Doctoral Thesis

A single-case series investigation of the efficacy of an internet delivered multi-session cognitive bias modification – interpretation task in a population with clinical levels of panic symptomatology.

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Abstract

Cognitive bias modification for interpretation bias (CBM-I) has been shown to successfully modify interpretative biases across psychological presentations including social anxiety, generalised anxiety and depression. Despite the role catastrophic misinterpretations of bodily sensations are thought to maintain with panic disorder, to date no study has sought to explore the efficacy of CBM-I with individuals with clinical levels of panic symptomatology. Six individuals (19 to 53 years old) with clinical levels of panic symptomatology, as measured by the panic disorder severity scale, completed an internet administered seven-session CBM-I training programme at home. A single-case series design was adopted in order to investigate the efficacy of the CBM-I training programme. Participants were randomised to a seven, nine or eleven day baseline control phase. Daily measures and outcome measures were completed. Visual analysis revealed that four of the six participants responded to the CBM-I training programme. Three participants made clinically significant and reliable change on a measure of panic, whilst four participants made significantly reliable change on a measure of anxiety sensitivity. Interpretation bias was assessed using the ranking and believability tasks of the Brief Body Sensations Interpretation Questionnaire. Four of the six participants showed a significant change in interpretation bias on the ranking task, whilst only two participants showed a change in interpretation bias in the expected direction on the believability task. The results indicate the potential clinical utility of CBM-I in reducing levels of panic symptomatology. These results need to be interpreted with caution due to the small sample size. Future areas for research are considered, with the potential for CBM-I to serve a preventative, as well as a therapeutic, function discussed.

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1.0 Chapter Introduction

This chapter aims to provide an overview of panic disorder referencing diagnostic criteria, prevalence rates, co-morbidity and a review of the catastrophic misinterpretation model of panic (Clark, 1986). The focus will be on interpretation biases in the experience of anxiety disorders and literature on cognitive bias modification training paradigms is also considered. The role imagery may have to play in the refinement of cognitive bias modification will be appraised. The role of imagery in the experience of anxiety disorders is discussed alongside evidence which suggests imagery and emotion maintain a 'preferential link'. Finally, the rationale to target panic symptomatology with a cognitive bias modification training paradigm is presented.

1.1. Panic Disorder

It is not uncommon for individuals to experience a sudden increase in their heart rate or occasional episodes of dizziness, however it is suggested that the meaning attributed to such bodily sensations can have a profound effect on the experience of these symptoms (Kamieniecki, Wade, & Tsourtos, 1997). That is to say, benign physical sensations can be the cause of sudden episodes of panic if interpreted in a maladaptive manner. This section will build on this assertion, considering the theoretical underpinnings of panic disorder, culminating with a review of Clark's (1986) Cognitive Model of Panic Disorder. The prevalence and co-morbidity rates of panic disorder are discussed, alongside the impact this observed co-morbidity has on suicidal ideation and intent. The extent to which the needs of individuals who demonstrate clinical levels of panic symptomatology are met is also considered.

1.1.2. Panic disorder: diagnostic criteria

It is not until relatively recently that panic disorder has been recognised as a psychological condition. For over a century, panic disorder was conceptualised as a psychopathological condition, a position which was reflected in research following distinct medical and psychological paths (Angst, 1998). It was not until 1987 when both the physical and psychological symptoms of panic disorder were defined by the Diagnostic and Statistical Manual Third Edition (DSM III; APA, 1987) that panic disorder was recognised in its current form. In its current iteration, panic disorder is characterised by recurrent and unexpected panic attacks (APA, 2000). The DSM-IV manual defines a panic attack as a period which consists of feelings of 'intense fear' or 'discomfort' in which four or more of thirteen physical and psychological symptoms develop. In order for a diagnosis of panic disorder to be given, these recurrent and unexpected panic attacks must be present with one or more defined consequences which relate to ongoing concerns regarding subsequent attacks, the repercussions of the attacks and a notable change in behaviour. To meet diagnostic criteria for panic disorder, an individual's panic attacks must not be a consequence of the physiological effects of a substance, medication or a given medical condition (APA, 2000).

1.1.3. Panic disorder: prevalence

Panic disorder is a highly prevalent anxiety disorder that is associated with significant impairment across the breadth of an individual's life domains. In the United Kingdom, the prevalence of panic disorder has been reported as amongst the highest in Europe, (King et al., 2008). Despite this claim, there is a level of reported variability between prevalence rates in the general population ranging from 1.1% (Skapinakis et al., 2011) to 10.3% (King et al., 2008). Notwithstanding this variability in overall prevalence rates, research has consistently reported a clear female preponderance of panic disorder, with women suggested as twice as

likely as men to suffer with the condition (Angst, 1998; Bijl, Van Zessen & Ravelli, 1998; Grant et al., 2006; Kessler et al., 2006; King et al., 2008).

It has been suggested that panic disorder is particularly prevalent within primary care settings, with prevalence rates being suggested as high as 13% (Craske et al., 2002). Despite this, traditionally the needs of individuals with panic disorder have not been well met within such settings, with a failure to appropriately recognise panic symptomatology highlighted as a significant mediator in this observation (Roy-Byrne et al., 1999; Roy-Byrne, Wagner, & Schraufnagel, 2005; Spitzer et al., 1994; Teng, Chaison, Bailey, Hamilton, & Dunn, 2008). It has been evidenced that individuals with panic disorder demonstrate increased levels of disability, more utilisation of accident and emergency services and a greater reliance on their GP comparative to other primary care patients (Roy-Byrne et al., 1999). Additionally, individuals experiencing panic disorder have been shown to have a higher incidence of substance abuse and social isolation (Klerman, Weissman, Oullette, Johnson, & Greenwald, 1991; Mitte, 2005; Tsao, Mystowski, Zucker, & Craske, 2005; Weissman, 1990).

1.1.4. Panic disorder: co-morbidity

Panic disorder is often co-morbid with a wide range of psychological disorders including other anxiety disorders, mood disorders, somatoform and pain-related disorders and personality disorders (Taylor, Asmundson, & Wald, 2007). It has been suggested that individuals who develop panic disorder are at a greater risk of developing depression, especially when panic disorder is present with agoraphobia (Skapinakis et al., 2011). Indeed, it has been suggested that major depressive disorder occurs in 50% - 65% of individuals with a diagnosis of panic disorder (Baldwin, 1998). The importance of this observation is apparent when exploring the relationship that this co-morbidity appears to hold with suicidal ideation and behaviour (Diaconu & Turecki, 2007). Individuals who can be considered to have a

'pure' diagnosis of panic disorder have been shown to be twice as likely as individuals with other psychiatric disorders, and 18 times more likely than a control condition to ideate about, or attempt suicide at some point in their lifetime (Weissman, Klerman, Markowitz, & Ouellette, 1989). When focusing purely on actual suicide attempts, individuals with 'pure' panic disorder have been shown to be five times as likely as controls to make an attempt to take their own life. When extending this to consider co-morbid panic, this figure is seen to rise to twenty-three times as more likely (Johnson, Weissman, & Klerman, 1990). When breaking this down further, people with panic disorder who ideate about committing suicide tend be younger than those who don't report any suicidal ideation (Borden, 1994).

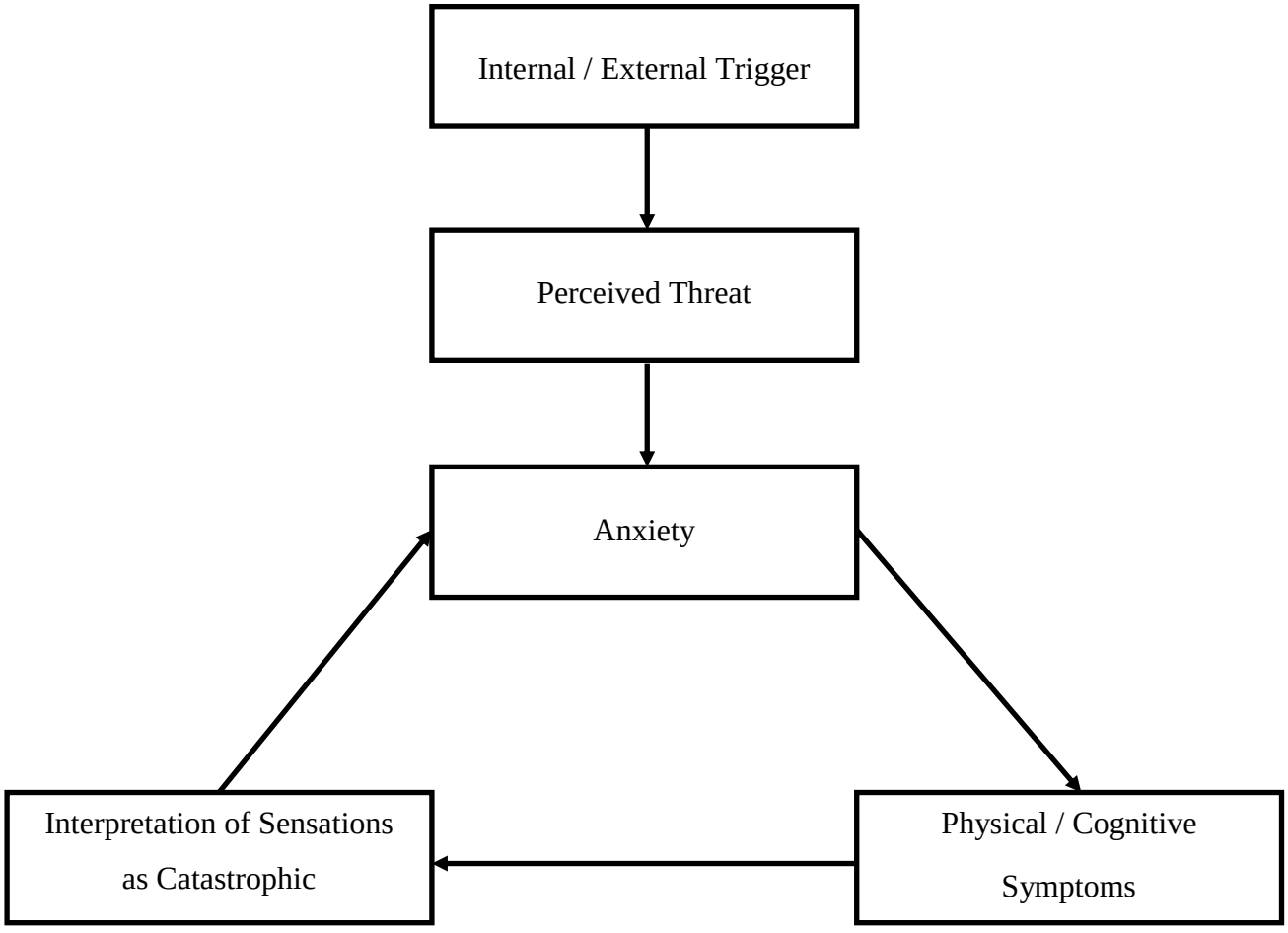
Whilst the figures pertaining to the presence of suicidal ideation and intent are clearly alarming, little is known regarding the mechanisms which underpin this relationship. One particular viewpoint has stressed the importance of the co-morbidity panic disorder shares with depression, suggesting that these two presentations serve to reinforce one another, subsequently impacting on levels of hopelessness (Noyes, 1991). Indeed, Diaconu and Turecki (2007) highlighted lower levels of functioning associated with co-morbid panic disorder and depression, which may in turn impact on levels of hopelessness.

1.1.5. Panic disorder: an overview of cognitive models

The precise aetiology of panic disorder is currently unknown; however there is a substantial body of evidence supporting a cognitive perspective on the disorder (Taylor et al., 2007). Cognitive theories (e.g., Beck, Emery, & Greenberg, 1985; Clark, 1986) posit that panic disorder is characterised by the catastrophic misinterpretation of interoceptive stimuli. Classically, an individual misinterprets a benign somatic sensation as an antecedent to an impending catastrophe (e.g., a heart palpitation may be interpreted as an impending heart attack). Clark's Model of Panic (1986; see Figure 1.1) suggests that the catastrophic misinterpretation of bodily sensations elicit and increase sympathetic arousal, which is then

interpreted by an individual as further evidence of impending catastrophe, with this feedback loop resulting in a panic attack. Clark's model is founded upon three core assumptions. The first states that individuals with panic disorder will make more harm related interpretations of ambiguous interoceptive stimuli relating to physical and psychological harm than non-anxious individuals. Secondly, Clark proposed that the catastrophic misinterpretation of bodily sensations was a unique characteristic of panic disorder. The third asserts that people with panic disorder maintain an interpretive bias towards internal stimuli but not for external events. The extent to which these assumptions are evidenced has implications for ones understanding of the aetiology, and subsequent treatment of panic disorder (Austin & Richards, 2001).

Figure 1.1 Catastrophic misinterpretation model of panic disorder (adapted from Clark, 1986)



To date a number of reviews have been undertaken to explore the level of empirical evidence that supports the central assumptions of the catastrophic misinterpretation model of panic disorder (Austin & Richards, 2001; Cox, 1996; Khawaja & Oei, 1998). Each review recognised substantial empirical support for the central role catastrophic misinterpretations maintain in panic disorder. These reviews have, in the main, centred on studies which are cross sectional in their design and rely upon the administration of questionnaires to infer the nature of catastrophic cognitions in participants. More widely, a lack of variation in methodologies used across studies poses a challenge when attempting to generalise findings (Cox, 1996; Khawja & Oei, 1998). The use of questionnaires is susceptible to confounding variables such as memory bias, with the completion of measures likely to be influenced by the emotional state of the participants (Dalgleish & Watts, 1990). Furthermore, this approach has been criticised as failing to capture the implied reflexive nature of catastrophic interpretations, as reflected in the cognitive model (Clark, 1986).

In light of the discussed focus on questionnaire-based methodologies, the following review aims to provide an up-to-date evaluation of the catastrophic model of panic disorder (Clark, 1986) encompassing a wider variety of methodological procedures. The review aims to evaluate whether there is a clear interpretive bias towards catastrophic outcomes for individuals with panic disorder when compared to non-anxious individuals, and whether this particular bias is specific to panic disorder.

1.1.6. Search protocol

Metlalib was used to search nine computerised databases, AMED, Cochrane Library, EBSCO, EMBASE, ERIC, MEDLINE, PsychINFO, Science Direct and Web of Knowledge. Metalib allows for the simultaneous search of multiple databases and was accessed through The University of East Anglia Network on the 3rd June 2014. The Boolean search terms used were Interoceptive Stimuli, Catastrophic Misinterpretation, and Panic Disorder. Interoceptive

Stimuli was also replaced with bodily sensations and body sensations. Catastrophic Misinterpretations was also replaced with interpret* bias. Truncation (*) was used in order to ensure all variant word endings were identified by the search. The search was supplemented by reviewing references of retrieved papers.

