present the mechanism by which symptom severity mediates reappraisal efficacy.

Additionally, evidence is presented for disruption of the down-regulation of amygdala activation (7). This is supported by (Liao et al., 2010) who found that the amygdala received decreased control from the inferior temporal gyrus (ITG), impacting on the ability to effectively process negative expressions in SAD. However, studies utilising CBT included within the review suggest that differences in neural responding and top-down control can be improved on completion of CBT; lending support for the Threat Reappraisal Mediation Hypothesis (Hofmann, 2008; Smits, Julian, Rosenfield & Powers, 2012).

Moderating and mediating variables have been identified across studies, including SAD symptom severity, experience of CBT, cognitive reappraisal stimuli, cognitive reappraisal self-efficacy, depression and chemosensory information. Therefore, it may be important for future research to take these factors into account when investigating cognitive reappraisal in SAD, or indeed directly assess their influence.

Although, this narrative review was not able to present results obtained consistently across cognitive reappraisal studies. One of the main difficulties in presenting the literature is the lack of demonstration of effective cognitive

reappraisal, coupled with missing temporal information for neural activation rendering it difficult to identify neural activity corresponding with the completion of cognitive reappraisal. An additional difficulty stems from the majority of fMRI studies, in comparison to few EEG studies, of which just two studies present differences in responding between groups. Whilst functional imaging provides information around behaviour and associated activity, a wider breadth of neuro-methodology and subsequent information is lacking.

1.5.1 Critical Review of the literature

As discussed, it is important to recognise the strengths and limitations of the studies included within this review. A critique of the literature included has been included throughout this narrative synthesis, however a short summary is presented here.

Included literature held strengths around the inclusion of comorbidity, employment of diagnostic and symptom severity measures and the adoption of healthy control groups (2, 4, 5, 6, 9, 12, 14). Furthermore, research demonstrated a range of cognitive reappraisal stimuli, with a more recent move towards more clinically relevant NSBs (6, 7, 14).

However, limitations observed across included studies include the omission of control emotion regulation strategy groups for comparison. This was adopted by Kivity et al (2018) who found no significant differences between groups, highlighting the importance of ensuring that the results are reliable and valid in demonstrating the underlying neural activation for cognitive reappraisal specifically, as opposed to emotion suppression, for example. Furthermore, cognitive reappraisal stimuli were often generic (1, 2, 3, 4, 5, 9, 10, 11, 13) and did not relate directly to participant symptomology, impacting on the assessment of reappraisal of emotive

and distressing stimuli in line with participant cognitions. These differences between study protocols and consequent validity may in part explain the inconsistencies in findings observed.

1.5.2 Limitations of the Review

This literature review holds several limitations. Firstly, whilst effort was made to utilise inclusive criteria as the first review of its kind, within a relatively novel and consequently limited evidence base; included studies recruited participants with a diagnosis of social anxiety in addition high levels of social anxiety. Therefore, this may have impacted on the integrity of findings for the SAD population, however both studies suggested that participants with high levels of social anxiety were within the clinical range indicated by their respective severity measure.

In addition to this, whilst this review includes a critique of research methodology, a formalised quality assessment tool was not incorporated as part of this review. This would provide a formal platform to evaluate methodological practices and reliability of results. However, it has been argued that a numerical score can be disadvantageous when synthesising results, with scores having the potential to overshadow unique contributions of included research (Booth, Sutton & Papaioannou, 2016). However, to the author's knowledge, there are no established quality assessment tools for neuro-imaging methodology and so a qualitative critique of study methodology has been incorporated throughout.

Consequently, the decision was made to exclude grey literature to ensure a high standard of quality across studies. However, this may have subjected the results of this review to publication bias, where research demonstrating treatment effects are more likely to be published than those which do not, leading to the "file drawer

problem" of hidden unpublished results, which if included, may present an alternative outcome (Borenstein, Hedges, Higgins & Rothstein, 2011).

1.5.3 Implications and Future Directions

The identification of neural regions implicated in cognitive reappraisal as a means of emotion regulation, hold clinical implications including the development of more targeted therapeutic interventions. Studies presented evidence for the beneficial effect of CBT for individuals with SAD, with evidence for the modulation of SAD related activation across reappraisal areas. Therefore, this evidence suggests that individuals presenting with this neural profile, may particularly benefit from a more cognitive focused CBT protocol in order to restore reappraisal neural mechanisms and facilitate reappraisal success.

However, further research is required to address the limitations discussed and utilise multi-modal imaging protocols, to provide differential qualities of information. For example, the use of fMRI event-related paradigms rather than the routinely used block-designs (Behroozi, Daliri & Boyaci, 2011) would provide temporal information to distinguish between emotion generation and emotion regulation neural correlates, across the temporal trajectory, as described within the process model of emotion regulation (John & Gross, 2004). In addition to this, the adoption of alternative imaging methodologies, such as non-invasive electromagnetic stimulation, can provide further support for role of reappraisal related neural regions in cognitive reappraisal in SAD, through the neuromodulation of activity to investigate causal relationships (Silvanto & Pascual-Leone, 2012).

1.5.4 Conclusions

To conclude, this review has presented evidence for altered activation across neural regions identified in emotion regulation, namely the dlPFC, dmPFC, dACC, inferior parietal lobe and STG, in comparison to controls, with moderators and mediators discussed. Whilst there are limitations of the included research and the conduction of this review, confidence in findings is provided by previous research. Additionally, findings suggest the neural mechanisms by which cognitive reappraisal, and more broadly, CBT exerts therapeutic effect, demonstrating a neural substrate consistent with the Threat Reappraisal Mediation Hypothesis.

Further research should aim to incorporate more clinically valid cognitive reappraisal stimuli, account for moderating variables and employ effective control groups and include multiple imaging protocols. This would ensure precise and distinct identification of neural mechanisms and allow for the exploration of the temporal features of cognitive reappraisal, to inform targeting of therapeutic interventions for individuals with SAD.

2 Chapter 2: The Effect of Transcranial Direct Current Stimulation (tDCS) on Emotion Regulation and Social Cognition in Adults with Symptoms of Social Anxiety

2.1 Introduction

2.1.1 Social Anxiety

As discussed in the previous chapter, social anxiety disorder (SAD) is defined within the Diagnostic and Statistical Manual (DSM-5) of Mental Disorders (American Psychiatric Association, APA, 2013) as an excessive and enduring (6 months or more) fear of social or performance situations, where the individual is exposed to unfamiliar people or potential social scrutiny. Approximately 10 percent of students report marked to severe levels of social anxiety (Russell & Shaw, 2009), with a larger proportion experiencing sub-clinical, elevated levels of social anxiety. Up to 12 percent of the population experience SAD in their lifetime (Kessler et al., 2005).

2.1.1.1 *Treatment*

The first line psychological therapy recommended by the National Institute for Health and Care Excellence (NICE, 2013) for adult SAD is Cognitive Behavioural Therapy (CBT),with evidence to suggest medium to large effect sizes post-treatment (vs. waitlist control) (e.g. Gil, Carrillo & Meca, 2001). CBT for social anxiety aims to restructure maladaptive beliefs about social situations by improving anxious individuals' cognitive reappraisal of social information, to reduce emotional impact and distress (Goldin et al., 2012) coupled with behavioural exposure techniques to feared social situations. However, research suggests that up to 40 percent of adults with SAD continue to experience symptoms post-treatment (Klumpp, Fitzgerald et

al., 2017), with evidence to suggest efficacy for a more cognitive-focused therapy (Clark et al., 2006; see chapter 1).

2.1.1.2 *Cognitive Reappraisal*

Neuro-imaging studies implicate the dorsolateral (dlPFC), dorsomedial (dmPFC), and ventrolateral (vlPFC) prefrontal cortices in addition to the dorsal Anterior Cingulate Cortex (dACC) in cognitive reappraisal (e.g. McRae et al., 2010) with support for pre-frontal top-down control of amygdala activity, consequently impacting on negative emotion experience (Ochsner & Gross, 2005; see chapter 1).

However, a recent functional magnetic resonance imaging (fMRI) study suggests that adults with SAD (in comparison to controls) show reduced activity in dmPFC and dlPFC during the cognitive reappraisal of negative facial expressions (Goldin, Manber et al., 2009); and delayed neural responses during reappraisal of autobiographical negative self-beliefs (NSBs) (Goldin, Manber-Ball, et al., 2009), consistent with the role of prefrontal hypo-activity in cognitive bias in SAD (Goldin, Manber et al., 2009). Although, Goldin et al (2013) observed that dlPFC and dmPFC responses were earlier and increased when cognitively reappraising NSBs following sixteen sessions of CBT, in comparison to waitlist controls; suggesting the neurological mechanisms through which CBT improves emotion regulation in SAD, supporting engagement of the dorsolateral and dorsomedial PFC during cognitive reappraisal. These findings are consistent with this conduction of a recent systematic literature review (see chapter 1).

There has been evidence to suggest that non-invasive brain stimulation of PFC can also improve emotion regulation in adults. For example, Feeser, Prehn, Kazzer, Mungee and Bajbouj (2014) randomised healthy participants to either

receive prefrontal transcranial direct current stimulation (tDCS) or sham whilst upregulating, downregulating, or maintaining emotional responses to negative and neutral International Affective Picture System images (IAPS; Lang, Bradley & Cuthbert, 2008). Results provided evidence that anodal stimulation over the right dlPFC enhanced emotional up-regulation (sham stimulation mean (*M*)=4.86, standard deviation (*SD*)=0.83; tDCS *M*=6.08, *SD*=0.59); and down-regulation (sham *M*=3.46, *SD*=0.71; tDCS *M*=2.17, *SD*=0.88). Consequently, tDCS of dlPFC may usefully further enhance cognitive behavioural exercises that target emotion regulation deficits in social anxiety, although this has not yet been explored.

Therefore, this study aimed to test whether tDCS of the PFC modulates cognitive reappraisal in adults experiencing symptoms of SAD, using an adapted version of autobiographical NSB task described by Goldin, Manber-Ball et al (2009).

2.1.2 Methodological considerations: Active Control site

Recent critiques of tDCS research (e.g. Parkin, Ekhtiari & Walsh, 2015) highlight the need to include appropriate control conditions. For example, Feeser et al (2014) omitted an active-stimulation control group, making it difficult to reliably conclude that the main effect observed of PFC tDCS on cognitive reappraisal, is not the result of general brain stimulation to a nonspecific brain region. A lack of task control comparison also makes it difficult to reliably conclude that improvement in performance could not be demonstrated on any nonspecific cognitive task (Parkin, Ekhtiari & Walsh, 2015).

Therefore, this study aimed to use a more robust tDCS methodology, whereby the cerebellum was recruited as an active-stimulation control group (cerebellar stimulation) in addition to a sham-control condition, to dissociate the

effects of PFC stimulation on reappraisal in adults with social anxiety; in addition to a control task comparison.

2.1.3 Emotion Recognition

The inclusion of a cerebellar control site and recommended control task allowed for the exploration of cerebellar tDCS on cognition, extending emerging evidence from lesion and neuroimaging studies that implicate the cerebellum in social information processing (e.g. emotion processing, Fusar-Poli et al., 2009; Van Overwalle, Baetens, Marien & Vandekerckhove, 2014; emotional face processing, D'Agata et al., 2011; Adamaszek et al., 2014; and pictures of eyes, Hoche, Guell, Sherman, Vangel & Schmahmann, 2016).

The role of the cerebellum in social cognition and emotion processing is mediated by interconnectivity between the cerebral cortex and the cerebellum (Zagon, McLaughlin & Smith, 1977) within multiple 'closed-loop' cerebro-cerebellar circuits (Kelly & Strick, 2000; 2003) between the cerebellum and areas including the limbic system, PFC, parietal cortex and temporal cortex (Baillieux, De Smet, Paquier, De Deyn & Mariën, 2008). This demonstrates the neural substrate through which the cerebellum may influence emotion processing and social cognition, in addition to motor functioning.

A recent neuro-stimulation study reported that repetitive transcranial magnetic stimulation (rTMS) to the midline cerebellum produced enhanced implicit processing of happy faces (as measured by slower colour naming within a masked faces task) (Schutter, Enter & Hoppenbrouwers, 2009); while Ferrucci et al (2012) found that both anodal and cathodal tDCS to the cerebellum enhanced recognition (reduced reaction times) of negative facial emotions (vs. null effects of PFC

stimulation). Consequently, this study aimed to further explore the effects of tDCS on emotional face processing in social anxiety.