1.1.6.1. Selection criteria

Studies were included in the review if the primary aim of the study was to explore the tendency to catastrophically misinterpret interoceptive stimuli. Other inclusion criteria consisted of the need for the study to include quantitative analysis and to be published in English language peer-reviewed journals.

Papers were excluded from the review if they met a number of predetermined exclusion criteria. Papers that examined the role of catastrophic cognitions through the use of treatment programmes were not included in the review. Likewise, papers which focused on attentional rather than interpretive biases as their primary aim were excluded alongside papers that reported levels of catastrophic misinterpretations as a secondary aim.

The initial Metalib search resulted in 263 returned articles, which were subsequently combined into 198 articles. Following this, initial screening identified 12 potentially relevant articles. Subsequent screening of the articles abstracts identified 8 articles that met inclusion criteria. A hand review of suitable papers resulted in an additional 3 articles being included in the review. The selection criteria adopted resulted in the identification of 11 peer reviewed articles, summarised in Table 1.1.

Table 1.1

Summary of Studies Investigating the Catastrophic Misinterpretation Model of Panic Disorder (Clark, 1986): Grouped on Basis of Methodology

Reference	Aim	Participants	Data Collection	Main Findings
McNally & Foa (1987)	To examine the ways agoraphobics interpret ambiguous information.	N = 27 9 untreated agoraphobics 9 treated agoraphobics 9 nonanxious control	Interpretation Questionnaire, Subjective Cost Questionnaire, Subjective Probability Questionnaire	No group differences on narrow criterion of threat. Untreated agoraphobics made more threat related interpretations using broad criterion of harm ($p < .05$), and rated arousal related events as more costly ($p < .05$)than the other groups
Harvey, Richards, Dziadosz & Swindell (1993)	To clarify whether the catastrophic misinterpretation of internal stimuli is specific to PD	N=36 12 participants with PD 12 participants with SAD 12 nonanxious control participants	Interpretation Questionnaire	No group differences across narrow criterion of threat. Both PD and SAD groups more gave more catastrophic misinterpretations than controls when pooled over internal and external stimuli ($p < .05$). PD group gave higher threat ranking to internal stimuli than other groups ($p < .05$)
Kamieniecki, Wade, & Tsourtos (1997)	To examine whether people with PD misinterpret bodily sensations which are caused by nonanxious states	N=30 15 participants with PD 15 nonanxious participants	ISCNS, Ambiguous Stimuli Questionnaire	Harm related responses not included in analyses due to lack of responses. PD patients provided more anxiety related initial interpretations than control group ($p < .001$). PD patients provided greater costly anxious responses than controls ($p < .001$) but no sig. difference in threatening responses.
Clark et al. (1997)	To extend results of McNally & Foa (1987)and to further examine specificity of catastrophic misinterpretations to PD	N= 60 20 participants with PD 20 participants with other anxiety disorders 20 nonanxious control group	BSIQ	PD patients made more negative interpretations of bodily sensations than other groups ($p < .05$) using narrow criterion of harm, and also using the broad criterion of harm ($p < .001$). PD patients ranked negative explanations as more likely for internal stimuli than other groups ($p < .001$)

Richards, Austin, & Alvarenga (2001)	To investigate whether people at risk of developing PD demonstrate similar cognitive biases as those diagnosed with PD	N=114 20 participants with PD 25 participants with non clinical PD 69 nonanxious controls	BBSIQ	No significant group differences based on narrow criterion of threat. PD and non clinical PD participants made significantly more threat interpretations than controls on broad criterion of threat ($p < .01$). PD participants gave significantly higher threat ratings than controls ($p < .01$) but no observed difference with non clinical PD group
Austin & Richards (2006)	To replicate the results of Clark et al. (1997)	N=113 38 participants with PD 20 participants with NCP 21 participants with SAD 34 nonanxious controls	BSIQ-M	PD participants gave more harm related responses than NAC's on both initial interpretation and outcome response, and more than both NAC's and NCP's on the initial interpretation. PD group made significantly more harm interpretations than all groups on both measures using broad criterion of threat.
Austin & Kiropoulos (2008)	To examine whether people with PD make more catastrophic misinterpretation that nonanxious individuals, and indeed if this is specific to PD	N=88 30 participants with PD 28 participants with SAD 30 nonanxious controls	Internet administered BSIQ-M	PD group gave more harm related responses than NAC group on both initial interpretation and outcome response, and more than both the NAC and SAD groups on the outcome item using the narrow criterion of harm. On broad criterion of harm PD and SAD groups made significantly more harm related responses on both measures than the NAC group. No sig differences on response ranked task
Schniering & Rapee (1997)	To examine if individuals with PD are characterised by an enhanced tendency to associate benign somatic symptoms with catastrophic outcomes	N=75 47 participants with PD 28 nonanxious controls	Modified lexical decision task	No sig group differences at long SOA condition or short SOA condition

Schneider & Schulte (2007)	To investigate whether individuals with PD demonstrate stronger semantic priming effects that NAC's for ideographically selected targets	N=80 48 PD participants 32 nonanxious controls	Semantic Priming Task	No group differences with semantic priming scores at long ISI. PD patients demonstrated significantly higher priming for catastrophic targets at zero ISI p =.012
Hermans et al. (2010)	To examine whether PD is characterised by spontaneous catastrophic misinterpretations and if this is specific to PD	[1]N=86 31 participants with PD 25 anxious controls 30 nonanxious controls [2]N=70 20 participants with PD 20 anxious controls 15 professionals 15 non professionals	Semantic Priming Task	[1]Significant main effect of trial type in panic group (p <.0001). Shorter latencies for panic-panic trials. Similar priming effect not evident in anxious control group. Significant priming effect (p < .05) observed in nonanxious control group. [2]Both PD patients (p <.005) and mental health professionals (p <.05) responded significantly faster on panic-panic trials. There were no significant differences for both the anxious and non professional control group on panic-panic tasks.
Breitholtz, Johansson & Ost (1999)	To evaluate PD and GAD patients in relation to their self-reported cognitions	N=74 36 participants with PD 38 participants with GAD	Self Observation	Significant distribution of overall cognitions between the groups (p <.00001). PD patients had significantly more catastrophic cognitions than the GAD patients (p< .00001).

Note: PD = Panic disorder; ISCNS = Interpretation of sensations caused by nonanxious states; BBSIQ = Brief body sensations interpretation questionnaire; BSIQ = Body Sensations Interpretation Questionnaire; BSIQ-M = Body sensations interpretation questionnaire modified. Hermans et al. (2010) reported two pieces of researched denoted by [1] and [2].

1.1.7. Review of literature: is panic disorder characterised by an enhanced tendency to catastrophically misinterpret ambiguous interoceptive stimuli?

1.1.7.1 Questionnaire based studies

McNally and Foa (1987) examined the ways in which individuals with agoraphobia and panic disorder interpret ambiguous information and whether they make more catastrophic interpretations of internal information than non-anxious controls. Three questionnaires were adapted and used from earlier measures used by Butler and Mathews (1983). Participants were required to rate the negative valence, the subjective probability and subjective cost of a variety of events. Responses were coded using broad and narrow criterions of threat. The broad criterion of threat included cognitions such as "I'm going to panic"; whereas a cognition that is consistent with the narrow criterion of threat would be "I'm going to have a heart attack". In essence, the narrow criterion of threat was used to identify cognitions which identified a specific concern relating to physical or mental catastrophe. Those with untreated agoraphobia interpreted scenarios as more threatening than both treated individuals and non-anxious controls for the broad criterion of threat but not the narrow criterion of threat. Data from subjective cost and probability measures suggested that non-treated individuals were characterised by the enhanced interpretation of threat for events relating specifically to arousal. As with all self-report measures, the data obtained is subject to distortion through processes such as emotional bias and social desirability effects (Furnham & Henderson, 1982; Hirotsune & Kawahara, 2011). Despite this limitation, the conclusions offered by the authors provided general support for the catastrophic misinterpretation model of panic (Clark, 1986).

Harvey, Richards, Dziadosz and Swindell (1993) investigated whether the catastrophic misinterpretation of interoceptive stimuli was a process specific to panic disorder. The interpretation questionnaire as used by McNally and Foa (1987) was employed

to investigate catastrophic misinterpretations and was completed by individuals with panic disorder, social anxiety and a group of non-anxious controls. Individuals with panic disorder demonstrated an enhanced tendency to misinterpret ambiguous internal information, comparative to both socially anxious and non-anxious controls, for a ranked response task only. This task required participants to rank the likelihood of ambiguous internal information as coming to mind in various situations. Harvey et al. (1993) suggested the activation of relevant core schemas accounted for the observed differences in the ranked response task. That is to say, ambiguous information was presented that activated a given threat-related thought process in individuals. Strengths of this study including the rating of independent scores, one of whom was a clinical psychologist, who were blind to subject diagnosis adds clinical relevance to the conclusions drawn. However, a fundamental criticism is the non-exclusion of individuals with social phobia who previously experienced panic attacks (Clark et al., 1997). This criticism relates to the possibility that previous experiences of panic attacks could be consistent with a non-clinical presentation of panic symptomatology. As such catastrophic misinterpretations may be evident in this group questioning the specificity of this interpretation bias (Clark et al., 1997).

Clark et al. (1997) developed the Body Sensations Interpretation Questionnaire (BSIQ) in response to a number of criticisms of earlier measures. The BSIQ is a modified version of the Interpretation Questionnaire used by McNally and Foa (1987). Individuals are asked questions across four domains, panic body sensations, social items, general items and other symptoms. The criticisms which motivated the development of the BSIQ included an oversight of belief ratings and an over representation of anxiety related explanations in the ranked response task. In their study, the authors had three groups complete the BSIQ, a panic group, an anxiety control group and a non-clinical group. The authors found, using the BSIQ, that individuals with panic disorder were more likely to infer threat related interpretations of

interoceptive stimuli than individuals with social anxiety, generalised anxiety and non-anxious controls across both the narrow and broad criterions of threat. Furthermore, individuals with panic disorder ranked panic bodily sensation explanations as more probable than all other groups, as well as being more likely to believe these interpretations. A strength of this study focuses on the inclusion of participants with social anxiety and generalised anxiety. This enabled a more comprehensive assessment of the observed differences between panic disorder and other anxiety disorders (Austin & Richards, 2001). A potential weakness of this investigation is the ineffectiveness of the BSIQ in assessing the hypothesised automatic and reflexive nature of catastrophic misinterpretations (Schneider & Schulte, 2007).

Kamieniecki et al. (1997) investigated whether individuals with panic disorder misinterpret bodily sensations which are caused by non-anxious states. The Interpretation of Sensations Caused by Non-anxious States instrument (ISCNS) was designed to measure catastrophic misinterpretations. The ISCNS coded participant's response as overt explanations and covert explanations. Should a response be classified as covert, it was rated as 'anxiety-related', harm-related' or 'benign'. The ISCNS was administered to fifteen individuals with panic disorder and fifteen control individuals. Participants with panic disorder were unable to identify as many harmless explanations for bodily sensations as non-anxious controls, with no group differences being observed across groups on threatening interpretations. Harm related responses were not included in the analyses resulting from a lack of this type of response being provided. Kamieniecki and colleagues suggested that the lack of harm related responses was a consequence of the concise definition they attached to 'harm related'. This definition centred on recognition of a serious threat to an individual's physical or emotional well-being. This assertion has been challenged by Austin and Richards (2001) who noted that the criteria used by the authors to describe 'harm related' as lacking

clarity, alternatively citing the verbal presentation, as contributing to this lack of observed interpretation type. Furthermore, the results obtained by Kamieniecki et al., (1997) are limited by the only modest internal reliability of the ISCNS.

Richards, Austin and Alvarenga (2001) compared cognitive biases in the misinterpretation of ambiguous somatic sensations in individuals with panic disorder to a group who were considered at risk of developing panic disorder and a control group using the Brief Bodily Sensations Interpretation Questionnaire (BBSIQ; Clark et al., 1997). Individuals who were deemed to be at risk of developing panic disorder had experienced at least one spontaneous panic attack during the previous six months, but did not satisfy DSM-IV criteria for panic disorder. Inconsideration of the broad criterion of threat, both individuals with panic disorder and those at risk of developing panic disorder made more threat interpretations than non-panic controls on open ended questions. There was no significant difference observed across the two panic groups. However, on a ranked task the individuals with panic disorder rated internal panic related events as significantly more likely non-anxious controls to come to mind. The inclusion of a non-clinical panic group offers an additional theoretical dimension to ones understanding of panic disorder, alongside a clinical insight into potential preventative measures associated with panic disorder. It follows that should an interpretation bias be common in both individuals with clinical levels of panic symptomatology and those at risk of developing clinical levels of panic disorder, a single clinical intervention may be able to serve a therapeutic and preventative function.

Austin and Richards (2006) aimed to clarify the core assumptions of catastrophic misinterpretation model of panic disorder (Clark, 1986). They modified the BSIQ to include a follow up question in order to identify the underlying cognitions preceding an individual's initial interpretation. The modified BSIQ was administered to a group of participants with panic disorder, a group of participants with social anxiety and a non-anxious control group.

Individuals with panic disorder gave more catastrophic interpretations using the narrow criterion of threat than non-anxious controls only. However, it was found that individuals with panic disorder gave more harm-related interpretations than all other groups when based on the broad criterion of threat. Additionally, individuals with panic disorder ranked anxiety-related interpretations significantly higher than both the non-anxious controls and the socially anxious groups; no differences were observed between the panic and non-clinical panic groups. Individuals with a history of uncued panic attacks were excluded from the socially anxious group, which addresses a criticism of the sample employed by Harvey et al. (1993). Although, the study should be commended for the attempt to assess underlying cognitions, it is implausible to conclude that the inclusion of "And then what might happen" sufficiently achieves this. As such it would be unwise to conclude that this modification addresses this short fall in the BSIQ.

Austin and Kiropoulos (2008) aimed to further explore the core assumptions of the catastrophic misinterpretation model of panic disorder through the online administration of the BSIQ-M. Three groups were administered the online version of the BSIQ-M, a group of participants with panic disorder, a group with social anxiety and a non-anxious control group. When focusing on the narrow criterion of threat, individuals with panic disorder were shown to make more catastrophic initial interpretations and subsequent outcome responses than non-anxious controls. Differences between participants with panic disorder and all other groups, using the narrow criterion of threat, were evident on outcome items only. The results obtained by Austin and Kiropoulos mirrored those of Austin and Richards (2006) when exploring the broad criterion of threat. Internet administration of psychological questionnaires has demonstrated the potential to become an important means of gathering psychological information that is less susceptible to social desirability effects and is therefore feasibly more representative than traditional pen and paper measures (Buchanan, 2002; Fiegelson &

Dwight, 2000; Joinson, 1999). However, as both experimental groups consisted mainly of females, the extent to which the findings can be generalised is open to debate (Paul, 1967).