Therefore, an exploratory investigation into the effects of cerebellar tDCS on emotion recognition was conducted; primarily acting as an active control site and task to the main effect of PFC tDCS on cognitive reappraisal.

2.1.4 Research aims

The primary research aim of this study was to investigate the selective effects of PFC stimulation on cognitive reappraisal in adults experiencing symptoms of SAD in comparison to active (cerebellar tDCS) and sham control groups.

Secondary, more exploratory aims were to investigate the selective effects of cerebellar stimulation on emotion recognition in individuals with symptoms of SAD, in comparison to active (PFC tDCS) and sham control groups.

2.1.5 Hypotheses

The primary hypothesis for this study was that individuals who receive PFC tDCS will experience less negative affect (i.e., a main effect of stimulation group) and that this will be greatest when instructed to 'reframe' NSBs (cognitively reappraise), in comparison to the 'react' condition; in comparison to individuals who receive cerebellar or sham tDCS.

The secondary, more exploratory hypotheses were (1) Individuals who experience cerebellar tDCS will demonstrate increased accuracy in the recognition of emotions within the emotion recognition task, in comparison to individuals who experience PFC or sham tDCS.

(2) Individuals who experience cerebellar tDCS will demonstrate decreased reaction times in the correct recognition of emotions within the emotion recognition task, in comparison to individuals who experience PFC or sham tDCS.

2.2 Methodology

2.2.1 Design

This study utilised a multi-site, mixed double-blind design, where both participants and researchers were unaware of stimulation condition. Participants were randomly allocated to independent groups of stimulation site (PFC, cerebellum or sham); with all participants completing the cognitive reappraisal (within groups; 2 levels 'react' and 'reframe') and emotion recognition tasks (within groups; 6 levels fearful, angry, happy, sad, disgusted and surprised).

This study was completed as part of an undergraduate student consortium following the initiative outlined by Button, Lawrence, Chambers and Munafo (2016); in which approximately 5 undergraduate and 2 postgraduate students across the University of Southampton and the University of Bath were involved in the recruitment and completion of this study, under the close supervision of the study lead (GH, doctoral student on the DClin Psych programme at Southampton) and their academic supervisors (KSB, MG). The study lead completed comprehensive training and observation at both sites with all student researchers, to ensure standardisation of testing and safety procedures.

2.2.2 Participants

A total sample of 33 eligible students (28 female; 5 male) were recruited across two sites, University of Southampton (n=18) and the University of Bath (n=15), using an opportunistic sample. Participants were aged 18-30 (M=21.42; SD=3.30) and described their ethnicity as White (n=23), Asian (n=7), Black (n=1) or Other (n=2). Participants scored between 16 and 54 on the Social Phobia Inventory (SPIN; Connor et al., 2000) questionnaire (M=27.79; SD=9.35). Participants received course credit or financial compensation for their time.

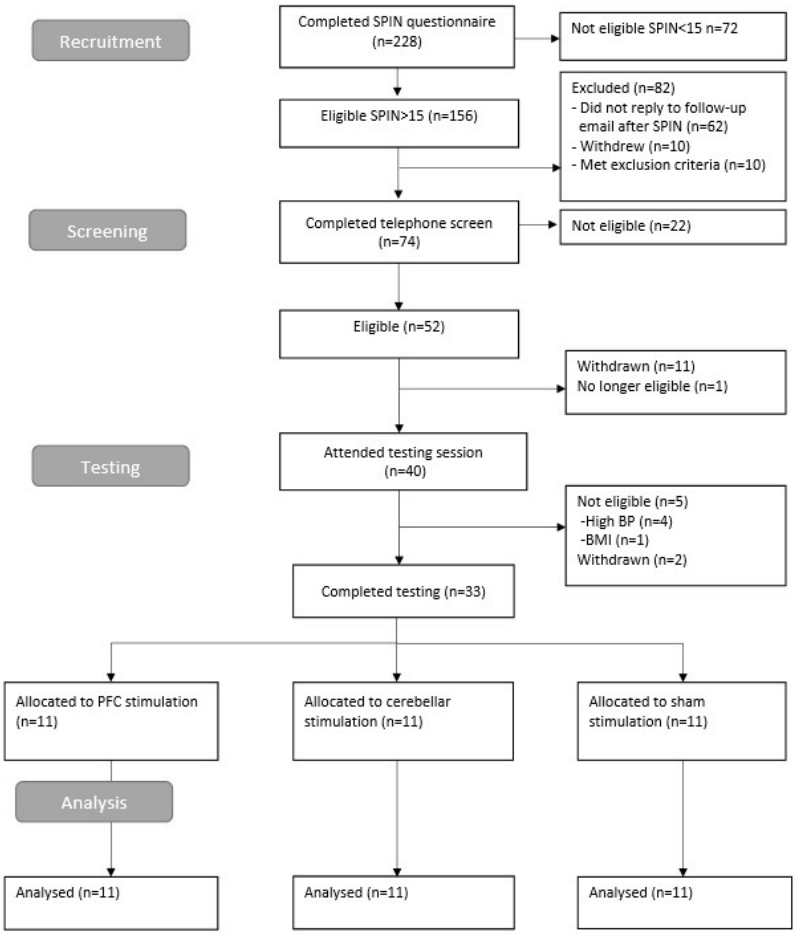

Figure 3. Schematic image showing the flow of participants included and excluded across recruitment, screening, testing and analysis.

2.2.3 Exclusion Criteria

Participants underwent a telephone physical and mental health screen using a structured diagnostic interview (Mini International Neuropsychiatric Interview MINI; Sheehan et al, 1998) prior to the testing session and on the day of the testing. A physical health checklist screened participants against current and lifetime physical illness exclusion criteria. Inclusion criteria comprised scoring above 15 on the Social Phobia Inventory, aged 18-55 years and right handedness. Exclusion criteria includes metal or electronic implants, epilepsy, recent medication (past 8

weeks bar topical treatment, paracetamol, oral, injectable, or skin patch contraception), pregnancy, elevated blood pressure (>140/90 mm Hg), cardiovascular or neurological disease (Feeser et al., 2014), lifetime history of psychiatric illness/alcohol/drug dependence, current smoker, body mass index (BMI) <18 or ⩾28 kg/m2, and recent use of alcohol (confirmed by breath test).

2.2.4 Randomisation

The randomisation sequence was computer generated and followed a block randomisation procedure stratified by gender, to ensure balanced recruitment across the stimulation groups, across sites. This was completed by supervisors at both sites, who were not directly involved in participant testing, ensuring condition blinding across testing researchers.

2.2.5 Materials

2.2.5.1 *The Social Phobia Inventory (SPIN)*

An online version of the SPIN was used as a 17-item self-report screening measure of symptoms of SAD (see appendix A). Participants were required to report their experience of fear, avoidance and physiological arousal in the past week on a 5-item Likert scale (0 = not at all to 4 = extremely). Connor et al (2000) state that evidence for scores over 19 indicating mild symptoms; however, they also demonstrated that a lower cut-off of 15 differentiates individuals with social phobia from healthy controls with 78% efficiency. As this design excludes participants with current mental health diagnoses, the lower cut-off was more appropriate. The SPIN holds good internal consistency, validity and test-retest reliability (Connor et al., 2000) and is routinely used within mental health services within the UK.

2.2.5.2 *Autobiographical Social Anxiety Situations questionnaire (ASAS)*

In line with the cognitive reappraisal task developed by Goldin, Manber-Ball et al (2009), an adapted version of the ASAS was developed in order to obtain details of participants' emotive autobiographical situations and NSBs (see appendix B). The ASAS asked participants to recall 4 autobiographical social anxiety situations characterised by social anxiety, humiliation or embarrassment and to write a paragraph describing the events, thoughts and feelings and five NSBs, as described by Goldin, Manber-Ball et al (2009). Participants were asked to provide their age at each situation and rate on a 9-point scale (1=not at all to 9=very much) the vividness of the memory, the experience of shame at the time of the situation, current shame, disturbance, avoidance and frequency of talking about the situation (Goldin, Manber-Ball et al., 2009).

2.2.5.3 *Cognitive reappraisal task*

This involved an adapted computerised task constructed in E-Prime (Schneider, Eschman & Zuccolotto, 2012) which utilised participants' ASAS responses to form personalised trials including their own reported situations and consequent NSBs generated by the researcher. At the beginning of each trial, the participant was instructed to 'react' or 'reframe' before being presented with one of their ASAS descriptions and corresponding NSBs. Within the 'react' condition, participants were required to reflect on how the NSB exhibits some truth about them as an individual, whereas the 'reframe' condition required the participant to reappraise/downregulate the NSB (Goldin, Manber-Ball et al., 2009). Participants were then asked to rate their negative emotion on a 5-point likert scale, as the dependent variable from this task. This was then repeated for the remaining three situations provided, in addition to response to neutral situation created by the researcher. Therefore, a total of five

trials (2 react, 2 reframe and 1 neutral) were presented to each participant within this 15-minute task (see figure 4 for a breakdown of one autobiographical social situation trial, adapted from Goldin, Manber-Ball et al., 2009).

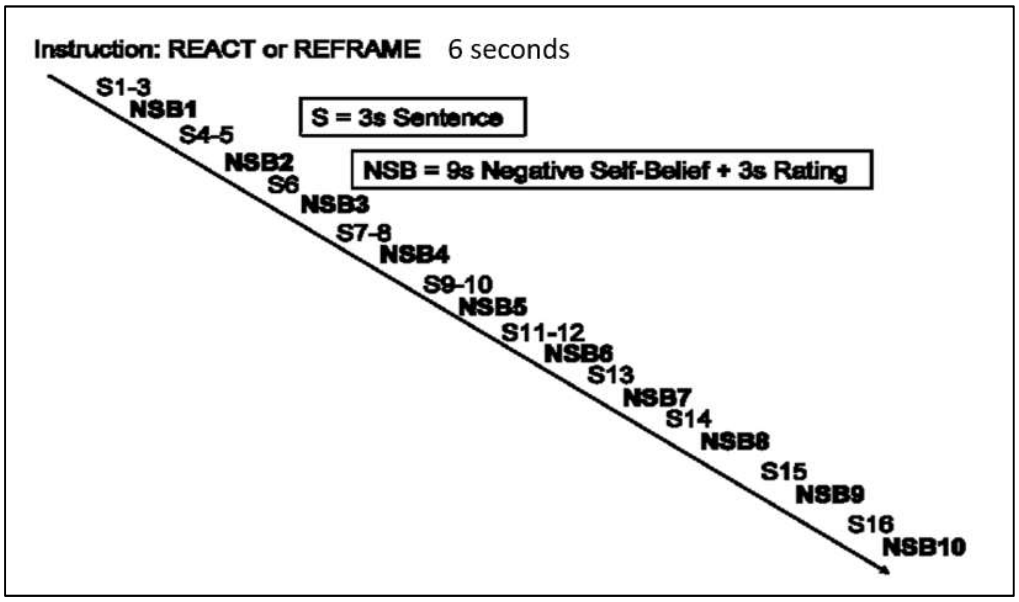

Figure 4. Components and structure of one autobiographical social situation trial adapted from Goldin, Manber-Ball et al (2009). Participants first received a 6 second instruction (REACT or REFRAME) followed by a 3 seconds sentence (16 in total per situation) in white font against a black background describing the situation. Participants were then shown their NSB (9 seconds each, 10 in total per trial) embedded in the unfolding story in uppercase letters that flashes 9 times (850 milliseconds on + 150 milliseconds off). Finally, participants completed a 3 seconds negative emotion rating on a 1-5 scale.

2.2.5.4 *Emotion recognition task*

An adapted version of the Cambridge Cognition Emotion Recognition Task was utilised as developed by Bamford et al (2015) in E-Prime (Schneider, Eschman & Zuccolotto, 2012), as a measure of emotion recognition sensitivity. This involves 90 trials in which participants are asked to name the emotion represented in each face display as quickly and as accurately as possible, from a selection of six options displayed on-screen (fearful, angry, happy, sad, disgusted and surprised). The emotion expression 15-image morphed continua (low to full intensity stimuli) developed by Bamford et al 2015 was utilised for each emotion group (see figure 5). Each trial commenced with a central fixation cross shown on-screen for 1500-2500ms, followed

by the presentation of the face stimulus (350 × 457 pixels) for 150ms. A noise mask is then activated for 250ms to prevent afterimage effects (Bamford et al., 2015). The six response options are shown on-screen for 10,000ms, or until the participant responds by selecting the emotion judged to be the most suitable descriptor (Bamford et al., 2015), within this 8-minute task.

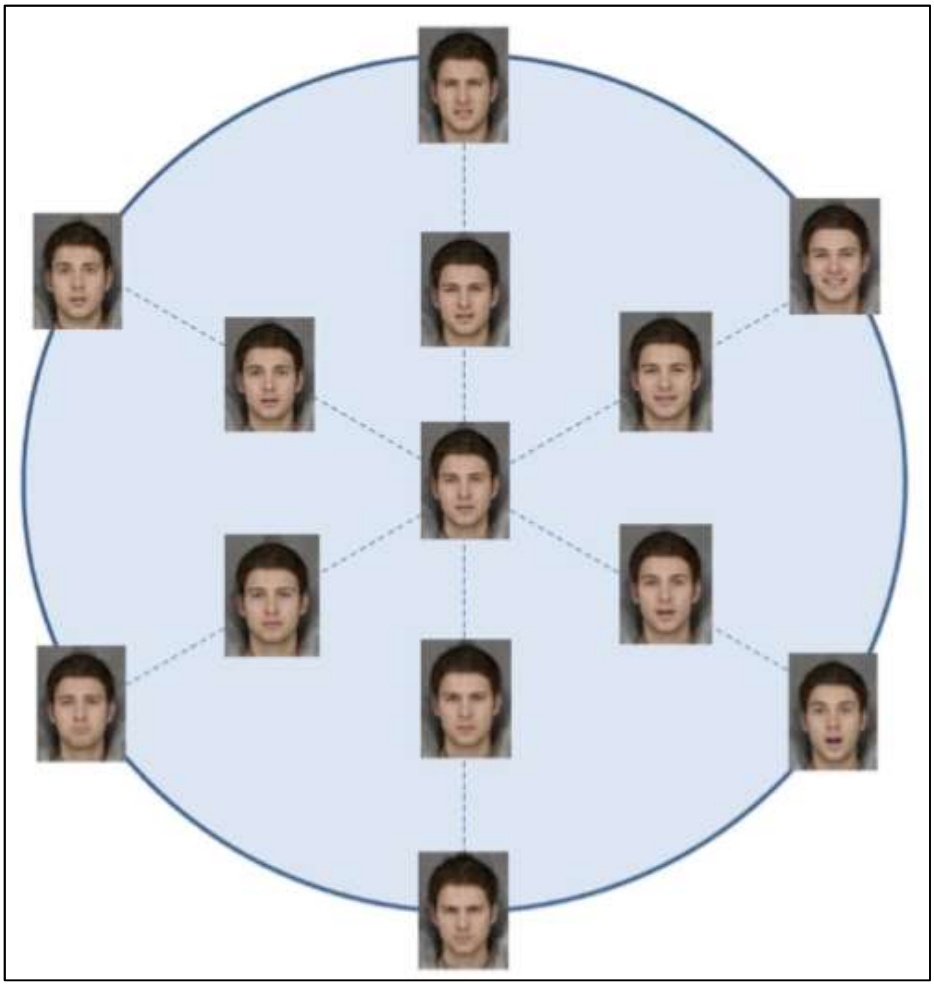

Figure 5. An example of emotion expression stimuli utilised within the Emotion Recognition task across low to full intensity (Bamford et al 2015).

2.2.5.5 *Omron M2 upper arm monitor*

An Omron M2 upper arm monitor measured heart rate and systolic and diastolic blood pressure.

2.2.5.6 *tDCS*

Participants were randomly allocated to receive active PFC tDCS, cerebellar-tDCS or sham tDCS. For the PFC tDCS group (*n*=11), the anode electrode was placed over F4 in order to stimulate the right dorsolateral PFC. A constant current of 2 mA was applied for 20 minutes (Feeser et al., 2014).

For the cerebellar tDCS group (*n*=11), the active electrode (anode, Ferrucci et al., 2012) was placed over the cerebellum at 1–2cm below and 3–4cm lateral to the inion as the most frequent placement for cerebellar stimulation (Ferrucci, Cortese & Priori, 2015; Van Dun, Bodranghien, Mariën & Manto, 2016; see figure 6). A constant current of 2 mA was applied for 20 minutes (Ferrucci et al., 2012; 2015).

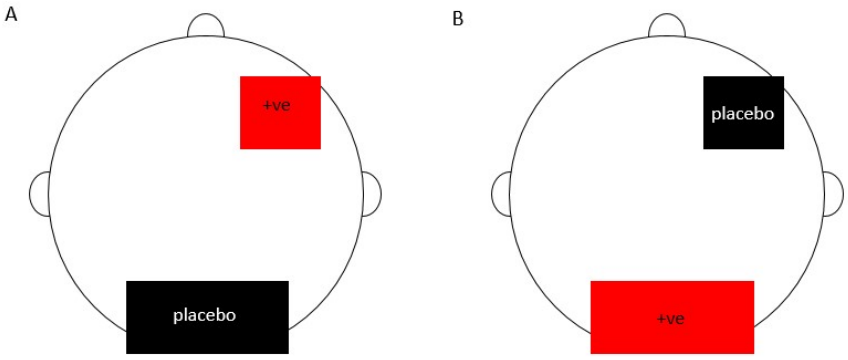

Figure 6. Schematic Image of tDCS anode placement (+ve), which received either active or sham stimulation (double blind); in addition to a placebo electrode which was utilised to blind participant to stimulation site.

For the sham tDCS condition (*n*=11), 30-seconds of stimulation was applied to the cerebellum (*n*=4) or PFC (*n*=7) only. A common reference node was employed across conditions over the left deltoid muscle (Ferucci et al., 2012). The stimulation commenced 4 minutes before starting the cognitive reappraisal task and continued for the duration of the task (total of 20 minutes), as described by Feeser et al (2014).

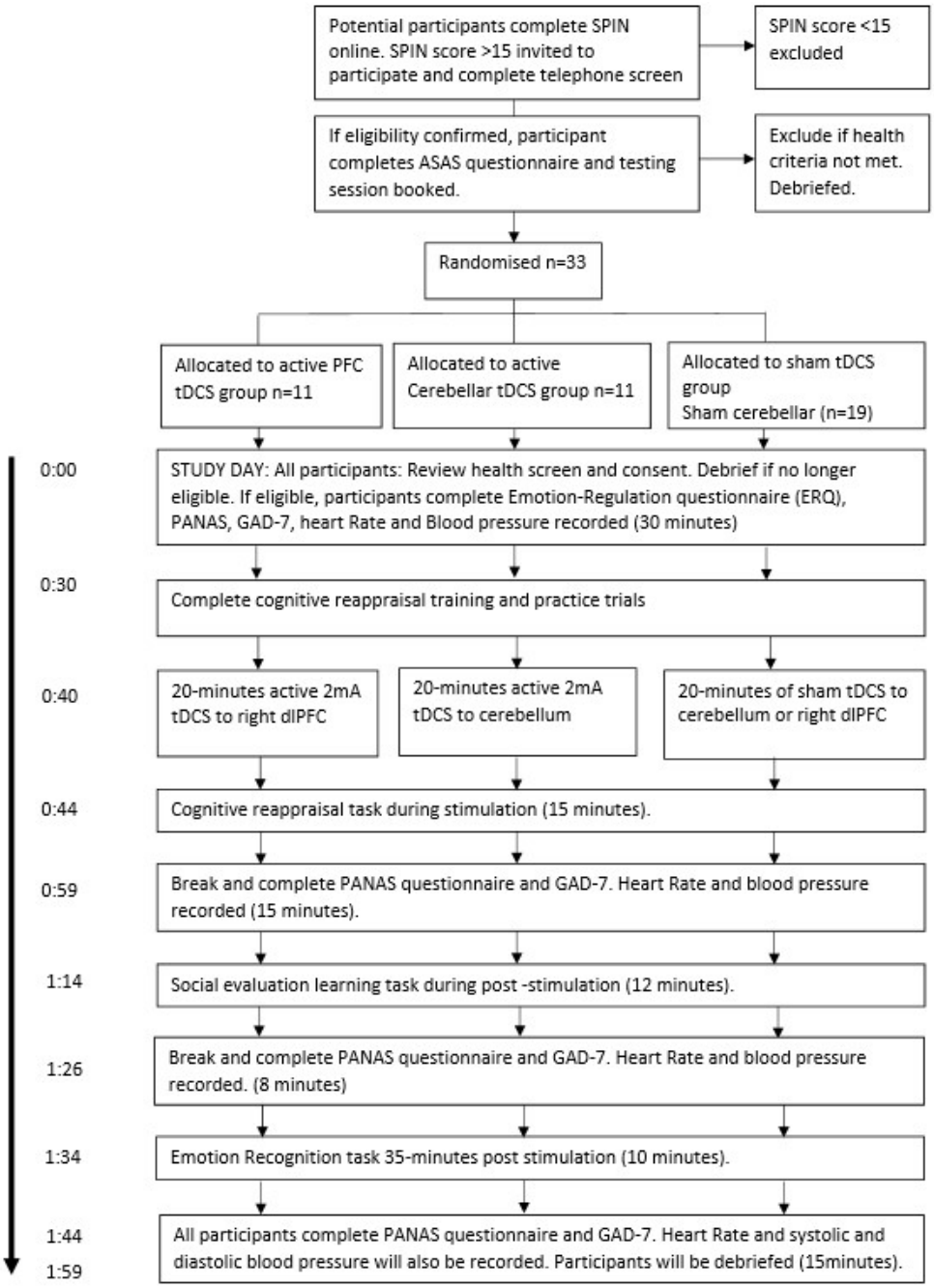

Figure 7. Schematic image of study day procedure (*n*=33). SPIN=Social Phobia Inventory; ASAS= Autobiographical Social Anxiety Situations questionnaire; PFC=prefrontal cortex; tDCS=transcranial direct current stimulation; ERQ=Emotion Regulation Questionnaire; PANAS= Positive and Negative Affect Schedule; GAD-7= Generalised Anxiety Disorder Assessment; dlPFC=dorsolateral prefrontal cortex.

2.2.5.7 *Emotion regulation questionnaire (ERQ)*

To control for individual differences in emotion regulation, the ERQ (Gross & John, 2003) was completed at the beginning of the testing session, as utilised by Feeser et

al (2014). This requires participants to respond to 10-items focusing on emotional control including both emotional experience and expression, on a 7-point likert scale (1=strongly disagree to 7=strongly agree; see appendix C).

2.2.5.8 *Positive and Negative Affect Schedule (PANAS)*

To examine changes in mood the PANAS (Watson, Clark & Tellegen, 1988) was completed at the beginning and end of each task. The PANAS consists of 20-items of both positive and negative affect requiring response using a 5-point likert scale (1=very slightly/not at all to 5=Extremely; see appendix D); with higher scores indicating higher levels of positive and negative affect respectively. Good reliability and validity of the PANAS have been reported (Crawford & Henry, 2004).

2.2.5.9 *Generalised Anxiety Disorder Assessment (GAD-7)*

To examine changes in state anxiety, the GAD-7 questionnaire (Spitzer, Kroenke, Williams & Löwe, 2006) was completed at the beginning and end of each task. This consists of 7-items measuring worry and general anxiety, to which participants respond from 4 options. The first time-point included standard options as a measure of trait anxiety generally over the past 2 weeks (not at all, several days, over half the days, nearly every day; see appendix E). Each subsequent time-point used an adapted version to measure changes in state anxiety across the session, asking around worry in the last 20 minutes, with options of not at all, some of the time, most of the time, and all of the time (see appendix F); with cut-off points of 5, 10 and 15 used to indicate mild, moderate and severe levels of anxiety (Spitzer, Kroenke, Williams & Löwe, 2006).