1.1.7.2 Semantic priming studies

Schniering and Rapee (1997) employed a semantic priming task in order to address the reflexive nature of catastrophic misinterpretation and to investigate whether or not such interpretations are apparent in panic disorder. In order to measure automatic and controlled processes involved in panic disorder, groups were required to make lexical decisions relating to neutral and threatening word pairs, across two time delay intervals. In this lexical decision task participants were required to determine whether words presented in the word pairs consisted of a proper English word. Although a significant facilitation effect was observed for the threatening word pairs, the effect was found to be equally strong across both the panic group and the non-clinical control group. That is to say, when presented with a threatening prime word, recognition of the target word was significantly quicker than for neutral word pairs for both groups. This observed effect was consistent across both time delay conditions. As such the conclusions made by Schniering and Rapee contradict the notion of a specific misinterpretation bias in panic disorder as the threatening word facilitated an effect across both groups. A strength of this study lies in its methodology as this addressed many of the biases which are associated with self-report measures (Schneider & Schulte, 2007).

Schneider and Schulte (2007) investigated whether individuals with panic disorder more strongly associated catastrophic outcomes with somatic sensations than a non-clinical sample. Participants were required to name catastrophic and neutral target words that followed primes sentences immediately or with a 1500ms delay. Consistent with Schniering and Rapee (1997), no differences were observed across the groups for semantic priming effects. However, participants with panic disorder demonstrated the expected stronger immediate semantic priming effects for catastrophic outcomes when using ideographically

selected stimuli. The outcome of this research suggested that whilst panic disorder is characterised by an increased tendency to misinterpret stimuli, the nature of these interpretations are highly idiosyncratic. The authors concluded that the experience of panic disorder and the cognitive errors which underlie this vary greatly and as such may not have been represented in the word pairs.

Hermans et al. (2010) explored whether panic disorder is characterised by the catastrophic misinterpretation of bodily sensations and whether this is a characteristic specific to panic disorder. In order to overcome the limitations of research based on verbal report, the authors used an associative priming procedure with three groups, a group of individuals with panic disorder, an anxious control group and a non-anxious control group. During this procedure participants were required to categorise words presented on a computer screen as 'words' or 'non-words'. These words included panic related words alongside neutral non-panic related words. Individuals with panic disorder demonstrated significantly shorter response times for panic control trials. Whilst a similar effect was not observed for the anxious control group, a significant panic priming effect was observed for the non-anxious control group. The authors speculated that this difference was due to the high proportion of mental health professionals contained within the non-anxious control group, hypothesising that these primes are strongly associated with their professional knowledge. The authors investigated this hypothesis by separating the non-anxious control group with both a 'professionals' non-anxious group and a 'non-professionals' control group. The results showed no significant differences in relation to priming effects for panic-panic trials suggesting that in certain cases groups maintain a bias similar to those seen in individuals with panic disorder. A particular strength of this piece of research is that the clinical participants were not actively engaged in a psychological intervention. Findings from CBT treatment studies into panic disorder have shown that cognitive interventions impact on the

extent to which individuals with panic disorder make catastrophic misinterpretations, (Casey, Newcombe, & Oei, 2005; Teachman, Marker, & Smith-Janik, 2008).

1.1.7.3 Self-report studies

Breitholtz, Johansson and Ost (1999) investigated whether individuals with panic disorder report more cognitions relating to physical and mental catastrophes than a sample of individuals with a diagnosis of generalised anxiety disorder. As part of a pre-treatment assessment, patients were asked to record experiences of panic attacks or heightened states of anxiety. Two independent observers, who were blind to the participants associated diagnoses, classified the reported cognitions using a pre-determined classification instrument. Individuals with panic disorder had significantly more cognitions relating to physical catastrophes in comparison to those generalised anxiety disorder, allowing for the conclusion that panic disorder is characterised by such catastrophic cognitions. The strength of methodology employed by the authors lies in the randomisation of cognitions and that the independent raters were blind as to diagnosis (Schmidt & Hunter, 1996). An omnipresent limitation of self-report measures lies in the potential that data are subject to distortion through extraneous variables such as desirability effects and emotional bias (Furnham & Henderson, 1982; Hirotsune & Kawahara, 2011).

1.1.8. Summary of literature review

This review proposed to evaluate the extent to which panic disorder is characterised by an enhanced tendency to catastrophically misinterpret interoceptive stimuli and whether this is disorder specific. As evidenced by this review, research has provided empirical support for the role, and specificity, of catastrophic misinterpretations in panic disorder (e.g., Austin & Richards, 2006; Clark et al., 1997). One of the main areas of discrepancy, as highlighted by this review, is the variation of results obtained by the studies across narrow and broad criterions of threat. That is, results based on the broad criterion of threat consistently

supported the core assumptions of Clark's (1986) cognitive model of panic disorder (e.g., Austin & Kiropoulos, 2008; Kamieniecki et al., 1997), whereas such a level of consistency was not observed across the narrow criterion of threat. Clark et al. (1997) suggested this discrepancy relates to the underlying cognitive content of anxiety responses, specifically anxiety responses mask catastrophic misinterpretations. More generally, McNally (1999) discussed this inconsistency as being reflective of the largely unfalsifiable nature of the catastrophic misinterpretation model of panic disorder. With this in mind, future research exploring the underlying cognitions in panic disorder would help to address this seemingly omnipresent criticism. Alongside this, consideration should be given to wider, subtle, issues including the nature of samples, such as their professional backgrounds and genders, and how this can markedly influence results as observed by Hermans at el. (2010).

The articles contained in this review offer a wide ranging evaluation of the catastrophic misinterpretations of bodily sensations in panic disorder. The results and conclusions discussed are susceptible to subtle variations in sample dynamics and procedural intricacies. In the main, the studies reviewed support the position that panic disorder is characterised by an enhanced tendency to catastrophically misinterpret somatic sensations and that this is a distinguishing attribute specific to panic disorder.

1.2. Cognitive Bias Modification for Interpretation (CBM-I)

As previously discussed, there is a substantial body of evidence supporting the central role of the catastrophic misinterpretation of interoceptive stimuli in the onset and maintenance of panic disorder (e.g., Austin & Richards, 2001; Cox, 1996; Khawaja & Oei, 1998). This section will consider and evaluate a growing body of evidence exploring the causality of interpretive biases more widely in anxiety disorders through the modification of such biases. The potential clinical value of interpretation modification paradigms is then considered within the context of panic disorder.

1.2.1. Causality of interpretation bias in anxiety disorders

The importance of interpretation biases has long been recognised by cognitive models of anxiety (e.g., Beck et al., 1985; Clark, 1986) with these biases often representing a target of cognitive interventions such as cognitive behavioural therapy (CBT; Grey & Mathews, 2000; Koster, Fox, & MacLeod, 2009). The importance of these biases is further substantiated when reflecting on the efficacy of the interventions which cite them as contributory factors to distress. Indeed, CBT has been shown to be an efficacious intervention for a wide range of psychological disorders (Butler, Chapman, Forman, & Beck, 2006).

Building on the causality of interpretation bias in anxiety disorders, Mathews and Mackintosh (1998) proposed a model of 'selective processing' in which it is suggested that incoming information is processed by competing evaluation systems. It is the role of these systems to categorise information as threatening or positive. Threatening information is screened by the 'threat evaluation system' (TES), whilst positive information is processed by the 'positive evaluation system' (PES). When incoming information is received, it is attended to and processed by both systems. The resulting emotional outcome is a consequence of an interaction between stored representations and prior experience. This interaction ultimately dictates whether the TES or the PES is activated. The activated system then becomes dominant suppressing the other system, strengthening a given emotional experience. It is proposed that individuals who are deemed to be susceptible to anxious states, process information that corresponds to information held within in the TES. The processing of this information by the TES then inhibits the PES, over time resulting in the strengthening of a threatening interpretation bias. Furthermore, it is suggested that this established interpretation bias becomes more sensitive to activation when presented with potentially ambiguous stimuli. The 'selective processing' model conceptualises the TES and the PES as competing processes. Mathews and Mackintosh suggest that by explicitly attending to the positive

attributes of received information at an early stage of processing, negative biases can be inhibited through the activation of the PES.

1.2.2. Cognitive bias modification for interpretation (CBM-I)

In order to provide evidence for their 'selective processing model', Mathews and Mackintosh (2000) developed a task called Cognitive Bias Modification for Interpretation (CBM-I), in which individuals were presented with a scenario which remained ambiguous until the final word which was presented as a word fragment. Participants were required to read each scenario before completing the word fragment. Upon resolution of the word fragment, the scenario is either valenced in a benign, positive or negative way. To ensure that participants understood the information presented to them in the scenario, they were then required to complete a comprehension question to verify their understanding. Participants were required to complete numerous scenarios, all of which were related to social threat, an example follows:

'*Your partner asks you to go to an anniversary dinner that their company is holding. You have not met any of their work colleagues before. Getting ready to go, you think that the new people you will meet will find you (bo___g or fri____y)'.*

Will you be disliked by your new acquaintances? (Mathews & Mackintosh, 2000).

Through the repeated presentation of ambiguous scenarios, it is proposed that interpretation biases in a given direction are able to be induced in individuals (Mathews & Mackintosh, 1998).

CBM-I provides a platform from which to investigate the amenability of cognitive biases to be modified or induced through the repeated exposure of a particular emotional

valence. It permits the measurement of change in emotion and the potential establishment of an interpretive bias in an individual. To establish causality between interpretation biases and anxiety, CBM-I needs to be successful in inducing given processing biases, and the effects this has on emotion quantified.

1.2.3. Cognitive bias modification for interpretation (CBM-I): analogue studies

Early research was conducted by Mathews and Mackintosh (2000) in order to further investigate the principles underpinning their 'selective processing' model. Initially, they reported findings from five different experiments. In the first of these experiments, an analogue sample was randomised to positive or negative text based CBM-I training. The authors employed a recognition test and a recognition time task to measure interpretation. The recognition time task measured the time it took participants to complete positive and negative word fragments. They found that individuals who were subjected to positive CBM-I training resolved positive word fragments quicker than participants who had been assigned to the negative training group. These results, paired with an observed change in anxiety in the expected direction, were identified as evidence of the causality interpretive biases in anxiety. Next, Mathews and Mackintosh removed the necessity for participants to complete word fragments in the training phase to investigate whether completing word fragments was necessary in observing change. Despite removing the need to complete word fragments, changes in interpretive bias were comparable to those elicited in experiment one. However, no changes in levels of state anxiety were evident. The authors then conducted a further three experiments focusing in part on the implications of 'active' training and 'passive' training. 'Active' training refers to the 'active' resolution of the word fragments, where as in 'passive' training individuals are presented with the emotionally valenced scenario in its entirety. In summary, these three experiments showed that the 'active' generation of relevant meanings was fundamental to the observation of changes in state anxiety. This active generation of

personally relevant meanings within CBM-I training has since been substantiated (Hoppitt, Mathews, Yiend, & Mackintosh, 2010). Of importance was the assertion that results of their studies were consistent with a causal link between an interpretive bias and emotion.

Yiend, Mackintosh, and Mathews (2005) explored the temporal characteristics and durability of induced interpretative biases. Yiend and colleagues demonstrated that induced interpretative biases, using the CBM-I, were durable over a 24 hour period within an analogue sample. Despite the significance of this finding, the authors highlighted the lack of a baseline measure of interpretation bias as a limiting factor in the extent to which conclusions could be drawn regarding the causality of interpretation biases in anxiety. The omission of a baseline measures raises questions regarding the potential performance of participants prior to completing CBM-I training.

Similarly, Mackintosh, Mathews, Yiend, Ridgeway, and Cook (2006) investigated the durability of interpretation biases in an analogue sample and the extent to which they survive changes in context. Participants completed CBM-I training in one of two groups, either via a computerised platform or through a pencil and paper format, accessed in a group setting. The effects of training were measured 24 hours following CBM-I training with all participants completing the pencil and paper group format. As such, half of the participants experienced a change in context between sessions. Mirroring Yiend et al. (2005), interpretation biases were found to persist for a period of at least 24 hours and additionally they were shown to survive changes in context. Furthermore, the authors demonstrated evidence of change in emotional vulnerability congruent with the training condition to which a participant was assigned. Mackintosh and colleagues summarised the importance of these results in relation to their clinical relevance, and the potential for CBM-I to be developed into a therapeutic intervention.

Whilst the studies discussed to date have sought to comprehend the impact CBM-I has on state anxiety, Mathews, Ridgeway, Cook and Yiend (2007) explored the effects CBM-I has on trait anxiety. Individuals who were considered to be 'high-trait anxious' were required to complete four sessions of positive CBM-I text-based training over a four week period. Following completion of the four sessions of CBM-I, individuals made more positive interpretations of novel descriptions compared to individuals in a control condition who did not receive CBM-I training. Additionally, it was observed that individuals who received CBM-I training demonstrated a significant reduction in trait anxiety scores when compared to the test-retest control group, with this effect observable at one week follow up. These results offer an important bridge highlighting the impact that CBM-I training has on state and trait anxiety. With this in mind, the authors provided further support to the causal role interpretation biases maintain with anxiety, and further hint at the potential clinical utility of CBM-I.

In a further study, Salemink, van den Hout, and Kindt (2007) examined the validity of the CBM-I paradigm. They proposed that tools typically used to measure interpretation bias in this field of research, the recognition task and the reaction time measure, were related to the training paradigm to such a degree that it may impact on observed outcomes. In expanding this point the authors highlight this closeness leads participants to be aware of the valence of their training condition and therefore potentially leading to confounding variables. As such, the authors included two additional measures of interpretation bias, one a homograph task, the second an open-ended questionnaire. The recognition task and a reaction measure were also included. When comparing positive and negative text-based CBM-I training, Salemink and colleagues found the positive training paradigm to be successful in changing interpretations when measured by the recognition and reaction time test only. Following positive training, participants demonstrated a reduction in trait and state anxiety

scores, with levels of state anxiety increasing following negative interpretation training. No changes were observed for the negative training condition. When using the additional measures of interpretation bias, no effects of the interpretation training were indicated. The authors suggested a number of reasons which may motivate this lack of observed bias. Firstly, the additional measures of interpretation bias lack the appropriate power to identify changes, with a subsequent power calculation confirming this suggestion specifically relating to the homograph task. With regards to the open-ended questionnaire, they discussed the potential for the measure to lack the sensitivity to identify a non-clinical interpretation bias owing to its development using a clinical sample. The authors highlighted the potential for higher baselines of anxiety, compared to those evidenced in Mathews and Mackintosh (2000), as a factor behind this lack of significant change.