2.2.6 Experimental procedures

The study was advertised on posters within the Psychology department at the University of Southampton and the University of Bath, on social media, with participants able to sign up via respective research portals. Potential participants were first instructed to complete the SPIN online to assess their eligibility to participate. Eligible participants were then sent an information sheet and consent form to consider and invited to arrange a telephone screening interview, complete with an *initial number* to maintain anonymity. On confirmation of eligibility, the participant was invited to complete an online version of the ASAS, complete with an assigned *study number*, used for the duration of the study, to maintain anonymity.

On arrival, participants were given the information sheet again in addition to a consent form. On consent the health screen was reviewed to ensure that the participant continued to meet health eligibility criteria. Participants were then asked to complete the ERQ, GAD-7 and PANAS questionnaires and physiological measures of blood pressure and heart rate was obtained (see figure 2 for a schematic image). Participants then completed training in cognitive reappraisal (see appendix G for a copy of the training script) and two practice trials, as described by Goldin, Manber-Ball et al (2009). Participants then received tDCS as per their randomly allocated condition, which commenced 4 minutes before the appraisal task. On completion of the cognitive reappraisal task and stimulation (20 minutes), participants were asked to complete the GAD-7 and PANAS online in addition to physiological measures and had a break to re-baseline their mood.

Participants then completed a second task (to be reported elsewhere, write-up to be led by Bath team), followed by the completion of the GAD-7, PANAS and physiological measures and a break, before completing the Emotion recognition task.

Ferrucci et al (2012) explain that the effects of cerebellar stimulation are most evident 35-minutes post stimulation. Therefore, a 35-minute delay was adopted between the end of stimulation and the emotion recognition task (see figure 7). On completion of this final task, the GAD-7, PANAS and physiological measures were taken for a final time.

On completion of the study, participants were debriefed, and a follow up phone-call was arranged for the following day.

2.2.6.1 *Ethical Considerations and Informed Consent*

Ethical approval was obtained from the University of Southampton Ethics Committee, and the University of Bath Ethics Committee. The nature, purpose and risks of the study were explained to the participant, both at the testing session and on signing up to participate online. Participants were informed that they are free to withdraw at any time.

2.2.7 Data analysis

The data analysis script was compiled prior to completing and viewing data collection using Statistical Package for the Social Sciences software (SPSS; IBM Corp, 2013) syntax. Additionally, the researcher was blind to stimulation conditions on initial analysis completion, to reduce risk of bias in data processing and analysis.

2.2.7.1 *Testing Primary Hypotheses: Cognitive reappraisal*

Outcome variables of average negative feeling ratings were calculated in SPSS, across conditions (neutral, react and reappraise). To explore the factor of time across the reappraisal task, average ratings were also calculated across trial blocks (neutral, react 1, reappraise 1, react 2, reappraise2). Total score variables for questionnaire

data were computed for GAD, PANAS (positive and negative) and ERQ (cognitive reappraisal and expression suppression scale).

A one-way repeated measures Analysis of Variance (ANOVA) was utilised to investigate differences in negative feeling across within-groups factor of cognitive reappraisal task conditions (3 levels; Neutral, React, Reappraise) to confirm cognitive reappraisal success in comparison to neutral and passive react conditions. In addition to this, the relationship between baseline data (SPIN, GAD, ERQ, PANAS), site, age, ASAS ratings and self-reported negative feeling was investigated using one-way ANOVAs. Additionally, associations between down-regulation efficacy (react minus reappraise) and baseline data and age was explored, as completed by Goldin, Manber-Ball et al (2009).

To assess the effect of tDCS on cognitive reappraisal as an emotion regulation strategy, a two-way mixed ANOVA was utilised, to examine the interaction effects between the between-groups factor of stimulation condition (3 levels; PFC, cerebellar, sham) and within-groups factor of task conditions (3 levels; Neutral, React, Reappraise) on ratings of negative feeling. This was repeated in separate ANOVAs for block one and block two of the cognitive reappraisal task, to explore any change in group differences over time.

2.2.7.2 *Testing Exploratory Hypotheses: Emotion recognition*

To calculate the dependent variable of 'emotion recognition sensitivity', the 'hit' (e.g. number of times correctly identified anger stimuli as 'anger') and 'false alarm' (e.g. number of times stimuli mislabelled as 'anger' when not anger) rates were first computed, as described by Bamford et al (2015). The 'hit' rate was calculated as the mean accuracy across trials for each emotion (15 trials). The 'false alarm' rate was

calculated by computing the number of times each participant responded with 'anger' for example, on the 75 trials where the anger emotion stimulus was not presented, for each emotion respectively. The dependent variable of 'emotion recognition sensitivity' was then computed across emotion type by subtracting the 'false alarm' rate from the 'hit' rate as described by Bamford et al., (2015); with scores ranging from -1 to 1. An 'emotion recognition sensitivity' score of 1 represents greater accuracy demonstrated by a high hit rate in addition to a low false alarm rate.

Initially, associations between emotion recognition sensitivity and baseline data (SPIN, GAD, PANAS), site and age were explored. To investigate the interaction effects of emotion stimulus intensity (3 levels; weak, medium, strong) and tDCS (3 levels) on 'emotion recognition sensitivity' (Bamford et al., 2015), a 3x3 mixed model two-way ANOVA was conducted for each emotion. Where significant effects are revealed, two-way 3x6 mixed-model ANOVAs were performed to investigate the interaction effects of tDCS (between-groups independent variable, 3 levels) and emotion (within-groups independent variable, 6 levels) on emotion recognition accuracy ('hits') and bias ('false alarms)', in order to explore whether it is hits or false alarms driving the effect (Bamford et al., 2015).

Finally, in order to investigate the effects of tDCS (3 levels) and emotion (within-groups variable, 6 levels) on reaction time, a 3x6 mixed model ANOVA was completed.

2.2.7.3 *Data Cleaning*

Before completing the analysis, descriptive statistics, stem-and-leaf diagrams and histograms were completed to assess data against test assumptions, including data

distribution, missing data or outliers and homogeneity of variance was assessed. Although, evidence suggests when there are equal group sizes, the F-statistic is robust to violations of normality, maintaining control of the type 1 and type 2 error rate (Field, 2009; Schmider, Ziegler, Danay, Beyer & Bühner, 2010; Glass, Peckham & Sanders, 1972; Lix, Keselman & Keselman, 1996). However, the F-statistic can be sensitive to outliers (Osbourne & Overbay, 2004) and so when present, data transformations were considered; however, this method can impact the accuracy of ANOVA (Games and Lucas, 1966; Zimmerman, 1998). Therefore, on confirmation that severe outliers (greater than 3 SDs from the total sample mean) were not a result of error, scores were truncated to next highest/lowest score plus/minus 1 unit (Field, 2009; Osbourne & Overbay, 2004) to maintain equal groups and data quality. Stem-and-leaf diagrams were then completed again to confirm the outliers had been truncated effectively. Where the assumption of sphericity was violated, corrected Greenhouse-Geisser degrees of freedom are reported as a more conservative statistic (Field, 2009). An alpha level of .05 was utilised for all statistical tests.

2.3 Results

2.3.1 Group Characteristics

Participants across tDCS groups did not differ in age, trait social anxiety (SPIN), baseline state anxiety (GAD-7), baseline mood (PANAS), baseline use of cognitive reappraisal and expression suppression to regulate emotions (ERQ), or blood pressure (see table 3 for group characteristics). There were no significant differences on cognitive reappraisal task performance between sites (no significant interaction $F(2,62) = .52$, $p = .079$, $\eta_p^2 = .08$; or main effect of site $F(1, 31) = 2.16$, p=.152, $\eta_p^2 = .07$).

Table 3

Participant characteristics across active PFC and Cerebellar tDCS and sham groups

	PFC *n*=11	Cerebellar *n*=11	Sham *n*=11	*F*
Sex				
Mean Age	20.91(2.91)	21.64(3.20)	21.73(3.95)	.19
SPIN	29.27(8.44)	25.27(7.88)	28.82(11.66)	.59
GAD-7	3.64(2.77)	3.73(2.80)	4.73(3.47)	.44
PANAS positive	29.09(7.57)	28.91(9.73)	27.18(7.21)	.18
PANAS negative	13.09(3.81)	12.55(2.84)	14.73(5.71)	.77
ERQ cognitive reappraisal	29.73(5.82)	26.45(6.17)	28.18(7.03)	.73
ERQ expression suppression	16.64(4.57)	13.27(5.88)	14.45(4.48)	1.27
Systolic BP	118.09(13.04)	114.36(12.89)	114.18(9.72)	.37
Diastolic BP	74.00(7.43)	71.09(6.76)	69.91(4.70)	1.19

Note. Values represent Mean (standard deviation); GAD-7=Generalised Anxiety Disorder Screener; PANAS=Positive and Negative affect; BP=Blood Pressure.

Additionally, there were no significant associations (all $p>.05$) between cognitive reappraisal down-regulation efficacy and age, social anxiety (SPIN), baseline state anxiety (GAD-7), baseline mood (PANAS) or baseline cognitive reappraisal and expression suppression (ERQ).

2.3.2 Autobiographical Social Situations

Table 4
Autobiographical situation characteristic and participant reported responses to situations

	PFC	Cerebellar	Sham	*F*
Characteristics of situation				
Age at situation (years)	18.03(2.68)	16.53(2.06)	17.82(4.24)	.74
Vividness of memory	7.43(.87)	6.64(1.36)	6.20(1.34)	2.91
Shame at situation	7.32(1.67)	7.14(.86)	7.09(1.22)	.10
Responses to situation				
Current shame	4.73(1.70)	4.14(1.49)	4.43(1.59)	.38
Current disturbance	4.95(1.73)	4.77(1.62)	5.41(2.13)	.35
Current avoidance	4.32(2.33)	5.14(1.85)	4.86(.91)	.59
Current talk	3.25(2.17)	2.32(.84)	2.14(.17)	1.99

Note. Values represent Mean (standard deviation).
*=$p<0.05$.

No significant differences were found between tDCS groups across autobiographical situation characteristics (age at situation, vividness of memory, shame at situation) or responses to situations (current shame, disturbance, current avoidance of similar situations, frequency of talking about situation) (see table 4).

A one-way repeated measures ANOVA found significant differences across time-points (4 levels; T1, T2, T3, T4) for GAD $F(2.14, 68.40) = 16.67$, $p<.001$, $\eta_p^2=.34$, with significantly lower anxiety reported across T3 (mean, $M=1.64$) and T4 ($M=1.64$), in comparison to T1 ($M=4.03$) and T2 ($M=3.36$). Significant differences were also presented for positive PANAS $F(2.27, 72.55) = 10.82$, $p<.001$, $\eta_p^2=.25$,

with significantly increased positive mood reported at T1 (*M*=28.39), in comparison to T2 (*M*=25.18), T3 (*M*=24.09) and T4 (*M*=23.09); and negative PANAS scores $F(2.18, 69.91) = 5.73$, $p=.004$, $\eta_p^2=.15$, with T2 (*M*=13.58) demonstrating significantly increased negative mood in comparison to T3 (*M*=12.00) and T4 (*M*=11.46).

2.3.3 Cognitive Reappraisal: Behavioural response

A one-way ANOVA revealed significant differences across all task conditions (3-levels, neutral, react, reappraise), $F(2, 64) = 161.49$, $p<.001$, $\eta_p^2=.84$; with participants reporting significantly lower negative feeling within the neutral task than react and reappraise(see table 5) and significantly increased negative feeling within the react condition in comparison to the neutral and reappraise.

Table 5

Mean reported negative feeling across cognitive reappraisal task and tDCS conditions

	PFC (*n*=11)	Cerebellar (*n*=11)	Sham (*n*=11)	Total (*n*=33)
Neutral	1.12(.15)	1.03(.05)	1.16(.18)	1.10(.14)
React	3.28(.71)	2.84(.87)	3.20(.70)	3.11(.76)
Reappraise	2.16(.62)	1.83(.42)	2.47(.80)	2.16(.67)

Note. Values represent Mean (standard deviation).

2.3.4 Effect of tDCS

The completion of a 3x3 mixed ANOVA revealed a significant main effect of task condition $F(2, 60) = 163.66$, $p<0.001$, $\eta_p^2=.85$, indicating that participants demonstrated significant differences in negative ratings across task conditions, with a large effect size. A Bonferroni post-hoc test revealed that participant reported

negative feeling was significantly different between all task instruction groups (p<0.001; neutral M=1.10; react M=3.11; reappraise M=2.16) (see figure 8).