In an attempt to explore the aforementioned, Salemink, van den Hout, and Kindt (2009) aimed to modify a negative interpretation bias in highly anxious individuals, and assess the impact this has on various clinical measures. Participants were randomised to either a positive CBM-I training condition or a control CBM-I training condition and were required to complete eight daily sessions of CBM-I. In an attempt to resolve some of the ambiguities brought by their previous research, the authors supplemented their research with a more comprehensive battery of measures which were completed pre and post-training. Reflecting the methodology adopted by Mackintosh et al. (2006), they included a stressor task as a means of measuring the effect CBM-I may have on emotional vulnerability. Participants who completed the positive CBM-I training were found to be less state and trait anxious than those individuals who received the control CBM-I training. Consistent with their previous research (Salemink et al. 2007), no bias was observed when using the open-ended questionnaire with this being attributed to the potential that CBM-I fails to impact on 'self-reported' interpretations.

Steinman and Teachman (2010) examined the role of negative interpretations in individuals with high anxiety sensitivity. This paper can be seen to be of particular importance within the context of the present study, due to the links anxiety sensitivity is believed to hold with panic disorder (Cox, Endler, & Swinson, 1995; McNally, 2002; Smits, Powers, Cho, & Telch, 2004). Anxiety sensitivity has been identified as a risk factor in developing clinical levels of panic symptomatology (McNally, 2002; Plehn & Peterson, 2002). Additionally, anxiety sensitivity has also been suggested as the mechanism that motivates Clark's (1986) vicious cycle of panic (Taylor, 1994). Participants were randomised to a positive CBM-I training condition or one of two control conditions in which participants received neutral CBM-I training or no training at all. Participants who received positive CBM-I training demonstrated a significant shift in interpretations of novel scenarios in the anticipated direction. Furthermore, participants assigned to the positive training condition demonstrated a reduction in levels of anxiety sensitivity. Based on the close links anxiety sensitivity is thought to maintain with panic disorder, the authors also included the BBSIQ as an exploratory measure of interpretation bias. Despite positive CBM-I training having no significant effect on the BBSIQ, a small to moderate effect size was observed in the anticipated direction. The authors suggested that the lack of significant effect may be due to the close proximity between pre and post administration of the measure. Whilst the results pointed to the potential of CBM-I to have clinical utility, there are a number of limitations that need to be considered. Firstly, as only the immediate impact of training was assessed, it is difficult to surmise the durability of the observed effects. Secondly, adopting multi-session CBM-I rather than the single-session methodology used would have enabled the authors to better determine the effects of training on emotional vulnerability (Steinman and Teachman, 2010).

1.2.4. Cognitive bias modification for interpretation (CBM-I): clinical samples

CBM-I research employing analogue samples has demonstrated that it is possible to induce interpretive biases in individuals (e.g., Steinman & Teachman, 2010; Yiend et al., 2005). Furthermore, this body of evidence suggested that by inducing a positive interpretation bias, levels of state and trait anxiety could be reduced (e.g., Mathews et al., 2007; Salemink et al., 2007). In order to assess the potential for CBM-I to be considered as a therapeutic tool, it is necessary to replicate these results using clinical samples. To date there has been an increasing number of studies exploring the effects of CBM-I training paradigms with a number of anxiety disorders. Studies exploring the efficacy of CBM-I training paradigm in those with clinical levels of depression is discussed in section 1.3.3.

1.2.4.1. Social anxiety

One of the first studies to explore the effects of CBM-I training within a clinical sample was conducted by Murphy, Hirsch, Mathews, Smith and Clark (2007) who examined the modification of interpretive biases in social anxiety. Participants were randomised to single-session positive, benign (non-negative) or control conditions. In a departure from the studies that have previously been discussed, the authors presented training scenarios aurally. Using a recognition task as a measure of interpretation bias, participants randomised to the benign training conditions (positive and non-negative) generated less negative interpretations of ambiguous social situations when compared to the control condition. Furthermore, participants who received benign training reported lower levels of anticipatory anxiety in relation to future social situations when compared to controls, as well as expectations of better social performance, although this trend was non-significant. Although speculative, the authors suggested that the acquisition of an interpretation bias impacts subsequent self-imagery, although this assertion requires further research.

Beard and Amir (2008) utilised a varied multi-session approach which comprised eight training sessions completed over a four week period. In a departure from the widely used test-based training paradigm developed by Mathews and Mackintosh (2000), Beard and Amir developed a task which required participants to determine whether a positive, benign or threat word related to an ambiguous socially orientated sentence. Following their responses, participants received feedback which was intended to reinforce a benign interpretation bias. Completion of the benign training task successfully decreased threat interpretation in participants. This decrease in threat related interpretation was accompanied with significant reductions in levels of trait anxiety, depression and social anxiety when compared to a control condition. In order to determine whether the change in interpretation bias mediated the change social anxiety, Beard and Amir conducted a mediation analysis using both threat and benign interpretations as potential mediators. The subsequent analysis revealed that the induction of a benign interpretation was a significant mediator in the reduction of reported levels of social anxiety, whilst change in threat interpretation bias was not. The authors concluded that whilst their findings suggest the induction of a benign bias and a reduction in threat bias may lead to reductions in social anxiety, it is unclear as to whether or not both types of bias need to be modified to elicit change in social anxiety. Additionally the authors cited the lack of long-term follow up, as impacting the extent to which the durability of the effects of training can be concluded.

To explore the feasibility and acceptability of CBM-I, Turner et al. (2011) adopted a single-case series methodology with six individuals recovering from first episode psychosis. Participants demonstrated clinical levels of social phobia as measured by the Structured Clinical Interview for DSM-IV-TR Axis I disorders (SCID; First, Spitzer, Gibbon, & Williams, 2002). Participants completed a computerised single-session CBM-I training session with mood and interpretation bias being measured pre and post-session. Following

CBM-I training participants engaged in a behavioural task which aimed to make them experience moderate levels of anxiety. The authors reported that following completion of CBM-I all participants reported an improvement in mood, with three participants evidencing a successful modification of negative interpretation bias. The extent to which the results of the study support the feasibility of CBM-I as a clinical intervention appears rather fragile in light of a number of limitations relating to the methodology. Firstly, a multi-session methodology would have been preferable to the single-session approach used in light of previous evidence (Beard & Amir, 2008; Salemink et al., 2009). Secondly, the in-vivo behavioural task assessing social anxiety may have skewed findings with the authors speculating the potential for this behavioural task to impact on interpretation bias. In light of these limitations, the extent to which the results of the study can be generalised is uncertain, although one can cautiously construe them as hinting to the potential feasibility of CBM-I as a clinical intervention.

1.2.4.2. Generalised anxiety disorder

Hirsch, Hayes, and Mathews (2009) randomised participants with high levels of worry comparable to generalised anxiety, to either a benign CBM-I training condition or a control condition. The authors assessed the results by use of a breathing focus task which required participants to categorise the emotional valence of cognitive intrusions. Participants who were randomised to the benign CBM-I training were shown to record fewer negative thought intrusions and greater residual working memory during the breathing focus task. Whilst the inclusion of assessor-rated measures strengthened the reliability of the study, the lack of an interpretation bias measure is a fundamental weakness of the methodology used. Consequently, conclusions relating causality cannot be made with any confidence, however it is important to note the encouraging impact that completion of the CBM-I training task had on the presentation of generalised anxiety.

In an adaptation of the methodology employed by the aforementioned study, Hayes, Hirsch, Krebs and Mathews (2010) included a measure of interpretation bias to explore causality. Mirroring the results obtained by Hirsch et al. (2009), participants who completed the benign CBM-I training task reported fewer negative cognitive intrusions than the control group. On the measure of interpretation bias, participants completing CBM-I successfully demonstrated an induced benign bias. When reflecting on causality, the authors suggested that the induced bias mediated the interaction between negative intrusions and the completion of the benign CBM-I training. Such suggestions offer evidence of the causation between interpretation biases and anxiety symptomatology, illustrating the potential for CBM-I to be developed into an efficacious clinical tool.

Moving the body of CBM-I research forward, Salemink, Kindt, Rienties, and van den Hout (2014) conducted a randomised controlled trial of CBM-I with individuals with a range of anxiety disorders including panic, social anxiety and generalised anxiety. Participants completed eight sessions of CBM-I training online, with a three month follow-up assessment included in the study. Individuals who were randomised to the positive training condition endorsed more positive interpretations, and less negative ones than a placebo control group. Interestingly, a reduction in anxiety, depression and overall psychological distress was present for both conditions. The authors highlight the potential for confounding variables relating to the accessing of CBM-I at home and the lack of specificity of disorder relevant training material as potential limiting factors to the observed effects of training. Additionally, the authors cite a lack of baseline measure of interpretation bias alongside a relatively small sample size which impacts on the ability to draw inferences regarding the causality of interpretative biases in emotion.

1.2.5. CBM-I research: what's next?

Research has demonstrated that interpretive biases can be induced in individuals and that said biases can be seen to impact on levels of state and trait anxiety (e.g., Mathews et al., 2007). A significant proportion of this research has focused largely on analogue samples to demonstrate the causality of interpretive biases in anxiety (e.g., Yiend et al., 2005). One of the most apparent research implications arising from previous research is the need to further extend the application of CBM-I training to clinical samples. When considering the potential clinical utility of CBM-I, it is important that future research continues to develop and expand upon earlier clinical studies (e.g., Hirsch et al., 2009; Turner et al., 2011) to include other anxiety disorders such as panic disorder. This shift towards a greater focus on samples with clinical levels of psychological distress will enhance and further validate the causal relationship interpretive biases are said to maintain with anxiety, whilst also enabling an appreciation of the potential clinical utility of CBM-I.

When contemplating the future of CBM-I research, it is important to consider how methodologies can be optimised and refined. A key variation across past research has been the number of CBM-I training sessions participants have been required to complete. This distinction has been split broadly into single-session CBM-I (e.g., Steinman & Teachman, 2010) and multi-session CBM-I (e.g., Beard & Amir, 2008). When comparing the efficacy of CBM-I, Hallion and Ruscio (2011) found that multi-session CBM-I demonstrated significantly larger effect sizes when compared against single-session CBM-I. Despite this observed difference between single-session and multi-session CBM-I, the construct of multi-session CBM-I is crude and lacks specificity. Future research which focuses on the optimum exposure to CBM-I training would serve a purposeful function in clarifying this position (Beard, 2011).

In moving towards demonstrating the clinical utility of CBM-I, the extent to which the effects of an induced bias are durable needs to be better understood. To date, a common omission from CBM-I research has been the lack of follow up point (e.g., Beard & Amir, 2008). Consequently, whilst well positioned to evidence the causality of interpretation bias in anxiety, research has largely failed to adequately demonstrate that these changes are durable. Future CBM-I research needs to address this shortcoming if CBM-I is to be seen as clinically beneficial. Similarly, the majority of CBM-I research has been based in the laboratory which restricts the extent to which observed changes are generalisable to more naturalistic settings. Future research is required to shift from its focus on laboratory-based analogue studies to naturalistic clinical studies in order to observe if changes are generalised to real-world contexts (MacLeod, Koster, & Fox, 2009).

1.3. Imagery, Emotion and Cognitive Bias Modification

This section will consider the link imagery is said to maintain with emotion and the evidence base upon which this link is founded. The importance of imagery in psychological disorders is discussed and considered. With reference to the importance of imagery in established psychological interventions, the potential for imagery to optimise CBM-I training will be evaluated. Research which has sought to determine the importance of imagery in CBM-I will be reviewed and discussed.

1.3.1. Mental imagery and emotion

Mental imagery can be considered to be a wide ranging construct encompassing a variety of processes which draw upon a number of neuronal pathways (O'Craven & Kanwisher, 2000). Despite this variability, mental imagery can be best understood as the recreation of perceptual experiences which can be seen to straddle sensory domains (Kosslyn, Ganis, & Thompson, 2001; Pearson, 2007). Indeed, mental imagery is underpinned by

neuronal processes which are similar to those activated by the initial perception of actual events (Holmes & Mathews, 2010).

Despite the complexities involved in the experience of mental imagery, it has been suggested that mental imagery and emotion maintain a 'preferential link' comparative to other processing modalities (Holmes, Mathews, Mackintosh & Dalgleish, 2008). A consequence of this 'preferential link' resides in the understanding that mental images induce more pronounced affective responses in comparison to relative verbal representations (Mathews, Ridgeway, & Holmes, 2013; Picet, Coughtrey, Mathews, & Holmes, 2011). Despite the potential clinical and research related importance of this held belief, empirical research supporting this assumption remains inadequate (Holmes & Mathews, 2005).

When aiming to better understand the mechanisms supporting this 'preferential link', Holmes and Mathews (2010) highlighted three relevant bodies of evidence. The first of these perspectives focuses on an evolutionary sensitivity between imagery and basic emotion. That is, the evolution of basic emotions preceded the evolution of more complex cognitive abilities. Ohman and Mineka (2001) suggested that emotional responses extend from systems which are relatively detached and protected from the influence of higher order cognitive processing abilities. A second body of evidence explores the link between imagery, perception and emotion and the overlap between these domains. Baddeley and Andrade (2000) demonstrated that simultaneous performance of a visuo-spatial and auditory task, negatively impacts on the vividness of visual and auditory image. Further evidence of such an overlap between cognitive processes emanates from research utilising neuro-imaging techniques (e.g., Cabeza & St Jacques, 2007; Ganis, Thompson, & Kosslyn, 2004; Kosslyn & Thompson, 2003; Sharot, Riccardi, Raio, & Phelps, 2007). Finally, the relationship between mental imagery, emotion and autobiographical memory is discussed. Conway and Pleydell-Pearce (2000) suggested that emotional events are stored in an individual's autobiographical

memory in the form of images, dictating that newly formed images are representative of such personally significant emotions.

When considering the multitude of pathways that mental imagery and emotion may interact with, it seems implausible to suggest that a single factor is responsible for the relationship mental imagery is said to hold with emotion. Whilst the very nature of this relationship remains unclear, it is apparent that mental imagery and emotion maintain a close, if not inextricable, relationship.

1.3.2. Mental imagery and psychological disorders

When considering the evidence detailing the link that mental imagery is believed to hold with emotion, it can be of little surprise that mental imagery is said to play a central role in a number of psychological disorders. One of the most researched psychological disorders in relation to imagery has been post-traumatic stress disorder (PTSD; APA, 2000). The driving force behind this focus on PTSD relates to imagery in the form of flashbacks constituting the hallmark of the disorder (Ehlers, Hackman, & Michael, 2004).