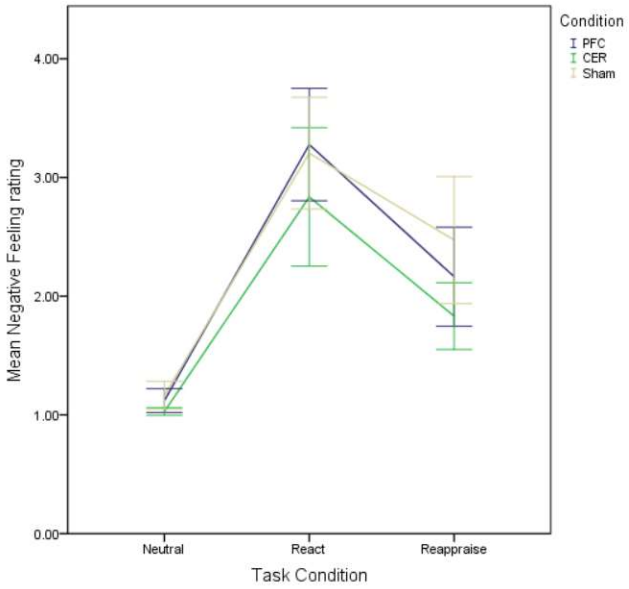

Figure 8. Line graph showing the effect of tDCS condition (PFC, Cerebellar, Sham) and task condition (Neutral, React, Reappraise) on participant reported negative feeling across the cognitive reappraisal task.

There was no significant main effect of tDCS condition on reported negative feeling, $F(2, 30) = 2.20$, p=.128, η_p^2=.13; or interaction effect between task instruction and tDCS condition, $F(4, 60) = 1.21$, p=.314, η_p^2=.08.

2.3.5 Time Analysis

2.3.5.1 *T1 and T2: Behavioural response*

A 2x2 repeated measures ANOVA investigating react and reappraisal trials across two trial blocks demonstrated a significant main effect of time $F(1, 32) = 5.67$, p=0.023, η_p^2=.15, with participants reporting significantly higher levels of negative feeling in the second block, in comparison to the first block. A significant main effect of trial instruction $F(1, 32) = 78.89$, p<0.001, η_p^2=.71, was also present, with participants reporting significantly lower negative ratings when instructed to

reappraise in comparison to react. No significant interaction effect was presented $F(1, 32) = .04$, $p=.851$, $\eta_p^2=.001$.

2.3.5.2 *T1: effect of tDCS*

A significant main effect of task instruction was present $F(1.68, 50.37) = 102.74$, $p<0.001$, $\eta_p^2=.77$, indicating that participants demonstrated significant differences in negative ratings across task conditions, with a large effect size. A Bonferroni post-hoc test revealed that participant reported negative feeling was significantly different between all task instruction groups ($p<0.001$; neutral $M=1.10$; react $M=2.99$; reappraise $M=2.06$). There was no significant main effect of tDCS condition on negative feeling, $F(2, 30) =1.74$, $p=.193$, $\eta_p^2=.10$, or interaction effect between task instruction and tDCS condition, $F(3.36, 50.37) = 1.65$, $p=.184$, $\eta_p^2=.10$.

However, simple contrasts suggested an interaction effect between neutral and reappraise task conditions. Therefore an exploratory follow-up ANOVA was conducted which found a significant interaction effect $F(2, 30)=3.57$, $p=.041$, $\eta_p^2=.19$ with a large effect size, demonstrating that the sham group reported significantly higher average ratings of negative feeling when reappraising negative self-beliefs ($M=2.49$), in comparison to PFC ($M=1.89$) and Cerebellar groups ($M=1.79$); in comparison to the neutral task with no differences between groups in reported negative feeling (Sham $M=1.17$; PFC $M=1.12$; Cerebellar $M=1.03$).

Significant main effects of task instruction $F(1, 30)=93.24$, $p<.001$, $\eta_p^2=.76$ with significant differences presented between both groups ($p<.001$); and tDCS condition was also present $F(2, 30)=4.92$, $p=.041$, $\eta_p^2=.25$. Bonferroni post-hoc tests found a significant difference between sham and cerebellar ($p=.016$), with a trend between sham and PFC ($p=.08$) (see figure 9).

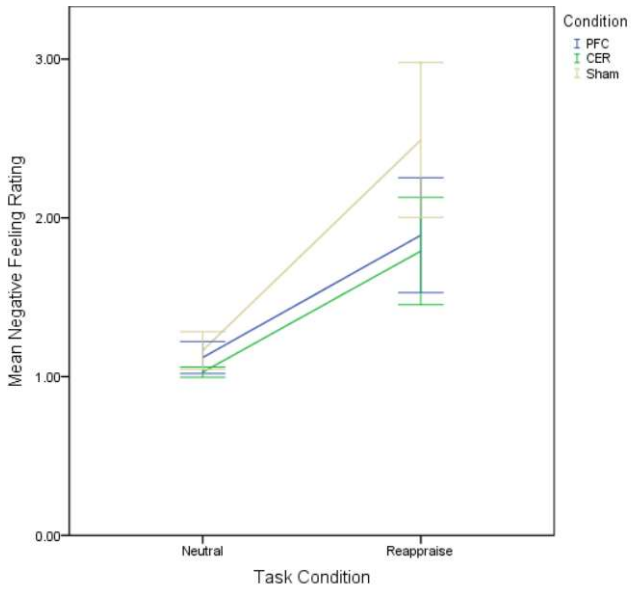

Figure 9. Line graph showing the effect of tDCS condition (PFC, Cerebellar, Sham) and task condition (Neutral, Reappraise) on participant reported negative feeling within the first task block of the cognitive reappraisal task.

2.3.5.3 *T2: Effect of tDCS*

A significant main effect of task instruction was present $F(2, 60) = 129.22$, $p<0.001$, $\eta_p^2=.81$, indicating that participants demonstrated significant differences in negative ratings across task conditions, with a large effect size; where negative feeling was significantly different between all task instruction groups ($p<0.001$; neutral $M=1.10$; react $M=3.22$; reappraise $M=2.26$).

There was no significant main effect of tDCS condition on negative feeling, $F(2, 30) =2.33$, $p=.114$, $\eta_p^2=.14$. There was no interaction effect between task instruction and tDCS condition, $F(4, 60) =.84$, $p=.505$, $\eta_p^2=.05$.

2.3.6 Emotion Recognition: Sensitivity Analysis

No significant differences were observed in emotion recognition sensitivity across weak, medium and strong intensities across 6 emotions between Bath and Southampton sites (all $p>.05$). Associations were found between recognition

sensitivity for strong anger stimuli and SPIN scores with a significant medium negative correlation $r(33)=-.36$, $p=.038$; recognition sensitivity for medium happy stimuli presented with a significant, negative association with GAD scores ($r(33)=-.35$, $p=.045$) and positively associated with PANAS positive scores ($r(33)=.47$, $p=.006$); recognition sensitivity for strong happy stimuli was significantly negatively associated with age ($r(33)=-.61$, $p<.001$). No other significant associations were found ($p>.05$). See table 6 for means and standard deviations across groups.

2.3.6.1 *Anger*

The completion of a 3x3 mixed ANOVA revealed a significant main effect of intensity, $F(2, 60) = 240.12$, $p<0.001$, $\eta_p^2=.89$, indicating that participants demonstrated significant differences in anger recognition sensitivity across intensities, with a large effect size. Bonferroni post-hoc tests revealed that recognition sensitivity was significantly different across intensities. Sensitivity was significantly lower for weak anger intensity ($M=.09$) in comparison to medium ($M=.68$) and medium sensitivity significantly reduced in comparison to strong ($M=.95$) (see figure 10).

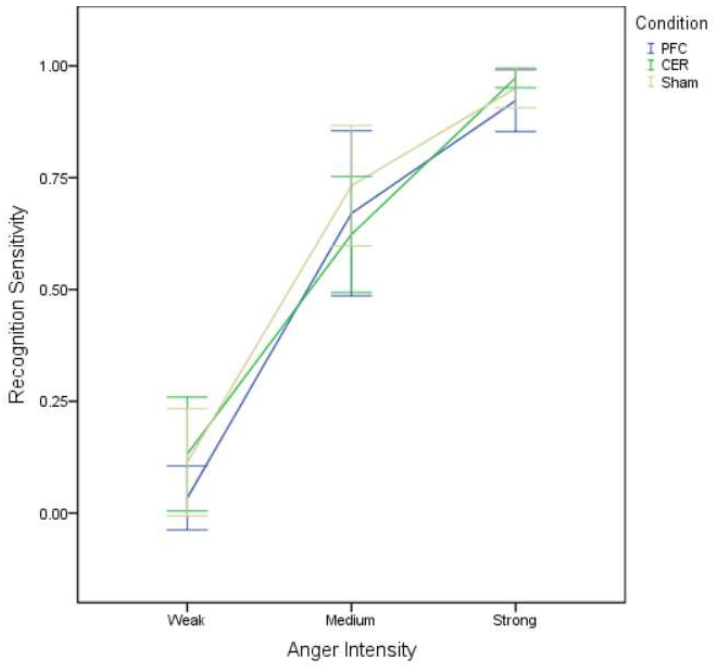

Figure 10. Line graph showing the effect of tDCS condition and anger stimuli intensity on anger recognition sensitivity on the emotion recognition task.

There was no significant main effect of tDCS condition on anger recognition sensitivity, $F(2, 30) = .89$, $p=.423$, $\eta_p^2=.06$, or interaction effect between intensity and tDCS condition, $F(4, 60) = .83$, $p=.514$, $\eta_p^2=.05$.

Table 6

Emotion Recognition 'Hits', 'False Alarms', Recognition Sensitivity and Reaction Time (RT) across tDCS groups

	PFC (n=11)	Cerebellar (n=11)	Sham (n=11)	Total (n=33)
Hits				
Anger	.58(.10)	.58(.10)	.63(.12)	.59(.11)
Disgust	.65(.23)	.72(.15)	.63(.13)	.66(.17)
Fear	.48(.26)	.39(.21)	.42(.22)	.43(.23)
Happy	.81(.14)	.79(.11)	.66(.16)	.76(.15)
Sad	.83(.08)	.78(.09)	.75(.15)	.78(.11)
Surprise	.75(.12)	.76(.08)	.70(.10)	.74(.10)
False Alarms				
Anger	.04(.04)	.01(.02)	.03(.04)	.03(.03)
Disgust	.07(.04)	.08(.07)	.09(.06)	.08(.06)
Fear	.08(.05)	.10(.03)	.12(.08)	.10(.06)
Happy	.04(.05)	.04(.04)	.03(.04)	.04(.04)
Sad	.07(.05)	.05(.07)	.05(.06)	.06(.06)
Surprise	.09(.05)	.11(.05)	.11(.06)	.10(.05)
Recognition Sensitivity				
Anger				
Weak	.03 (.11)	.13 (.19)	.11 (.18)	.09(.16)
Medium	.67 (.27)	.62 (.19)	.73 (.20)	.68(.22)
Strong	.92 (.10)	.97 (.03)	.95 (.07)	.95(.07)
Disgust				
Weak	.35 (.33)	.39 (.34)	.35 (.32)	.36(.32)
Medium	.69 (.18)	.73 (.19)	.60 (.22)	.68(.20)
Strong	.69 (.31)	.77 (.21)	.68 (.24)	.71(.25)
Fear				
Weak	.38 (.34)	.34 (.29)	.35 (.31)	.36(.30)
Medium	.40 (.34)	.34 (.26)	.40 (.38)	.38(.32)
Strong	.43 (.40)	.21 (.33)	.13 (.24)	.26(.34)
Happy				

Weak	.49 (.35)	.44 (.23)	.20 (.28)	.38(.31)
Medium	.87 (.18)	.87 (.15)	.73 (.24)	.83(.20)
Strong	.97 (.03)	.96 (.04)	.95 (.07)	.96(.05)
Sad				
Weak	.46 (.23)	.33 (.23)	.31 (.27)	.37(.24)
Medium	.86 (.13)	.89 (.10)	.82 (.23)	.86(.16)
Strong	.91 (.07)	.95 (.07)	.95 (.06)	.93(.06)
Surprise				
Weak	.31 (.28)	.24 (.23)	.20 (.15)	.25(.23)
Medium	.77 (.16)	.84 (.11)	.72 (.17)	.78(.15)
Strong	.91 (.05)	.89 (.05)	.89 (.06)	.90(.05)
RT				
Anger	1079.46(227.37)	1258.64(345.18)	905.67(109.21)	1081.26(280.23)
Disgust	1536.74(439.33)	1345.35(378.86)	1326.91(449.83)	1403.00(421.53)
Fear	1744.15(559.96)	1988.10(1146.41)	1490.09(556.17)	1740.78(804.98)
Happy	923.90(199.33)	895.36(201.63)	888.35(223.08)	902.53(202.28)
Sad	1224.68(389.61)	1184.57(326.25)	1066.34(256.99)	1158.53(325.57)
Surprise	1221.08(337.58)	1055.98(433.80)	1011.92(508.20)	1096.33(428.35)

Note. Values represent Mean (standard deviation).