A second psychological disorder in which imagery is understood to be centrally implicated is social anxiety. Individuals with social anxiety typically perceive social interactions in which they may be judged or evaluated by others as anxiety provoking. Socially anxious individuals repeatedly report distressing and recurrent imagery of a past event (Hackman, Clark, & McManus, 2000) with the experience of said imagery represented in contemporary cognitive models of the disorder (Clark, 1999; Rapee & Heimberg, 1997).

Of interest to the present study is the role of imagery in panic disorder, although this area of research has been identified as lagging behind research into imagery and other anxiety disorders (McTeague, Lang, Laplante, & Bradley, 2011). Ottaviani and Beck (1987) investigated the nature of imagery in individuals with panic disorder. The authors noted that individuals with panic disorder described experiencing imagery that centred on physical and

mental catastrophes. Whilst, the imaginal ideation of danger is central to the maintenance of panic disorder, the extent to which these conclusions are relevant in the context of the current discussion is tentative. More contemporary research has utilised neuro-imaging techniques to explore the role of imagery in panic disorder. For example, Bystritsky et al. (2001) employed fMRI techniques to identify neural constructs associated with the experience of imagery in panic disorder. The authors concluded that individuals with panic disorder showed increased activity in a number of brain areas comparative to non-panic controls. It can be suggested that imagery has a powerful impact upon felt emotion within panic disorder and psychopathology more generally. When considering the effects mental imagery has upon emotion and the maintenance of psychological distress, it is important to consider the ways in which this relationship can be utilised in the treatment of such psychological distress (Holmes & Mathews, 2010).

1.3.3. Mental imagery and cognitive bias modification for interpretation (CBM-I)

One of the challenges facing CBM-I research moving forward focuses on how these paradigms can be optimised in order to further demonstrate their clinical utility. Increasingly, CBM-I research has sought to utilise the link mental imagery holds with emotion in this process.

Holmes and Mathews (2005) reported two experiments which sought to compare the effects of mental imagery focused interpretation training against verbally focused interpretation training. Experiment one aimed to test the hypothesis that self-generated imagery accounted for the outcomes observed by Mathews and Mackintosh (2000). Participants followed a comparative procedure to that employed by Mathews and Mackintosh, with the additional instructions to imagine themselves in the event, or to focus on the meaning of the words presented. The authors reported that individuals who imagined

themselves in the event reported greater increases in state anxiety than those participants in the verbal-semantic training condition. Similarly, emotionality ratings of ambiguous test descriptions also increased more in the imagery than in the verbal-semantic training condition. However, the focus on negative emotionally valenced effects overlooks the potential implications of imagery in the induction of a benign or positive bias. In responding to this shorting-coming, Holmes and Mathews reported a second experiment which included a benign training condition. As in the earlier study, the authors observed that negative valenced imagery resulted in greater increases in anxious mood than did comparative verbal processing. Despite the role of imagery on negative bias being replicated, no evidence of an effect of imagery versus verbal processing was found with benign training. The authors noted that the sample of participants used by the study may have not had sufficiently high levels of state anxiety for benign training to reveal any significant reductions.

Holmes, Mathews, Dalgliesh and Mackintosh (2006) focused on the effect of an overtly positive interpretation training paradigm on mood. A group of non-clinical participants were randomised to either an imagery or verbal processing positive CBM-I training condition. Participants allocated to the imagery focused group were required to image the positive scenarios, whilst participants assigned to the verbal processing group were instructed to concentrate on the verbal meaning of the scenarios. The authors found that participants who were assigned to the mental imagery group reported greater increases in positive affect and greater decreases in state anxiety than did those participants who were in the verbal processing condition. Despite the small sample size adopted by the authors, these results offer support for position that positive interpretation training can be enhanced through imagery as opposed to verbal-semantic processing.

Holmes, Lang and Shah (2009) reported two experiments using non-clinical participants which sought to test whether positive imagery CBM-I would extend to a

depressive bias. Firstly, participants were randomised to either an imagery focused or verbally focused CBM-I training condition. In line with previous research (e.g., Holmes et al., 2006), participants who completed imagery based CBM-I training demonstrated greater increases in positive mood and interpretive bias than those participants randomised to the verbal-semantic condition. Unexpectedly, individuals who received verbally focused CBM-I training indicated increases in anxiety over the training phase. When contemplating this unforeseen consequence of the verbal training condition, the authors stressed the importance of comprehending what aspect of verbal processing may have lead to an increase in anxiety. Consequently, Holmes et al. (2009) reported a second experiment which explored the hypothesis that participants were making unfavourable comparisons between the overtly positive training materials and their own personal experiences. The authors noted that increases in anxiety in additional verbal comparison conditions supported the hypothesis that comparative verbal processing contributed to the findings of the first experiment. The outcomes of this research suggested that imagery focused positive CBM-I may have clinical utility in the context of depressed mood.

More recently, the clinical utility of imagery focused CBM-I for depression has been substantiated through the use of multi-session interpretation training paradigms (Blackwell & Holmes, 2010; Lang, Blackwell, Harmer, Davison, & Holmes, 2012). Blackwell and Holmes (2010) sought to determine the clinical value of CBM-I by testing the impact completion of imagery focused training has on interpretation bias and depressed mood outside of a laboratory setting. Participants completed interpretation training at home daily for a period of seven days with depressive symptoms assessed at a two week follow up point. Of the seven participants included in the research, four demonstrated improvements in mood and bias, with these improvements being maintained at follow up. The authors noted that feedback provided by the participants highlighted the importance of providing a rationale to engage in what can

be perceived as a long a tedious task. This point has clear implications in the utilisation of CBM-I training. When focusing on the role of imagery, the authors reported that imagery coaching elicited a reduction in negative mood for one participant, although this improvement was not maintained when prompts were removed.

Lang et al. (2012) further enhanced the support for the clinical utility of a positive imagery-focused CBM-I task for those with clinical levels of depression. In their study, individuals with depression completed either seven daily sessions of positive imagery focused CBM-I or a control condition at home. For individuals completing the positive imagery CBM-I condition, the authors reported significant improvements between pre-intervention and post-intervention measures of depressive symptomatology, cognitive bias and intrusive symptoms compared to the control condition. Whilst the results reported provide further support to the clinical utility of computerised CBM-I tasks, the authors highlighted that the methodology adopted by the study does not enable inferences to be made with regards to the mechanisms of change underpinning the observed improvements. As a means of addressing this limitation, Lang et al. (2012) suggested the inclusion of a non-imagery control group in future research as a prudent measure.

Steel et al. (2010) reported on an imagery focused CBM-I training programme which aimed to treat anxiety in individuals diagnosed with schizophrenia. Participants were randomised to a single-session CBM-I training task or a single control session, with participants in the CBM-I condition receiving instructions to simulate the scenarios via mental imagery. Unexpectedly, participants completing the CBM-I training task did not demonstrate a reduction in state anxiety or change in interpretation bias. Despite this lack of observed change, the authors noted a significant positive relationship between participants rated use of imagery within everyday life and change in interpretation bias, suggesting that

those individuals who had a tendency or ability to engage in mental imagery were more amenable to an induced positive interpretation bias.

1.3.4. Clinical and research implications

It would appear that mental imagery has an important role to play in the optimisation of CBM-I training procedures. The inclusion of mental imagery within both negative and positive interpretation training has demonstrated greater changes in interpretation bias and emotion comparative to verbally focused CBM-I training (e.g., Holmes et al., 2009). Despite the potential benefits of imagery focused CBM-I there are a number of points which warrant consideration.

Whilst exploring the potential benefits imagery may hold in CBM-I training, a number of studies have found an increase in negative affect in certain training conditions (Holmes et al., 2006; Holmes et al., 2009; Standage, Ashwin, & Fox, 2009). In order to determine the effects of imagery on CBM-I training, research has typically sought to draw participant's attention to the semantics of a training scenario or to fully immerse themselves in the imagery associated with such tasks via auditory presentation of stimuli (e.g., Holmes et al., 2006). Holmes et al., (2006) highlighted the possibility that a focus on the semantics of a scenario may have proved arduous, the experience of which underpinning the observed change in mood. Seeking to determine the optimum methodology to enhance the effects of CBM-I training, Standage et al., (2009) compared the visual and auditory presentation of information. Assuming the importance of engaging in mental imagery, the authors instructed participants to imagine themselves in each scenario regardless of assigned training condition. They hypothesised that the auditory presentation of information would be preferable as it could be considered more conducive with the processing of information via mental imagery. Contrary to their hypothesis, they found that auditory presentation of information led to a deterioration in mood. When attempting to account for this unexpected observation, the

authors noted the increase in testing time associated with the auditory condition may have influenced the deterioration in mood. This point can be seen to hold important similarities with the assertion of Holmes and colleagues, that a task which is arduous in nature may temper, or even nullify, the potential benefits of CBM-I training. When considering this point clinically, it seems important that participants engaging in CBM-I training have the ability to control the pace at which they engage with the training task and that this can be best facilitated through the visual presentation of stimuli (Standage et al. 2009).

An important question to consider, when appreciating the potential role imagery has to play in CBM-I training, focuses on the ability or tendency for individuals to engage in mental imagery. Firstly, it is important to note that there are differences in the extent to which an individual is fundamentally able to engage in mental imagery. Indeed, neuro-imaging has highlighted a number of neural correlates with mental imagery ability (Cui, Jeter, Yang, Montague, & Eagleman, 2007). Furthermore, psychometric measures have been developed which have demonstrated their ability to measure various aspects of imagery such as vividness (VVIQ: Marks, 1973) and tendency (SUIS: Reisberg, Pearson, & Kosslyn, 2003). In order to position CBM-I training to fully utilise the preferential link mental imagery holds with emotion, it is vital that individual differences in mental imagery are comprehended. Indeed, the extent to which an individual engages in mental imagery in everyday life has been highlighted as a factor in the successful induction of an interpretation bias (Steel et al., 2010). Further work is needed to replicate the observation that the tendency for an individual to engage in mental imagery makes them increasingly amenable to CBM-I training paradigms. With this in mind, it is important for future research to consider whether an individual's ability or tendency to engage in mental imagery can be enhanced.

1.4. Rationale

Research has successfully demonstrated the ability for CBM-I training paradigms to successfully induce interpretive biases in both analogue and clinical samples (e.g., Blackwell & Holmes, 2010; Steinman & Teachman, 2010). Such is the promise of CBM-I training paradigms in impacting upon negative affect through the modification of negative interpretation biases, research has sought to investigate the potential clinical utility of such training programmes. To date, this increasing focus on clinical samples has assessed the effectiveness of CBM-I training with samples demonstrating clinical levels of social anxiety (Turner et al., 2011), generalised anxiety (Hayes et al., 2010) and depression (Blackwell & Holmes, 2010). To date, there have been no clinical studies specifically assessing the clinical effectiveness of CBM-I training in those presenting with clinical levels of panic symptomatology. This section will identify and discuss the theoretical underpinnings which may highlight panic symptomatology as a presentation which may be particularly amenable to CBM-I training.

1.4.1. Interpretive biases and panic disorder

The Cognitive Model of Panic Disorder (Clark, 1986) posits that the catastrophic misinterpretation of bodily sensations elicit and increase sympathetic arousal, which is then interpreted by an individual as further evidence of impending catastrophe, with this feedback loop resulting in a panic attack. When considering such interpretive biases in the treatment of panic disorder, it is beneficial to consider the mediators of change in established efficacious interventions such as cognitive behaviour therapy. Hofmann et al. (2007) highlighted the implementation of cognitive challenging techniques, which focus on catastrophic cognitions relating to physical symptoms, as a central component to the mediation of treatment change in CBT. Consideration of such evidence, underlines the potential clinical benefits of targeting such cognitive biases in those with clinical levels of panic symptomatology. It is the aim of

the present study to assess whether CBM-I is able to successfully modify these cognitive biases. Despite the theoretical suitability for panic disorder and those with clinical levels of panic symptomatology to be a suitable target for CBM-I, the author is aware of no research exploring the potential clinical utility of CBM-I with these populations. It is important that the current clinical evidence base pertaining to the clinical utility of CBM-I is expanded to consider other anxiety disorders such as panic disorder (Beard, 2011).

1.4.2. Anxiety sensitivity and panic disorder

Further support for the assertion that panic symptomatology represents a suitable target disorder for CBM-I training resides in the close link between panic disorder and anxiety sensitivity. Whilst there are no studies to date exploring CBM-I with panic disorder, completion of a single-session CBM-I training task has demonstrated its ability to modify interpretive biases in an analogue sample with high levels of anxiety sensitivity (Steinman & Teachman, 2010). Changes in anxiety sensitivity have been found to wholly mediate changes in panic related impairment following cognitive behaviour therapy (Smits et al., 2004). Additionally, completion of CBT for panic disorder, which has been deemed clinically successful, has resulted in lower levels of anxiety sensitivity (Otto & Reilly-Harrington, 1999). The constructs of anxiety sensitivity and panic disorder are clearly closely related and share a degree of overlap in the importance they place on fear of somatic sensations. The observation that CBM-I training can reduce scores of anxiety sensitivity after only a single session, further substantiates the rationale underpinning the application of CBM-I to a sample of participants demonstrating clinical levels of panic symptomatology. In continuing to demonstrate the clinical utility of CBM-I across anxiety disorders, the present study will explore the impact that completion of CBM-I training has on levels of anxiety sensitivity.

1.4.3. CBM-I and contemporary healthcare provision

Currently, CBT is recommended as the intervention of choice in the United Kingdom with access to psychological therapy gained through a stepped care approach (NICE, 2011). Furthermore, the treatment option of choice should be made accessible to the patient 'promptly', a point which can present a number of challenges. As a means of addressing this requirement to provide evidence based support in a timely manner, computerised CBT has been recommended in the treatment of depression and panic disorder (NICE, 2006). Indeed, computerised CBT has been described as an 'efficient treatment strategy', although low adherence rates have been identified (Gerhards et al., 2010). Building upon the success of computerised CBT programmes, CBM-I is required to demonstrate clinical utility in naturalistic settings with clinical samples if it is to be considered complimentary to current guidance. As such, the present study aims to assess the clinical effectiveness of an internet accessed multi-session CBM-I training paradigm with individuals experiencing clinical levels of panic symptomatology.

1.5. Aims of the Present Study

The present study aims to assess the effects of a CBM-I training paradigm with a sample of individuals with clinical levels of panic symptomatology. As a means of addressing the need for CBM-I research to take place with a real-world clinical setting, the present study will utilise an internet delivered CBM-I training programme enabling participant to access the paradigm in their own home. The methodology adopted by the presented study draws upon previous CBM-I literature in order to fully exploit the potential benefits of the CBM-I training paradigm.

1.6. Research Hypotheses

Hypothesis one: A seven-session internet administered CBM-I training programme will reduce levels of panic in individuals experiencing clinical levels of panic symptomatology, with these changes evidenced at follow up.