2.3.6.2 *Disgust*

The completion of a 3x3 mixed ANOVA revealed a significant main effect of intensity, $F(1.60, 47.84) = 18.35$, $p<0.001$, $\eta_p^2=.38$, indicating that participants demonstrated significant differences in disgust recognition sensitivity across intensities, with a large effect size. Post-hoc tests recognition sensitivity for disgust was significantly lower for weak intensities (M=.36), in comparison to both medium (M=.68) and strong (M=.71) (see figure 11).

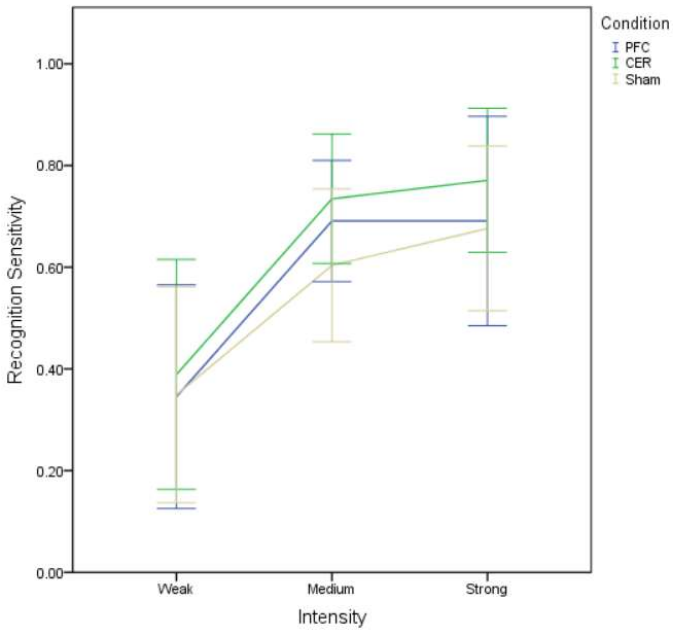

Figure 11. Line graph showing the effect of tDCS condition and disgust stimuli intensity on disgust recognition sensitivity.

There was no significant main effect of tDCS condition on disgust recognition sensitivity, $F(2, 30) = .86$, $p = .434$, $\eta_p^2 = .05$, or interaction effect between intensity and tDCS condition, $F(3.19, 47.84) = .13$, $p = .948$, $\eta_p^2 = .01$.

2.3.6.3 *Fear*

The completion of a 3x3 mixed ANOVA revealed a trend for a main effect of fear intensity, $F(1.67, 50.14) = 2.60$, $p = .094$, $\eta_p^2 = .08$, with post-hoc tests demonstrating a significant difference between medium and strong intensities of fear, with recognition sensitivity significantly worse for strong ($M = .26$) intensities than medium ($M = .38$) (see figure 12).

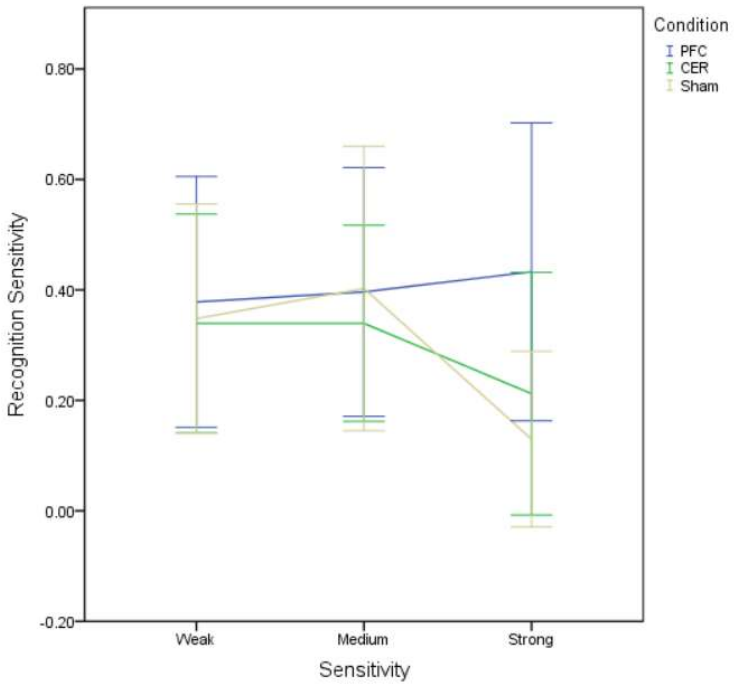

Figure 12. Line graph showing the effect of tDCS condition and fear stimuli intensity on fear recognition sensitivity.

No significant main effect of condition, $F(2, 30) = .60$, $p = .557$, $\eta_p^2 = .04$, or interaction effect between fear intensity and tDCS condition, $F(3.34, 50.14) = 1.54$, $p = .212$, $\eta_p^2 = .09$ was present. However, simple contrasts suggested an interaction effect between medium and strong intensities $F(2, 30) = 3.74$, $p = .035$, $\eta_p^2 = .20$, with significantly improved recognition sensitivity in the PFC condition ($M = .43$) compared to Sham ($M = .13$) or Cerebellar ($M = .21$) for strong intensities, with no difference between groups in recognition sensitivity to medium fear stimuli (Sham $M = .40$; PFC $M = .40$; Cerebellar $M = .34$).

A follow up one-way ANOVA revealed no significant differences between tDCS groups on fear recognition 'hits' $F(2, 30) = .39$, $p = .678$, $\eta_p^2 = .03$ or 'false alarms' $F(2, 30) = 1.79$, $p = .185$, $\eta_p^2 = .11$. However, less sensitive LSD post hoc tests reveal a trend ($p = .07$) for a significantly increased false alarm rate for the Sham

group (*M*=.13), in comparison to participants who received PFC tDCS (*M*=.08); suggesting that this trend for interaction is driven by recognition 'false alarms'.

2.3.6.4 *Happy*

The completion of a 3x3 mixed ANOVA revealed a significant main effect of intensity, $F(1.60, 47.96)=88.62$, $p<0.001$, $\eta_p^2=.75$, indicating that participants demonstrated significant differences in happy recognition sensitivity across intensities, with a large effect size. Post-hoc tests revealed that recognition sensitivity was significantly different across groups. Sensitivity was significantly lower for weak happy intensity (*M*=.38) in comparison to medium (*M*=.83) and medium sensitivity significantly reduced in comparison to strong (*M*=.96) (see figure 13).

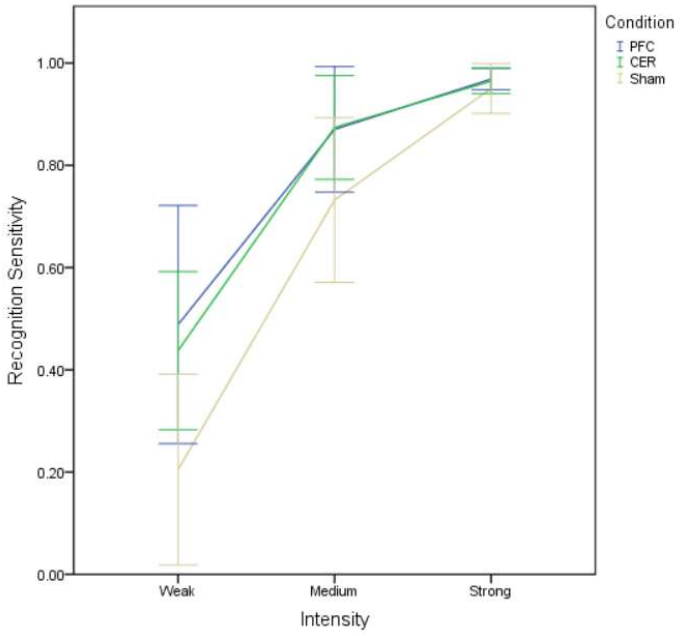

Figure 13. Line graph showing the effect of tDCS condition and happy stimuli intensity on happy recognition sensitivity.

A significant main effect of condition was also revealed, $F(2, 30) = 3.92$, $p=.031$, $\eta_p^2=.21$, indicating that participants demonstrated significant differences in

happy recognition sensitivity across tDCS condition, with a large effect size. Post-hoc tests revealed that recognition sensitivity for happy was significantly reduced for Sham (*M*=.63) in comparison to PFC, (*M*=.78; *p*==.047) with a trend for significant difference between Sham and Cerebellar (*M*=.76; *p*=.093) (see figure 13).

No significant interaction effect between intensity and condition was revealed, $F(3.20, 47.96)=1.61$, $p=.198$, $\eta_p^2=.10$, indicating that there were no significant differences between tDCS groups, in happy recognition sensitivity across different stimuli intensities. However, simple contrasts suggested a trend for an interaction effect between weak and strong intensities $F(2, 30)=2.60$, $p=.091$, $\eta_p^2=.15$, with lower recognition sensitivity in the Sham condition (*M*=.21) compared to PFC (*M*=.49) or Cerebellar (*M*=.44) for weak intensities, with no difference between groups in recognition sensitivity to strong happy stimuli (Sham *M*=.95; PFC *M*=.97; Cerebellar *M*=.97). A follow up one-way ANOVA revealed that the effect of tDCS condition on happy recognition sensitivity and trend for interaction is driven by recognition accuracy 'hits' $F(2, 30)=3.87$, $p=.032$, $\eta_p^2=.45$, rather than 'false alarms' $F(2, 30)=.075$, $p=.928$, $\eta_p^2=.07$, with a Bonferroni post-hoc test revealing that participants who received PFC (*M*=.81) stimulation were significantly more accurate (*p*=.049) in the recognition of happy faces than the sham group (*M*=.66), with no significant difference between tDCS groups in the number of 'false alarms'.

2.3.6.5 *Sad*

A significant main effect of intensity, $F(1.53, 45.95) = 114.12$, $p<0.001$, $\eta_p^2=.79$, was present indicating that participants demonstrated significant differences in sadness recognition sensitivity across intensities, with large effect size. Post-hoc tests revealed that recognition sensitivity was significantly different across groups.

Sensitivity was significantly lower for weak sad intensity (*M*=.37) in comparison to medium (*M*=.86) and medium sensitivity significantly reduced in comparison to strong (*M*=.94).

There was no significant main effect of condition, $F(2, 30) = .69$, $p = .512$, $\eta_p^2 = .04$, indicating that participants demonstrated no significant differences in sadness recognition sensitivity across tDCS condition. Additionally, there was no significant interaction effect $F(3.06, 45.95) = 1.25$, $p = .304$, $\eta_p^2 = .08$.

2.3.6.6 *Surprise*

A significant main effect of intensity, $F(1.56, 46.76) = 158.03$, $p < 0.001$, $\eta_p^2 = .84$, was present indicating that participants demonstrated significant differences in surprise recognition sensitivity across intensities, with a large effect size. Post-hoc tests revealed that recognition sensitivity was significantly different across groups. Sensitivity was significantly lower for weak surprise intensity (*M*=.25) in comparison to medium (*M*=.78) and medium sensitivity significantly reduced in comparison to strong (*M*=.90).

There was no significant main effect of condition, $F(2, 30) = 1.29$, $p = .290$, $\eta_p^2 = .08$, indicating that participants demonstrated no significant differences in surprise recognition sensitivity across tDCS condition. Additionally, there was no significant interaction effect $F(3.12, 46.76) = .79$, $p = .508$, $\eta_p^2 = .05$.