Hypothesis two: Individuals with clinical levels of panic symptomatology will demonstrate an increased positive interpretation bias following a seven-session internet administered CBM-I training programme, with these changes evidenced at follow-up.

Hypothesis three: Individuals with clinical levels of panic symptomatology will demonstrate a decrease in anxiety sensitivity following a seven-session internet administered CBM-I training programme, with these changes evidenced at follow-up.

Hypothesis four: Individuals who are better able to vividly imagine the training scenarios will evidence the greatest decrease in scores across outcome measures.

Chapter Two: Methodology

2.1. Chapter Introduction

This chapter outlines the methodology of the present study. It begins with a rationale of the study design alongside a description of the core features of a non-concurrent multiple baseline single-case series design. Next, a brief participant profile is presented and the inclusion and exclusion criteria are discussed. All screening and outcome measures adopted by the present study are then described and their psychometric properties considered. Finally, the procedure is described and the ethical considerations highlighted.

2.2. Design

The present study employed a single-case research design with follow-up (Barlow & Hersen, 1984). Single-case design methodology has been identified as a means of expanding and complementing the yield of a traditional quantitative research perspective (Kazdin, 2007). Additionally, single-case research design has been identified as being inimitably suited to appraising treatment effects with individual participants (Hayes, 1981; Kazdin, 1978). With the present study in mind, such a methodology offers an opportunity for researchers to appraise the efficacy of potential interventions which may be considered in their infancy. This opportunity has been reflected in a renewed focus on the role that single-case designs may play in the development and continued establishment of a scientific basis for psychological interventions (Kratochwill, 2007). With a specific focus on CBM-I, a number of studies have adopted a single-case design to evaluate the effectiveness of CBM-I paradigms across a variety of populations (e.g., Blackwell & Holmes, 2010; Turner et al., 2011).

A non-concurrent multiple-baseline across participants design (Barlow & Hersen, 1984) was used by the present study (see Figure 2.1). A multiple-baseline research design has been suggested as an appropriate, and potentially advantageous, methodology for evaluating

population based research (Hawkins, Sanson-Fisher, Shakeshaft, D'Este & Green, 2007). The basis for this assertion relates to the requirement of a smaller number of participants, in which each participant acts as their own control, (Hawkins et al., 2007). Indeed, as the design does not require a return to baseline level it can be considered ethically sound (Barlow, Nock & Herson, 2009). The inclusion of multiple baselines, allows for an appreciation of the specific effect of an intervention, through the introduction of participants to baselines of varying length (Kazdin, 2010). That is, if baseline changes are observed subsequent to the introduction of the CBM-I task, it is plausible to attribute this change to the completion of the CBM-I task, as opposed to any unaccounted variables (Kazdin & Kopel, 1975). Within the present study, participants were randomly allocated to varying baseline periods of seven, nine or eleven days.

Figure 2.1. Phases of multiple baseline design

2 Participants	Pre-Baseline Assessment	Baseline Assessment 7 Days	Pre-Intervention Assessment	CBM-I 1 Week	Post CBM-I Assessment	Follow up Assessment 1 Week		
2 Participants	Pre-Baseline Assessment	Baseline Assessment 9 Days		Pre-Intervention Assessment	CBM-I 1 Week	Post CBM-I Assessment	Follow up Assessment 1 Week	
2 Participants	Pre-Baseline Assessment	Baseline Assessment 11 Days			Pre-Intervention Assessment	CBM-I 1 Week	Post CBM-I Assessment	Follow up Assessment 1 Week

Watson and Workman (1981) summarised that the combination of varying baseline conditions and random assignment to groups bolsters the potential of a research study to demonstrate experimental control. Adherence to this suggested practice aids levels of experimental control and minimises threats to internal validity (Carr, 2005).

This research design offered a plausible and established means of contributing to the development of psychological interventions (Kratochwill & Levin, 2010). The non-concurrent multiple-baseline design provided a framework in which the present study could

be conducted in an applied setting (Christ, 2007). Furthermore, Salkovskis (1995) discussed the importance of single-case series designs in contributing to the development of psychological interventions. In his 'hourglass' model, Salkovskis highlighted that single-case research designs act as a precursor to larger scale research designs.

2.2.1. Randomisation

As highlighted by Watson and Workman (1981), an important consideration when aiming to bolster the experimental control of a study adopting a single-case research design methodology is the randomisation of participants to baseline conditions. Bolstering experimental control is suggested as a prudent step when employing a non-concurrent design (Christ, 2007). As a means of randomising participants to baseline conditions a random number generator was used. This random number generator was accessed online at www.random.org. The initial digits of the number provided by the website were used to determine the baseline condition of each participant using the following sequence; 1-3 to seven day baseline, 4-6 to nine day baseline, and 7-9 to eleven day baseline. In the event that all three baselines were allocated the initial digit was overlooked and the next digit used.

2.3. Participants

Participants were recruited from two main sources. Firstly, a number of participants were recruited from Primary and Secondary Mental Health Services situated within Cambridgeshire and Peterborough Foundation Trust (CPFT). In total seven NHS sites were made available for recruitment. Secondly, participants were recruited from the University of East Anglia after responding to an email advertisement.

2.3.1. Inclusion criteria

The inclusion criteria required participants to be at least 18 years of age at point of referral into the study. Participants needed to demonstrate clinical levels of panic symptomatology as determined by the Panic Disorder Severity Scale (PDSS; Shear, Brown,

et al., 1997). This was evidenced by obtaining a score of 8 or greater on the PDSS (Shear et al., 2001). Due to the high prevalence rates of panic symptomatology with other mental disorders, it was not a requirement of the present that panic was considered their primary diagnosis. Relating to this point, it has been suggested that people with uncomplicated panic disorder represents fewer than a third of the people who demonstrate clinical levels of panic disorder (Johnson et al., 1990). Participants were required to be considered stable on psychotropic medication (if prescribed) at study inception. Due to the nature of the CBM-I training tasks, participants were required to be proficient in reading and comprehending English, able to use a computer and access the internet to an appropriate level.

2.3.2 Exclusion criteria

Individuals who demonstrated severe clinical levels of depression by scoring above 19 on the Patient Health Questionnaire (PHQ 9; Kroenke, Spitzer, & Williams, 2001) were excluded from the study. Individuals who exhibited suicidal ideation at study inception were also excluded. Likewise, individuals who were considered to abuse substances were excluded from the present study due to the potential interaction this behaviour may have with the presentation of panic disorder (Cowley, 1992; Cox, Norton, Swinson, & Endler, 1990). Interventions such as cognitive behaviour therapy (CBT) have been shown to reduce interpretative bias in individuals with panic disorder (Westling & Ost, 1995). Consequently, whilst potentially seeking support, those receiving psychological intervention at the commencement of the study were excluded due to the potential for this to act as a confounding variable. Other exclusion criteria consisted of individuals with a known learning disability, traumatic brain injury and psychotic illness.

2.3.3. Recruitment of participants

The present study had initially hoped to recruit nine participants from Improving Access to Psychological Therapies (IAPT) teams located within CPFT. Previous studies

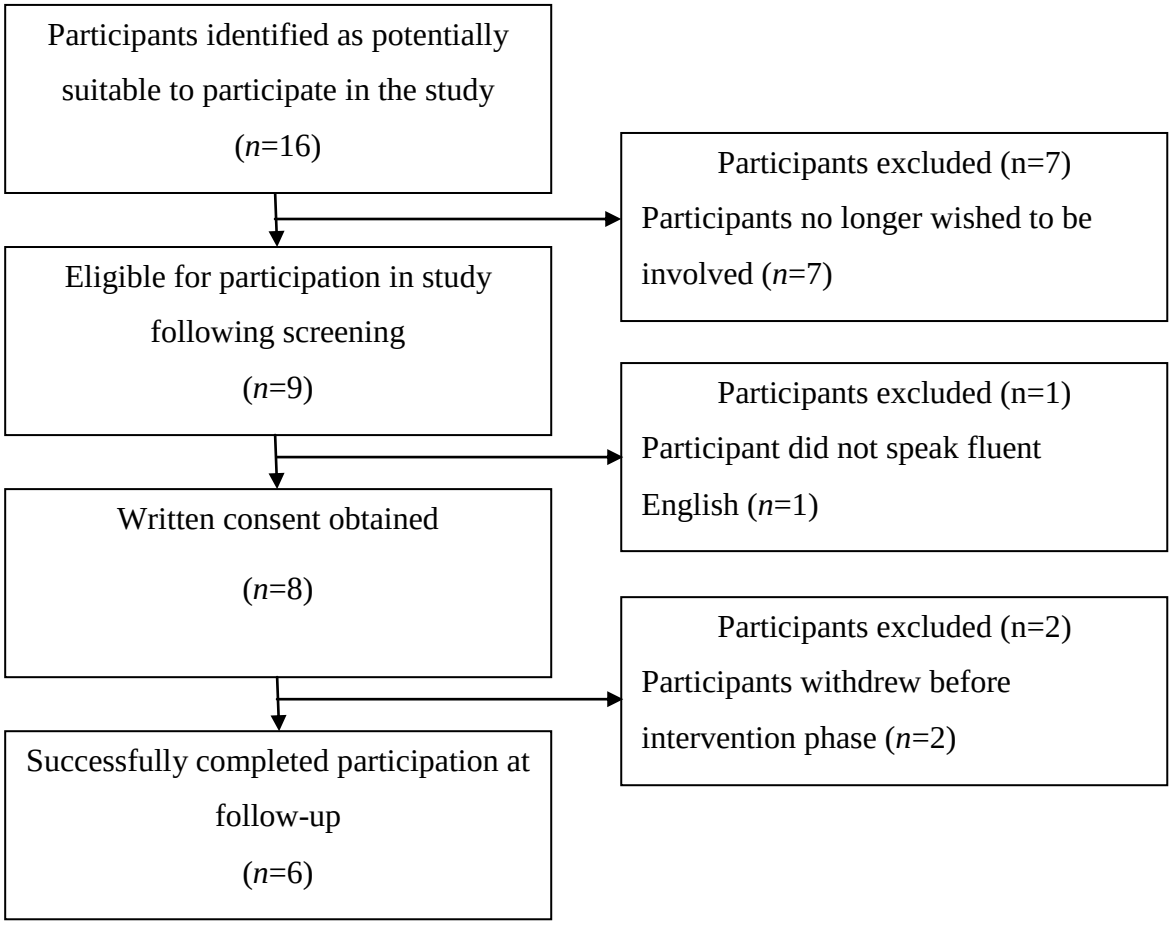
exploring the efficacy of CBM-I using single-case series methodology have utilised sample sizes between six and nine participants (e.g., Blackwell & Holmes, 2010; Turner et al., 2011). At the time of recruitment, mental health services within CPFT were subject to a major redesign with many members of staff uncertain about the future of their jobs. Given the context against which recruitment was set, the author made attempts to make the identification and referral of potential participants as least demanding as possible for clinicians. Throughout recruitment clinicians were asked to identify individuals they believed may have panic symptomatology at initial assessment or if an individual was being 'stepped up' to receive a higher intensity psychological intervention. The process of recruitment, as accepted by the ethical committee (see Appendix A), required referring clinicians to gain verbal consent from a potential participant to be contacted by the researcher. The researcher would then complete all screening measures in order to determine eligibility criteria had been met. Team meetings were attended with this referral process re-affirmed and channels of communication set-up. In total five IAPT services covering the whole of CPFT were utilised as recruitment sites. As recruitment progressed through its first two months a total of two potential participants were referred from across the five recruitment sites. In an attempt to boost recruitment, additional secondary mental health services were set up as recruitment sites. Despite this, recruitment continued to be problematic. Due to time constraints experienced by the researcher due to the present study forming part of a Doctorate in Clinical Psychology qualification, a change to the original ethical approval was sought. Subsequently, a substantial amendment (see Appendix B) was made in order to recruit from the staff and student population at the University of East Anglia. It should be emphasised that all participants recruited from the University of East Anglia met the same criteria as those referred from NHS services. Equally, all participants could be considered help-seeking as they were accessing support from their GP at the time of their participation.

2.3.4. Sample size

As a consequence of challenges with recruitment, six participants were recruited to the present study. In total sixteen individuals were identified as potential participants for the study. Of these sixteen, ten were identified through mental health services embedded within CPFT and six individuals responded to an email advertisement disseminated to students and members of staff at the University of East Anglia. Of these sixteen individuals, eight withdrew before written consent was obtained, and a further two individuals withdrew after completing the baseline phase. For a diagrammatic representation of the flow of participants through the study see Figure 2.2.

Despite the challenges faced with recruitment (see Appendix C for a recruitment timeline), the recruitment of six participants was in line with previous studies exploring the efficacy of CBM-I through the use of a case series design (e.g., Turner et al., 2011). A sample size of six participants has been highlighted as a sufficient sample size to adhere to the requirements of the design (Kazdin, 2010). Whilst not accessing support through a mental health service at the time of their participation in the present study, all participants recruited from the University of East Anglia were currently under the care of their GP for their ongoing difficulties with panic symptomatology.

Figure 2.2. Participant flow diagram



2.3.5. Participant demographics

The six participants who successfully completed all phases of the present study had an age range of 19 to 53 years, with a mean age of 34.8 years (*SD = 11.8*). The sample was comprised of four males and two females. Three of the six participants were referred from mental health services, with the remaining three participants responding to the email advertisement sent out to all staff and students at the University of East Anglia.

2.3.6. Participant profiles

2.3.6.1. Participant one

Participant one was a 19-year old male with a four year history of panic symptomatology. He was referred to an Adult ADHD service where he was assessed for symptoms of inattention and distractibility. It was felt that these symptoms were a

consequence of ongoing difficulties with anxiety rather than ADHD. He explained experiencing frequent panic attacks when leaving the family home. This had led to him becoming socially isolated having dropped out of college. His scores on the PDSS were consistent with a *moderately ill* clinical description.

2.3.6.2. Participant two

Participant two was a 30-year old male with a six year history of panic symptomatology. He was referred to an IAPT service after presenting to his GP with concerns his symptoms of panic were becoming more problematic. Participant two spoke of his particular concerns relating to his heart-rate and how this often triggers panic attacks. Recently, his symptoms of panic were resulting in him spending less time socialising with friends. His screening score on the PDSS indicated *slight* illness, although participant two noted his symptoms had been unusually minor during the preceding seven days.

2.3.6.3. Participant three

Participant three was a 53-year old male with a five year history of panic attacks. He was recruited to the study after he responded to an email advertisement. He reported experiencing panic attacks across different contexts. Participant three reported a difficulty in tolerating feelings of faintness and a rapid heartbeat. Participant three reported that he was awaiting a referral to be made to his local psychology service, with his current difficulties managed primarily by his GP. His screening score on the PDSS suggested an individual that was *markedly ill.*

2.3.6.4. Participant four

Participant four was a 40-year old woman who was referred following an assessment with her local IAPT service. She noted that she has experienced symptoms of panic for a period of six years. She stated that she avoided various situations to manage her panic

symptoms and wanted to change this. Her screening score on the PDSS was consistent with a *moderate* presentation of panic disorder.

2.3.6.5. Participant five

Participant five was a 27-year old woman who responded to an email advertisement. Although not currently on the caseload of her local psychological service, participant five manages her mood with psychotropic medication for which she is under the care of her GP. Participant five reported frequent panic attacks across various contexts over the past three years. She reported particular concerns that she will faint when experiencing a panic attack. Her screening score on the PDSS was consistent with a *slightly ill* profile of panic disorder.

2.3.6.6. Participant six

Participant six was a 39-year old man who self-referred to the study after responding to an email advertisement. Participant six highlighted that he was due to access privately funded person centred counselling in the coming weeks, and wished to pursue his participation in the present study prior to this. Participant six is under the care of his GP in relation to his ongoing psychological difficulties. He explained that he struggled to tolerate various bodily sensations, which would result in frequenting and distressing panic attacks. Participant six's screening score on the PDSS suggested an individual that was *markedly ill.*

2.4. Measures

Please see Table 2.1 for an outline of the measures adopted by the present study at the time points that these measures were administered.

Table 2.1. *Measures used by Present Study with Time Points when Administered*

Measure	Time point administered
BSI	Screening
PHQ 9	Screening
PDSS	Screening, Pre-Baseline, Pre-Intervention, Post-Intervention, Follow-up
PDSS Daily	Daily throughout baseline and intervention phases
BBSIQ	Pre-Baseline, Pre-Intervention, Post-Intervention, Follow-up
ASI	Pre-Baseline, Pre-Intervention, Post-Intervention, Follow-up

2.4.1. Screening and eligibility measures

The measures discussed below were used in order to determine the eligibility into the study.

2.4.1.1. Patient Health Questionnaire (PHQ 9; Kroenke, Spitzer, & Williams, 2001)

The PHQ 9 (see Appendix D) was used as a means of assessing levels of depression and is a widely used measure both within primary care and within a research context (Kroenke & Spitzer, 2002). The PHQ 9 is a self-report questionnaire assessing depressive symptoms as defined by the DSM-IV over the previous two weeks. The PHQ 9 is the depressive sub-scale of the Patient Health Questionnaire (Spitzer, Kroenke, & Williams, 1999). It consists of nine items which are scored on a four point scale ranging from 0 to 3; *not at all, several days, more than half the days and nearly every day.*

The PHQ 9 was administered mainly over the telephone, following consent being obtained by clinicians for the researcher to contact potential participants. An advantage of using the PHQ 9 in a research context centres on a completion time of approximately one minute (Kung et al., 2013).

The PHQ 9 can be seen to serve two functions. Firstly, the PHQ 9 focuses on the screening of depression in a given population and has shown strong psychometric properties across a number of domains. For example, Cameron, Crawford, Lawton, & Reid (2008) reported high internal consistency for the PHQ 9 when administered to primary care patients, both at baseline and at the end of treatment (α .83 and α .92). Furthermore, the PHQ 9 demonstrated superior 'operating characteristics' compared to the Hospital Anxiety and Depression scale (Zigmond & Snaith, 1983) and the Well Being Index (WHO, 1998a) when screening for major depression (Lowe et al., 2004). The PHQ 9 algorithm for major depression has indicated good sensitivity (73%-91%) and high specificity (89%-94%) when compared against a mental health professional (Spitzer et al., 1999). Secondly, the PHQ 9 enables clinicians and researchers to monitor change over time. The PHQ 9 has been shown to demonstrate high responsiveness to change in individuals being treated for depression (effect size 0.99) (Cameron et al., 2008).

2.4.1.2. Brief Symptom Inventory (BSI; Derogatis, 1993)

The BSI (see Appendix E) was used as a screening tool to assess co-morbidity of psychiatric disorders and has been identified as an effectual screening tool for differentiating across psychiatric disorders (Derogatis, 1983). The BSI enables profiling on nine independent dimensions, somatisation, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism (Schwannauer & Chetwynd, 2007). The measure takes approximately 10 minutes to complete.

As previously stated, panic disorder is often characterised by its co-morbidity with other mental health disorders (Johnson et al., 1990). Therefore, it was appropriate that the nature of this co-morbidity between participants was understood and appreciated. The BSI is a shorter version of the widely used Symptom Checklist-90-R (SCL-90-R; Derogatis, Rickels & Rock, 1976). The BSI comprises of 53 items which are designed to assess severity of

psychological problem during the past week. The items are rated on a 5 point scale of distress (0-4), *not at all, a little bit, moderately, quite a bit and extremely.*

Derogatis (1993) reported good levels of internal consistency from the original manual across the nine subscales (α = .71 to α = .85).These results have since been replicated by Schwannauer & Chetwynd (2007) who reported levels of internal consistency across a sample of 'GP attenders' and across a 'clinical psychology' sample. Within the 'GP attenders sample', levels of internal consistency were lowest for the 'paranoid ideation' dimension (α = .71) and highest for the dimensions of 'obsessive compulsive', 'depression', 'anxiety' and 'phobic anxiety' (α = .87). Within the 'clinical psychology sample' level of internal consistency were lowest for the 'paranoid ideation' dimension (α = .81) and highest for the 'depression' dimension (α = .91).

Convergent validity for the BSI has been established through analysis of the correlations between the clinical scales of the Minnesota Multiphasic Personality Inventory (MMPI; Dahlstrom, 1969), the Wiggins content scales of the MMPI (Wiggins, 1966), the Tyron Cluster Scores (Tyron, 1966) and the nine separate domains of the BSI. The SCL-90-R has demonstrated excellent convergent validity with the MMPI (Derogatis et al., 1976). Despite convergent validity being evidenced through significant correlations (r =0.30 to r = 0.72), the BSI can be considered to lack specificity due to the number of correlations between its scales which are considered independent of one another (Nezu, Ronan, Meadows & McClure, 2000). Nevertheless, the BSI offers a useful and important insight into the clinical presentation of the participants (Lam, Michalak, & Swinson, 2005).

2.4.1.3. Panic Disorder Severity Scale (PDSS; Shear et al., 1997)

The PDSS (see Appendix F) is a seven-item scale designed to assess overall levels of severity of panic disorder symptoms, (Lam et al., 2005). Clinician-administered and self-report versions of the PDSS are both widely used within research and clinical settings

(Wuyek, Antony, & McCabe, 2011). For the purpose of the present study, the use of the self-report PDSS scale was adopted. This version has been highlighted as an appropriate scale to measure treatment progress and is widely used within IAPT services as an outcome measure (IAPT Data Handbook, 2011; Keough et al., 2012). The PDSS consists of seven items which are coded on a 5 point ordinal scale ranging from 0 to 4; *none, mild, moderate, severe and extreme* (Shear et al., 1997). A cut-off score of 8 has been identified as a suitable screen for diagnosis-level symptoms of panic disorder (Shear et al., 2001). More recently evidence-based guidelines for interpreting scores have been published (Furukawa et al., 2009). The PDSS represents seven different indices, frequency of panic attacks, distress during panic attacks, panic-focused anticipatory anxiety, avoidance of agoraphobic situations, avoidance of panic-related physical sensations, and impairment in social and occupational functioning (Lam et al., 2005).

The PDSS served two main purposes within the present study. Firstly, the PDSS was administered as a screening tool to identify potential participants who met the central inclusion criteria of clinical levels of panic symptomatology. Secondly, the PDSS served the function of being a primary outcome measure, enabling the researcher to measure change in panic symptomatology over time. Completion of the PDSS takes less than 5 minutes.

Houck, Spiegel, Shear, and Rucci (2002) reported excellent levels of internal consistency for the self report version of the PDSS ($\alpha = .917$). This was comparable to levels of internal consistency reported for the clinician administered PDSS ($\alpha = .923$). The self report version of the PDSS also demonstrated good test-retest reliability (ICC = 0.81), which was broadly comparable to the value obtained for the clinician administered PDSS (ICC = 0.83).

Concurrent validity has been evidenced through significant correlations between items on the self report and clinician administered versions of the PDSS (Houck et al., 2002).

Each of the questions contained in the PDSS were found to correlate highly with one another ($r \geq .69$), except for question five (interoceptive fear / avoidance) ($r = .59$). When considering the total scores obtained by each version of the PDSS, a high intra-class correlation coefficient ($r = .81$) suggests that the self report version of the PDSS is a reliable format which has applications in both clinical and research contexts (Houck et al., 2002). Differences were identified between the mean total score of the two versions, with participants completing the self report measure scoring 2 points less than the clinician administered version (Houck et al., 2002). However, a number of potential factors limit the extent to which one can assume that a different cut off point is warranted by the self report version of the PDSS. Houck et al. (2002) discussed the potential for interviewer over-rating and the difference in the time-frame of the two formats to impact on this observed outcome. With this is mind, the present study maintained the original cut off score of 8 (Shear et al., 1997) when screening for clinical levels of panic.

2.4.2. Outcome and daily measures

All outcome and daily measures adopted by the present study were self-reporting and administered in a paper format. Measures were required to be completed daily across the baseline and intervention stages of the present study. The individual application of each measure will be discussed below.

2.4.2.1. Panic Disorder Severity Scale (PDSS; Shear et al., 1997)

Full details for this measure are contained in section 2.4.1.3. As discussed, the PDSS rates overall panic symptomatology severity in individuals over a seven day period. Within the present study the PDSS was completed daily, offering a profile of panic symptomatology over a 24 hour period. Participants were instructed to answer the questions in relation to their experienced symptomatology over the previous day, rather than the previous week. The seven indices contained within the PDSS enabled a wider appreciation of the impact of the CBM-I

task across various domains of panic disorder. Although, the PDSS is not a validated as a daily measure, it was deemed suitable due to the construct overlap it maintains with a validated panic diary (De Beurs, Chambless & Golstein, 1997).

2.4.2.2. Anxiety Sensitivity Index (ASI; Reiss, Peterson, Gursky, & McNally, 1986)

The ASI (see Appendix G) was used in the current study as an outcome measure to assess levels of anxiety sensitivity in participants. Anxiety sensitivity has been described as maintaining a close relationship to the catastrophic misinterpretation of interoceptive stimuli as evidenced in panic disorder (Cox et al., 1995; McNally, 2002). Lam et al. (2005) noted that in excess of 100 peer-review articles have demonstrated a link between high anxiety sensitivity and panic disorder. The ASI is a 16-item self-report measure designed to assess an individual's fear of anxiety-related symptoms centred on beliefs pertaining to their potential to bring about harmful consequences (Peterson & Heilbronner, 1987). Items are rated on a scale ranging from 0 (very little) to 5 (very much), with a total score ranging from 0 to 64 derived from the sum total of all items. The inclusion of the ASI in the present study was mainly exploratory in nature, given the links anxiety sensitivity maintains with panic disorder. Completion of the ASI takes fewer than 5 minutes.

The ASI has been identified as a psychometrically sound instrument for measuring response to treatment in patients with panic disorder (Lam et al., 2005). Peterson & Heilbronner (1987) reported high levels of internal reliability ($\alpha = .88$), whilst test-retest reliability ranging from .71 to .75 (Reiss et al., 1986) has been demonstrated. Factor analysis revealed a single factor structure, in which 13 of the 16 items had a loading of 0.4 or greater on the first factor (Reiss et al., 1986). Scale items are identified as interrelated to a 'fairly high degree' ensuring that the ASI reliably measures a coherent factor (Reiss et al., 1986). Furthermore, the ASI appears to offer an unmatched contribution to the prediction of fear-

related symptoms (Peterson & Heilbronner, 1987) and is considered a valuable measure in the present study.

2.4.2.3. Brief Body Sensations Interpretation Questionnaire (BBSIQ; Clark et al., 1997)

The BBSIQ (see Appendix H) was used to measure participant's interpretation bias. The BBSIQ is a short measure of interpretation bias, which is based on the Body Sensations Interpretation Questionnaire (BSIQ; Clark et al., 1997). The BBSIQ consists of 14 items in which participants are presented with ambiguous scenarios. Half of the items contained in the BBSIQ relate to external threats, such as social situations, whilst the remaining items pertain to bodily sensations. Completion of the BBSIQ takes approximately 5 minutes.

Following the presentation of each ambiguous event, participants are asked 'why?', and are then required to record the first thing that comes to mind. After completing their written response participants are asked to rank three possible explanations to disambiguate the scenario. One explanation is always negative, whilst the other explanations are either positive or neutral (Steinman & Teachman, 2010). Once participants complete all open-ended responses and ranking for each item, they are asked to go back and rate the extent to which they would believe each of the three alternative explanations offered for each scenario (Clark et al., 1997). Belief was rated on a scale of 0 – 8, with 0 being representative of 'not likely at all' and 8 corresponding to 'extremely likely to be true'. For the present study participants were required to complete only the ranking and belief rating panic related elements of the BBSIQ. This is in line with other research utilising the BBSIQ as an interpretation measure in CBM-I research (Steinman & Teachman, 2010).

An example of a bodily sensation item on the BBSIQ is:

"You notice that your heart is pounding, you feel breathless, dizzy and unreal, why?"

a. You have been overdoing it and are overtired (neutral)

b. Something you ate disagreed with you (neutral)

c. You are dangerously ill or going mad (negative)

Clark et al. (1997) reported alpha coefficients for each of the scales contained within the BBSIQ. Satisfactory internal consistency was reported for panic body sensation rankings ($\alpha = .86$) and panic body sensation belief ratings ($\alpha = .90$). Concurrent validity was established through comparison with a number of other validated measures, namely the Agoraphobic Cognitions Questionnaire (ACQ; Chambless, Caputo, Bright & Gallagher, 1984) and the State subscale of the Speilberger State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch & Lushene, 1970). Bodily sensations scores were found to correlate significantly ($r = .49$, $p < .001$) with those for the ACQ Physical Concern Factor, but not with those for the ACQ Social-Behavioural Consequences factor, or those for STAI State or Trait Anxiety subscales (Clark et al., 1997). Test-retest validity is rather variable, with ranking data demonstrating satisfactory reliability (.73 to .75), however more variance is observable for the belief rating with reliability ranging from poor to good (.48 - .81) (Clark et al., 1997). Sensitivity to change was evidenced by correlating changes in panic composite with changes in negative interpretation rankings ($r = .33$, $p < .05$) and belief ($r = .35$, $p < .05$). As can be evidenced, the BBSIQ demonstrates satisfactory psychometric properties. In addition to its satisfactory psychometric properties, the BBSIQ is considered a suitable measure of interpretation bias for the present study due to the close alignment it holds with the catastrophic misinterpretation model of panic disorder (Clark et al., 1997).