2.3.7 Emotion Recognition: Reaction Time

The completion of a 3x6 repeated measures ANOVA found a significant main effect of emotion $F(2.28, 68.49) = 19.91$, $p < .001$, $\eta_p^2 = .40$; with Bonferroni post-hoc comparisons indicating significant differences between anger and disgust, fear,

happy; disgust and happy, sad, surprise; fear and happy, sad, surprise; happy and sad (see table 6 for means and standard deviations).

No significant main effect of tDCS condition is presented $F(2, 30)=1.35$, $p=.28$, $\eta_p^2=.08$ or interaction $F(4.57, 68.49)=.987$, $p=.428$, $\eta_p^2=.06$. However, simple contrasts suggested a trend for an interaction effect, $F(2, 30)=6.95$, $p<.001$, $\eta_p^2=.32$, with faster recognition of angry faces in the sham condition ($M=905.67$) compared to PFC ($M=1079.46$) or cerebellar ($M=1258.64$), with no difference between groups in reaction time to happy stimuli (sham $M=888.35$; PFC $M=923.90$; cerebellar $M=895.36$) (see figure 14).

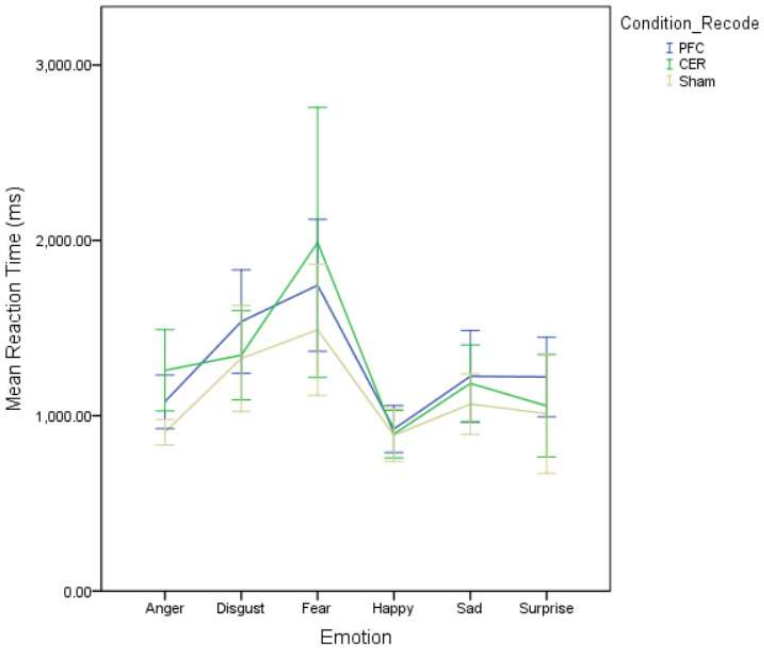

Figure 14. Line graph showing the effect of tDCS condition and emotion on reaction time across the emotion recognition task.

2.4 Discussion

This study presents evidence for successful cognitive reappraisal in adults with social anxiety in comparison to passively responding to NSBs in the context of autobiographical situations. Whilst there were no significant effects of tDCS on cognitive reappraisal across the entire cognitive reappraisal task, there was some evidence early in the task (block one) that cerebellar stimulation (vs. sham) might reduce ratings of negative feeling during cognitive reappraisal, and that PFC stimulation might achieve a similar effect.

In terms of emotion recognition, there was some evidence that participants who received PFC stimulation were better at discriminating happy faces (vs. sham), driven by significantly increased recognition accuracy, and that cerebellar stimulation might achieve a similar effect. There was also weak evidence that participants who received PFC stimulation were better at discriminating strong fear faces (vs. sham and cerebellar), driven by reduced false alarms. In terms of reaction time, participants (across groups) were quicker to recognise happy faces. Additionally, participants within the sham group were faster to respond to angry faces (vs. PFC and cerebellar).

Partial support is provided for the primary experimental hypothesis, as individuals who received PFC stimulation tended to experience less distress during cognitive reappraisal than participants who received sham tDCS. This finding corresponds with that of Feeser et al (2014) who reported anodal tDCS to the right dlPFC resulted in more efficient downregulation of emotion in healthy participants. Anodal tDCS elicits increased neuronal firing in dlPFC which research suggests may impact emotion regulation by exerting an inhibitory influence indirectly, potentially via medial PFC, to the amygdala (Urry et al., 2006), as described across top-down

theories of emotion regulation. However, this interaction effect was also present for cerebellar stimulation, and so *selective* effects for PFC tDCS are not demonstrated; with the cerebellum holding interconnectivity with the PFC and the limbic system, in addition to the parietal and temporal cortex (Baillieux, De Smet, Paquier, De Deyn & Mariën, 2008), which may be the neural mechanism through which the cerebellum modulates cognitive reappraisal. Although, this interaction was solely present between neutral and reappraise trials. Therefore, it is not clear if this effect is a direct result of reappraisal of NSBs, with evidence to suggest a role for the cerebellum in emotion reactivity (Ziv et al., 2013).

Additionally, this effect was only present across the first trial block, with significantly less effective reappraisal observed across the second block. This may demonstrate a cumulative effect of anxiety and low mood over the experience of responding to one's own idiosyncratic social anxiety related autobiographical situations and NSB. This is supported by significantly lower self-reported positive mood, coupled with a maintained negative mood, after the cognitive reappraisal task, in comparison to baseline, across participants.

There is evidence to suggest that the effects of online tDCS (during task completion) are dependent on the activations within the underlying neural network (Silvanto, Muggleton & Walsh, 2008) and so participant neuronal 'state' over the course of the task, impacts the neuromodulation of prefrontal activity (Silvanto & Pascual-Leone, 2008). Evidence suggests a role for the dlPFC in positive emotion, with feelings of happiness associated with stronger activity in the right dlPFC (Habel, Klein, Kellermann, Shah & Schneider, 2005) and reduced activity associated with depression (Schutter & van Honk, 2005). Therefore, changes in participant positive state over the course of the task may, in some part, explain this difference,

as a result of the 'state-dependency' of neuro-stimulation paradigms. Additionally, evidence suggests that individuals with social anxiety have reduced activation within the dlPFC in comparison to healthy controls (see chapter 1). Therefore, SAD baseline neuronal 'state' may present as reduced in comparison to healthy individuals, impacting on the stimulation intensity required to achieve similar results to Feeser et al (2014) in terms of improved efficacy of cognitive reappraisal.

Furthermore, inconsistencies in tDCS and task procedures can impact on results; including the adoption of the left deltoid muscle, as a contralateral reference resulting in an alternative flow of stimulation through the brain (Bikson, Datta, Rahman & Scaturro, 2010), or task differences with Feeser et al (2014) adopting IAPS in comparison to the present autobiographical social situations task (as discussed in chapter 1).

The exploratory analyses investigating emotion recognition also provide partial support for the secondary, exploratory hypotheses; with a trend for significant improvement in participants who received cerebellar or PFC stimulation, in emotion recognition sensitivity to weak happy faces. This is somewhat contrary to Ferucci et al (2012) who also found improved accuracy for faces; however, they reported improvement for negative emotions only, with no effect of right PFC stimulation on emotion recognition. However, support for this finding is demonstrated by Nitsche et al. (2012) who found that anodal tDCS to left dlPFC improved emotion facial recognition for positive content. Furthermore, evidence from PET and fMRI studies suggest a relationship between prefrontal activity and happy face recognition (Kilts, Egan, Gideon, Ely & Hoffman, 2003) or responding to pleasant stimuli (Herrington et al., 2005).

Additionally, all participants demonstrated similarly faster reaction times to happy faces, with participants within the sham group showing the fastest response when recognising angry faces. These findings present evidence against the second exploratory hypothesis of this study. However, this finding may be explained by the content-specificity hypothesis (Beck, 1976), which states that individuals demonstrate biases for information which endorses their underlying cognitions. Therefore, individuals with SAD require less information to recognise angry faces (Joormann & Gotlib, 2006), which may be the mechanism through which individuals within the sham group demonstrated faster reaction times, in comparison to participants within the stimulation groups which may be delayed by increased cognitive control exerted by tDCS and consequently less biased to angry faces. This is supported by the finding that participants who received PFC stimulation were better at discriminating strong fear faces (vs. sham and cerebellar), driven by reduced false alarms, with evidence to suggest amygdala sensitivity for fear stimuli (Fusar-Poli et al., 2009; Adolphs, 2008) which, when not inhibited by the dlPFC, may be the mechanism through which participants demonstrated increased errors in the identification of fear faces within the sham and cerebellar conditions.

2.4.1 Strengths

This study benefits from the utilisation of both active and sham control sites, in addition to a control task. Comparison against an active control site helps determine whether tDCS of distinct regional networks achieve selective effects on performance cognitive reappraisal. However, no selective effects have been revealed across analyses - instead effects of tDCS (vs. sham) were common across both cerebellar and PFC tDCS groups, in comparison to sham. This suggests that reappraisal might

be augmented by tDCS of cerebellar and PFC, or that non-specific tDCS is related to improvements in cognitive reappraisal, for example.

In addition to this, the methodology incorporated the use of a multi-site student consortium to support the recruitment of participants and increase generalisability across student populations and different laboratory settings.

Finally, the study benefits from the use of idiographic autobiographical reappraisal stimuli, which is specific to social anxiety and therefore more clinically valid when considering treatment for SAD (Buhle et al., 2014).

2.4.2 Limitations

There are also several limitations which should be considered when interpreting these results. Whilst participants received intensive training and live coaching in the completion of cognitive reappraisal and the results demonstrate that negative feeling was significantly reduced within the reappraise trials in comparison to neutral and react, it is not certain whether this is through the utilisation of cognitive reappraisal or other emotion regulation methods. To remedy this, Goldin et al (2014) utilised a self-report questionnaire at the end of their study to clarify strategies used. Alternatively, Kivity et al (2018) utilised an additional task condition of emotion suppression when completing an EEG investigation into cognitive reappraisal to allow for comparisons between emotion regulation strategies, improving validity of outcomes for the specific construct of cognitive reappraisal. This highlights the additional concern of self-report measures and the social desirability bias which may be present within individuals with social anxiety in particular (Schlenker & Leary, 1982). As discussed in chapter one, similar studies have utilised measures of social desirability to support the validity of self-report measures obtained.

In addition to this, whilst effort was made to include control stimulation neural sites and tasks, a non-socially anxious control group is absent from this methodology. Therefore, no conclusions can be made around the unique effects of neuromodulation for individuals experiencing symptoms of SAD, with no healthy comparison group. Whilst participant recruitment took place across two University sites, this study also utilised a relatively limited sample size and is consequently lacking in power, although sample sizes are in keeping with similar methods (e.g. Peña-Gómez, Vidal-Piñeiro, Clemente, Pascual-Leone & Bartrés-Faz, 2011). Additionally, the conduction of a large number of statistical tests further impacts on the power of this study and increases the chance of type 1 error. (Ranganathan, Pramesh & Buyse, 2016). Furthermore, the conduction of exploratory analyses should be interpreted with caution.

Finally, whilst this study provides a novel neuro-stimulation methodology to this area of research, there were some methodological issues when using the tDCS packs. Additionally, contact with the scalp was required to complete tDCS, which lead to the exclusion of participants with hair weaves, impacting on ethnic heterogeneity of the sample.

2.4.3 Clinical Implications

The findings present partial support for improved efficacy of cognitive reappraisal with tDCS, suggesting that neuromodulation of activity may support this key cognitive component of CBT when reappraising social anxiety NSBs. Therefore, this evidence contributes some understanding for the underlying neurophysiological mechanisms of cognitive reappraisal and CBT, from a neuro-stimulation protocol which has not been previously explored. Additionally, this suggests that individuals

with symptoms of SAD may benefit from increased cognitive reappraisal training to support reduced dlPFC activation.

The findings from participants emotion recognition support the Content-Specificity Hypothesis and contribute to literature around cerebellar and PFC involvement in social functioning; potentially identifying a neural mechanism for a negativity bias in SAD.

TDCS is a portable, painless, inexpensive and safe tool (Cohen, Levy, O'Shea, Shea & Savulescu, 2012) which may be utilised in supporting individuals with symptoms of SAD when attempting to cognitively reappraise salient NSBs and reduce negative bias, alongside therapeutic interventions.

2.4.4 Future directions

It is important for future research to recruit larger sample sizes and healthy comparison control groups across neuro-imaging studies, to obtain sufficient power to detect differences between groups. It will also be important to control for use of alternative emotion regulation strategies and consider the role of 'state dependency' in tDCS. Furthermore, the employment of SAD specific stimuli will be imperative to future studies within this area to ensure results are more clinically valid when investigating the neural underpinnings of cognitive reappraisal in SAD.

In addition to addressing the above limitations, future research could also explore the role of targeted tDCS in conjunction with CBT with individuals with a diagnosis of SAD, to further explore the clinical benefits on cognitive appraisal and bias.

2.4.5 Conclusions

In conclusion, the balance of evidence suggests that PFC and cerebellar stimulation improved cognitive reappraisal in comparison to sham in the first trial block; however, it is unclear if this is a direct result of cognitive reappraisal or emotion reactivity. The moderating impact of 'state' anxiety and mood across the course of the reappraisal task may account for cognitive reappraisal efficacy over time.

When recognising emotions, the evidence suggests that cerebellar and PFC tDCS improved recognition sensitivity for happy faces and increased reaction times to angry faces; with PFC tDCS also improving discrimination of fear faces. This provides evidence for a potential neural mechanism for negative bias in social anxiety which may be alleviated with PFC and cerebellar stimulation.

2.5 Appendices

2.5.1 Appendix A - The SPIN questionnaire

	Not at all	A little bit	Somewhat	Very much	Extremely
1. I am afraid of people in authority.	○	○	○	○	○
2. I am bothered by blushing in front of people.	○	○	○	○	○
3. Parties and social events scare me.	○	○	○	○	○
4. I avoid talking to people I don't know.	○	○	○	○	○
5. Being criticized scares me a lot.	○	○	○	○	○
6. I avoid doing things or speaking to people for fear of embarrassment.	○	○	○	○	○
7. Sweating in front of people causes me distress.	○	○	○	○	○
8. I avoid going to parties.	○	○	○	○	○
9. I avoid activities in which I am the center of attention.	○	○	○	○	○
10. Talking to strangers scares me.	○	○	○	○	○
11. I avoid having to give speeches.	○	○	○	○	○
12. I would do anything to avoid being criticized.	○	○	○	○	○
13. Heart palpitations bother me when I am around people.	○	○	○	○	○
14. I am afraid of doing things when people might be watching.	○	○	○	○	○
15. Being embarrassed or looking stupid are among my worst fears.	○	○	○	○	○
16. I avoid speaking to anyone in authority.	○	○	○	○	○
17. Trembling or shaking in front of others is distressing to me.	○	○	○	○	○

2.5.2 Appendix B – ASAS questionnaire

Autobiographical Social Anxiety Situations questionnaire (ASAS)

We would like you to recall 4 events in your life which you feel are characterised by social anxiety, humiliation and embarrassment. For each situation, please write a paragraph describing the events that occurred, your thoughts and feelings at the time, in addition to five negative self-beliefs (NSBs).

Negative Self Beliefs are self-representations we develop about ourselves and how others evaluate us, generated in social situations. Examples include 'I am weird' or 'Others do not like me'.

Please report your age at the time of each situation and provide ratings, on a scale of 1 (not at all) to 9 (very much), quantifying the vividness of the memory, the experience of shame at the time of the situation, as well as current shame, disturbance, avoidance and frequency of talking about the situation.

Event 1	**Age at time of event:**	

Event Ratings	**Not at All**								**Very Much**
Vividness	1	2	3	4	5	6	7	8	9
Shame at time	1	2	3	4	5	6	7	8	9
Shame now	1	2	3	4	5	6	7	8	9
Disturbance	1	2	3	4	5	6	7	8	9
Avoidance	1	2	3	4	5	6	7	8	9
Frequency of talking about this event	1	2	3	4	5	6	7	8	9

Negative self beliefs

Self	**Others**

Event 2	**Age at time of event:**	

Event Ratings	**Not at All**								**Very Much**
Vividness	1	2	3	4	5	6	7	8	9
Shame at time	1	2	3	4	5	6	7	8	9
Shame now	1	2	3	4	5	6	7	8	9
Disturbance	1	2	3	4	5	6	7	8	9
Avoidance	1	2	3	4	5	6	7	8	9
Frequency of talking about this event	1	2	3	4	5	6	7	8	9

Negative self beliefs

Self	**Others**

Event 3	**Age at time of event:**	

Event Ratings	**Not at All**								**Very Much**
Vividness	1	2	3	4	5	6	7	8	9
Shame at time	1	2	3	4	5	6	7	8	9
Shame now	1	2	3	4	5	6	7	8	9
Disturbance	1	2	3	4	5	6	7	8	9
Avoidance	1	2	3	4	5	6	7	8	9
Frequency of talking about this event	1	2	3	4	5	6	7	8	9

Negative self beliefs

Self	**Others**

Event 4	**Age at time of event:**	

Event Ratings	**Not at All**								**Very Much**
Vividness	1	2	3	4	5	6	7	8	9
Shame at time	1	2	3	4	5	6	7	8	9
Shame now	1	2	3	4	5	6	7	8	9
Disturbance	1	2	3	4	5	6	7	8	9
Avoidance	1	2	3	4	5	6	7	8	9
Frequency of talking about this event	1	2	3	4	5	6	7	8	9

Negative self beliefs

Self	**Others**

2.5.3 Appendix C - Emotion regulation questionnaire

1	2	3	4	5	6	7
Strongly disagree			Neutral			Strongly agree

1. ☐ When I want to feel more *positive* emotion (such as joy or amusement), I *change what I'm thinking about.*
2. ☐ I keep my emotions to myself.
3. ☐ When I want to feel less *negative* emotion (such as sadness or anger), *I change what I'm thinking about.*
4. ☐ When I am feeling *positive* emotions, I am careful not to express them.
5. ☐ When I'm faced with a stressful situation, I make myself *think about it* in a way that helps me stay calm.
6. ☐ I control my emotions by *not expressing them.*
7. ☐ When I want to feel more *positive* emotion, I *change the way I'm thinking* about the situation.
8. ☐ I control my emotions by changing the way I think about the situation I'm in.
9. ☐ When I am feeling *negative* emotions, I make sure not to express them.
10. ☐ When I want to feel less *negative* emotion, I *change the way I'm thinking* about the situation.

2.5.4 Appendix D –The PANAS questionnaire

1	2	3	4	5
Very Slightly or Not at All	A Little	Moderately	Quite a Bit	Extremely

_____ 1. Interested	_____ 11. Irritable
_____ 2. Distressed	_____ 12. Alert
_____ 3. Excited	_____ 13. Ashamed
_____ 4. Upset	_____ 14. Inspired
_____ 5. Strong	_____ 15. Nervous
_____ 6. Guilty	_____ 16. Determined
_____ 7. Scared	_____ 17. Attentive
_____ 8. Hostile	_____ 18. Jittery
_____ 9. Enthusiastic	_____ 19. Active
_____ 10. Proud	_____ 20. Afraid

2.5.5 Appendix E –The standard GAD-7 questionnaire

GAD-7

Generally how often have you been bothered by the following problems? Rate each word by drawing a vertical line (or a cross) on the DASH-LINE scale below each statement to indicate the extent you have felt that way.

FEELING NERVOUS, ANXIOUS OR ON EDGE			
Not at all sure	Several days	Over half the days	Nearly every day
| ..... |			
NOT BEING ABLE TO STOP OR CONTROL WORRYING			
Not at all sure	Several days	Over half the days	Nearly every day
| ..... |			
WORRYING TOO MUCH ABOUT DIFFERENT THINGS			
Not at all sure	Several days	Over half the days	Nearly every day
| ..... |			
TROUBLE RELAXING			
Not at all sure	Several days	Over half the days	Nearly every day
| ..... |			
BEING SO RESTLESS THAT IT IS HARD TO SIT STILL			
Not at all sure	Several days	Over half the days	Nearly every day
| ..... |			
BECOMING EASILY ANNOYED OR IRRITABLE			
Not at all sure	Several days	Over half the days	Nearly every day
| ..... |			
FEELING AFRAID AS IF SOMETHING AWFUL MIGHT HAPPEN			
Not at all sure	Several days	Over half the days	Nearly every day
| ..... |			

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2.5.6 Appendix F –The adapted GAD-7 questionnaire

GAD-7

During the last **20 minutes** how often have you been bothered by the following problems? Rate each word by drawing a vertical line on the scale below to indicate the extent you feel this way.

FEELING NERVOUS, ANXIOUS OR ON EDGE			
Not at all sure	Some of the time	Most of the time	All of the time
| ..... |			
NOT BEING ABLE TO STOP OR CONTROL WORRYING			
Not at all sure	Some of the time	Most of the time	All of the time
| ..... |			
WORRYING TOO MUCH ABOUT DIFFERENT THINGS			
Not at all sure	Some of the time	Most of the time	All of the time
| ..... |			
TROUBLE RELAXING			
Not at all sure	Some of the time	Most of the time	All of the time
| ..... |			
BEING SO RESTLESS THAT IT IS HARD TO SIT STILL			
Not at all sure	Some of the time	Most of the time	All of the time
| ..... |			
BECOMING EASILY ANNOYED OR IRRITABLE			
Not at all sure	Some of the time	Most of the time	All of the time
| ..... |			
FEELING AFRAID AS IF SOMETHING AWFUL MIGHT HAPPEN			
Not at all sure	Some of the time	Most of the time	All of the time
| ..... |			

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2.5.7 Appendix G – Cognitive Reappraisal Training Script

In the first task, you will be presented with your specific autobiographical events which you provided on the ASAS questionnaire, along with your reported negative self-beliefs and others created by our researchers.

At the beginning of each trial you will be instructed either to REACT or REFRAME the negative self belief (which will flash on the screen; white for react and green to reframe as a reminder). So what do we mean by that:

1. So when task asks you to REACT: this involves focusing on how the negative self belief reflects something true about yourself. Attend to and be aware of, but not to try to change, any feelings elicited by it. DO this for each negative self belief presented within the trial.
2. Alternatively, when you are instructed to REFRAME: this involves actively reframing the belief by thinking in a way that reinterprets the content of the belief and thereby make the belief less negative and toxic for you. Reinterpret the belief so that it no longer elicits a negative response. DO this for each negative self belief presented within the trial.

For example, if the belief is "NO ONE LIKES ME", REFRAMING may be telling yourself "That is not always true," "Some people like me", or "This is only a thought, not a fact." How else might you dispute this BELIEF?" This might involve focusing on the situational aspects of an event (i.e. only specific to this situation, but what about other times?).

However, when asked to reframe, it is important that you do not look away (unless completely necessary) or distract yourself with irrelevant and/or positive thoughts.

PRACTICE TRIALS

Have a go at the 2 practice trials which are in the same format as the first task. The first situation asks you to REACT and the second asks you to REFRAME. In the second set, you can have a go at generating *reframes* of the negative self-beliefs in these example situations. Verbally reinterpret the beliefs so that it no longer feels negative to you.

[2 situations – react or reframe on computer]

Researchers: you can speak to the participant throughout the practice trials. Explain that the negative ratings are for training purposes only in the practice trials – to get them familiar with the format of the task.

*1) After each/first few NSBs on the REACT trial – remind the participant of what they need to do "*focus on how the negative self belief reflects something true about yourself*"*

2) After each NSBs on the REFRAME trial - remind the participant of what they need to do and ask them to verbally say how they could reframe. Help as necessary – get them to give ideas. Give coaching and shaping to ensure that participants can reinterpret NSBs quickly and effectively.

EG1. reframing might be telling yourself "that is not always true" "I don't ALWAYS do the wrong thing, sometimes I do the right thing" or "This is only a thought, not a fact!"

Tip: What would you say to a friend if they told you they had this belief about themselves?

End: Do you have any questions?

Before starting testing trials:

Just do your best to reframe the belief when asked to do so, but it is difficult. So just report the strength of your negative emotion on the scale as ***honestly and accurately as possible, whether or not you feel that the reframe has been successful in changing the way you feel.***

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