2.4.2.4. Visual Analogue Scales – Panic Disorder (VAS)

Visual analogue scales (see Appendix I) were used as a means of obtaining an efficient and repeatable measure of subjective levels of distress associated with a number of panic related symptoms. Visual analogue scales have been widely used within anxiety disorder focused research owing to their suitability for frequent and repeated use (Tiplady, Jackson, Maskrey & Swift, 1998). Typically visual analogue scales consist of a ten centimetre line anchored at either end with maximal and minimal extremes of the dimension being measured (McCormack, Horne & Sheather, 1988). The visual analogue scales used in the present study were presented in this way and developed in relation to the DSM-IV diagnostic criteria for panic disorder. Visual analogue scales were completed by participants daily throughout the baseline assessment and intervention phases of the study. The four visual analogue scales in the present study aimed to evaluate the distress experienced by participants in relation to their bodily sensations, feelings of unreality, feelings of losing control and a feeling that they are going to die.

2.5. Cognitive Bias Modification (CBM-I) Training Materials

2.5.1. Cognitive bias modification: interpretation (CBM-I) scenarios for panic disorder

The CBM-I training materials used adhere to the original text based format as used by Mathews and Mackintosh (2000), in which participants learned to attribute negative or positive interpretations to various ambiguous scenarios. The aim was to evaluate the efficacy of a CBM-I training programme to train participants towards a more positive or benign interpretation of ambiguous scenarios relating to panic disorder. A small proportion of the scenarios used were taken from a study exploring the modification of interpretation biases in anxiety sensitivity (Steinman & Teachman, 2010). Additional scenarios were produced in line with diagnostic criteria for panic disorder as outlined in the Diagnostic and Statistical

Manual 4th Edition (DSM-IV; APA, 2000). All bodily sensations represented in the diagnostic criteria for panic disorder were equally represented in the additional scenarios. These additional scenarios adhered to the format as advocated by Mathews and Mackintosh (2000). All additional scenarios were checked by the primary supervisor of the present study and a fellow researcher investigating the efficacy of a CBM-I programme with another anxiety disorder to ensure scenarios related to the DSM-IV criteria for panic disorder (APA, 2000). Participants were required to complete 50 training tasks each day, over a seven day period. These tasks were presented to participants in blocks of 10, with the option to take short break in between these blocks. The training tasks presented over the course of the intervention phase were all unique and were not repeated, in order to manage potential training biases. The CBM-I programme was accessed through a designated webpage, with each participant receiving a personal username and password. Additionally, guidance was built into the CBM-I training programme to support participants in navigating the training programme.

Prior to the commencement of each days CBM-I training session, participants were required to complete an imagery exercise. During this exercise participants were required to explore an imaginary scenario, paying particular attention to the sensory elements of this picture. Participants are then required to provide a vividness rating of the image they formed of the imagery task. Additionally, participants were instructed to visualise themselves within each individual training scenario that they are presented with. The inclusion of imagery in this way is consistent with current studies exploring the efficacy of CBM-I paradigms (e.g. Blackwell & Holmes, 2010).

The following is an example of an imagery task taken from the present study:

Example Imagery Task

Close your eyes and imagine that you have just cut a fresh, juicy lemon in half.

Now imagine lifting it to your noise and have a smell.

What does it smell like? Now take a bite and suck the juice.

What does it taste like? What feelings do you get in your body?

Training scenarios were four lines in length, and were intended to remain emotionally ambiguous until the last word. Each scenario was disambiguated by the completion of the final word fragment. This resolution determined whether the scenario was valenced in a positive or benign direction. Participants completed the word fragment by typing the missing letter on their keyboard. Following this, a comprehension question that was designed to ensure that participants understood the associated scenario was administered. The following is an example of a training scenario taken from the scenarios used within the present study:

Example scenario

Whilst at a charity dinner you buy a number of raffle tickets to win

a holiday of your choice. The speaker announces the raffle is set to

begin. You check your tickets and suddenly start to sweat heavily.

You are sweating as you are

e x _ i t e d (excited)

Do you think sweating is dangerous?

Yes (incorrect) No (correct)

Completion of the daily CBM-I session took approximately 45 minutes to complete.

2.6. Ethical Considerations

Prior to contact being sought with any potential participants, ethical approval was granted by the proportionate review sub-committee of the NRES committee North-East – Newcastle and North Tyneside 2. Approval for the present study was also gained from the CPFT research and development department (see Appendix J).

2.6.1. Consent

When a potential participant had been identified by a clinician embedded within an NHS service, the clinician provided an overview of the present study and a brief description of what taking part in the study would entail. Following on from this, clinicians sought verbal consent for the researcher to contact potential participants in order to conduct screening measures. This was clearly documented in the patient notes held by the referring service. The chief investigator then contacted potential participants over the telephone to complete various screening measures and to ensure inclusion criteria had been met. Verbal consent to contact potential participants was not required for individuals recruited from the University of East Anglia as these individuals made initial contact with the researcher. If inclusion criteria had been met, a patient information sheet was mailed to potential participants (see Appendix K) that contained a detailed account of the present study and a follow up appointment arranged. This appointment would take place no fewer than 72 hours following receipt of the patient information sheet. It was during this meeting that written consent would be sought, before initial outcome measures were completed by participants. Participants were informed that they could withdraw from the study at any time and that participation in the study would not impact on their care as usual.

2.6.2. Confidentiality

Participants were informed that all personal data and information would remain confidential. Participants were informed as to the process and location of their data. Data

were anonymised and participants were assigned a ‘participant code’ to help maintain confidentiality. Data were stored in secure locked cabinets, and will be stored for five years before being safely destroyed. All procedures regarding the confidentiality of information obtained by the present study were guided by the Data Protection Act (http://www.dataprotection.gov.uk) and British Psychological Society (BPS) guidelines (British Psychological Society, 2005).

2.6.3. Impact of research

The application of CBM-I training programmes in both non-clinical (Mathews & Mackintosh, 2000) and clinical (Turner et al., 2011) samples has demonstrated encouraging results whilst maintaining participant wellbeing. Consequently, it is not believed that any harm would come to participants taking part in the present study. In the improbable event that a participant became distressed during the training programme they were encouraged to take a break from the task in the first instance. Should distress continue, a referral would be made to the participants GP or to the service that referred them into the present study. Where possible the researcher negotiated with participants a set time where they would be available to be contacted should any difficulties arise during the completion of the daily training tasks.

Due to the varying baseline lengths required by the design adopted by the present study, participation in the study ranged from 21 to 25 days. This was carefully managed with the participants who were referred from NHS services to ensure that treatment as usual was not impacted.

2.7. Procedure

Subsequent to ethical approval being granted, meetings were arranged with IAPT teams located within CPFT. The purpose of these meetings was to provide an overview and rationale of the present study and to consider recruitment protocol. As discussed, clinicians embedded within services identified potential participants, obtaining and documenting verbal

consent to be contacted by the researcher. Lines of communication were established to enable the passing of this information. Alongside this, an email advertising the study was included in the staff and student e-bulletin at the University of East Anglia (see Appendix L).

Potential participants who were identified by clinicians embedded within mental health services were verbally given an overview of what participation in the research would involve. Once consent to be contacted had been gained, the researcher contacted potential participants by telephone to complete screening measures and to ensure eligibility. The participant information sheet was forwarded to those meeting eligibility criteria and a face-to-face meeting was arranged for a time no fewer than 72 hours following receipt of the information sheet. For potential participants who responded to an email advertisement, a participant information sheet was emailed and screening measures completed via email, prior to a face-to-face meeting being sought.

During the initial face to face meeting the researcher sought to gain informed consent (see Appendix M) for the participation in the study. Once informed consent had been obtained, the researcher completed the participant details sheet with each participant. Participants were then randomly allocated to a baseline condition (7, 9 or 11 days). Participants prescribed psychotropic medication at study inception, were requested to inform the researcher of any changes to this during their participation in the study. During this initial meeting the researcher completed both the PDSS and the ASI with each participant. Paper copies of daily measures (VAS and PDSS) were given to participants, and email or text reminders set up if requested. The PDSS and VAS's were completed daily throughout the baseline condition.

Once participants completed the baseline length to which they were assigned, the researcher met with them again to complete the outcome measures once more. In addition to

the outcome measures at the beginning of the baseline phase, the researcher completed the BBSIQ with participants to obtain an initial measure of interpretation bias.

Participants were given a unique username and password and directed to a website that hosted the CBM-I training programme. The researcher met with participants at their home to guide them through their first training session consisting of 50 training scenarios. This was in order to familiarise them to the CBM-I training programme. During this socialisation process, time was dedicated to the completion of an imagery exercise and the rationale for the use of imagery reaffirmed. Participants were required to complete one training session per day for seven consecutive days. During this period, the daily measures were completed by participants. As in the baseline phase, reminders were arranged if requested by participants. Where possible, the researcher arranged times with each participant where they would be available to be contacted should the participant encounter any problems whilst completing the CBM-I training. It was explained that it would be preferable that participants would complete the CBM-I training in conjunction with the availability of the researcher to be contacted, although this was not always possible. Following the completion of the CBM-I training participants completed the outcome measures as adopted by the present study along with the BBSIQ.

The researcher met with participants one week post completion of the intervention phase to complete final outcome measures. Alongside completion of these outcome measures a semi-structured interview was completed with participants, with the data obtained from this interview written as a separate service based research project. The purpose of this semi-structured interview was to ascertain the views held by participants regarding their experience of accessing an internet administered CBM-I task. Once all participants had completed the present study, a prize draw was conducted and three participants awarded a £10 high street voucher. Clinicians who referred participants into the present study were informed that their

involvement was now complete. Participants were given the option of receiving a summary of findings of the study, with this information being forwarded upon completion of the study. Finally, an end of study report was sent to the relevant ethics committee and the NHS trust research and development department from which ethical approval for the present study was sought (see Appendix N for a receipt of acknowledgement).

Chapter 3: Results

3.1. Chapter Introduction

This chapter outlines the results and statistical analysis of the present study. In total data from six participants were collected and analysed in line with the aims of the present study. Initially through visual inspection, participant's scores on the PDSS and VAS are analysed across all time points to identify *responders* and *non-responders*. This analysis is consistent with the criteria advocated by Kazdin (2010). Reliable and clinical change is reported on outcome measures at pre-intervention, post-intervention and follow-up. The effects of imagery on outcome are also reported.

3.2. Visual Inspection of Data

In order to evaluate the effectiveness of the CBM-I training programme, participant's scores on the PDSS and VAS were graphed and visually inspected. Visual inspection draws upon the criteria suggested by Kazdin (2010). The aim of this visual inspection was to ascertain whether scores in the intervention phase were representative of a significant change comparative to the scores of a participant's baseline phase (Barlow & Hersen, 1984). To facilitate this analysis, Kazdin (2010) nominates two principles, magnitude of change and rate of change. Magnitude of change looks to determine whether there is a change in mean scores on outcome measures across phases and if there are any changes in level evident. Changes in level look to observe any changes in scores when the intervention is introduced. With this is mind, the need for a stable baseline is apparent. Rate of change looks to determine whether a graphical representation of data evidences a change in trend or slope. This criteria is supplemented by latency of change which focuses on the time between the introduction of the intervention and a change in slope or trend. Each participant is deemed to be a *responder* or *non-responder* based on their scores on the PDSS as this was used as the primary outcome measure in the present study.

To ensure reliable inspection of the data, baseline stability was calculated for each participant's daily outcome measures (see Appendix O) using Kendall's *tau* (Kendall, 1970) analysis. Kendall's *tau* correlations were calculated for participants scores on the PDSS and VAS's with the number of days completed during the baseline phase of their participation. A non-significant result of Kendall's *tau* suggests that there was no significant relationship between time and scores, therefore indicating a stable baseline suitable for visual analysis.

3.2.1. Visual inspection of data: participant one (*Responder*)

Participant one was randomly assigned to the seven-day baseline phase. Kendall's *tau* analysis indicated baseline instability on the PDSS (*tau* = .651, *p* = .046). Despite this, as scores increase during the baseline, indicating deterioration in mood, these data are interpretable. Additional Kendall's *tau* analyses revealed baseline stability for the bodily VAS (*tau* = -.169, *p*>.05), the unreality VAS (*tau* = 1.00, *p*>.05), the control VAS (*tau* = .451, *p*>.05) and the dying VAS (*tau* = -.117, *p*>.05). Change in mean scores for the PDSS across phases is small with a baseline mean score of 13.4 decreasing to 12.4 during the intervention phase (see Figure 3.1). Potentially this small change in mean is accounted for by an increasing trend of scores during the baseline phase. A clear change in slope is evident from the second day of intervention on the PDSS scores which is maintained to follow-up. For each of the four VAS measures a change in level can be observed with the start of the intervention phase which paired with a decreasing trend (see Figure 3.2). Participant one is cautiously identified as a *responder* to the CBM-I training programme.

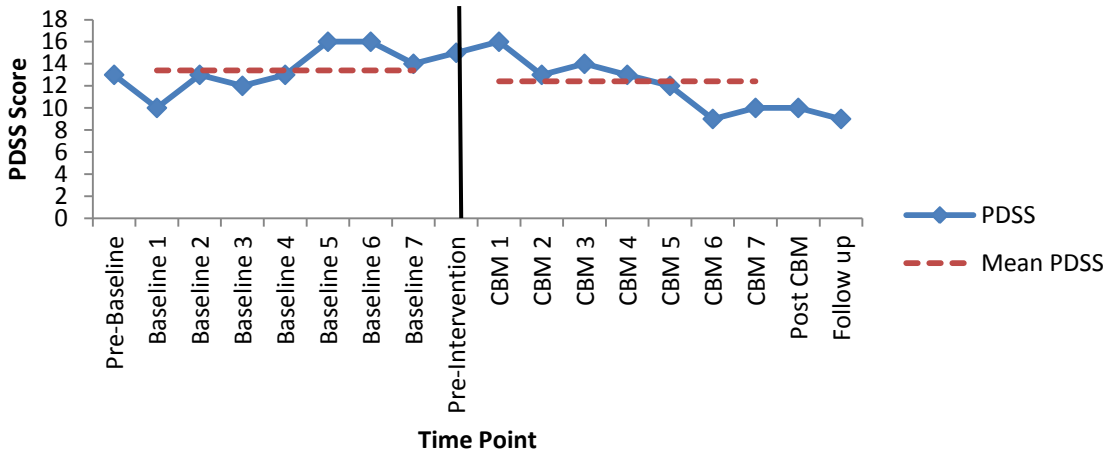


Figure 3.1. PDSS scores across time points for Participant 1 (*Responder*).

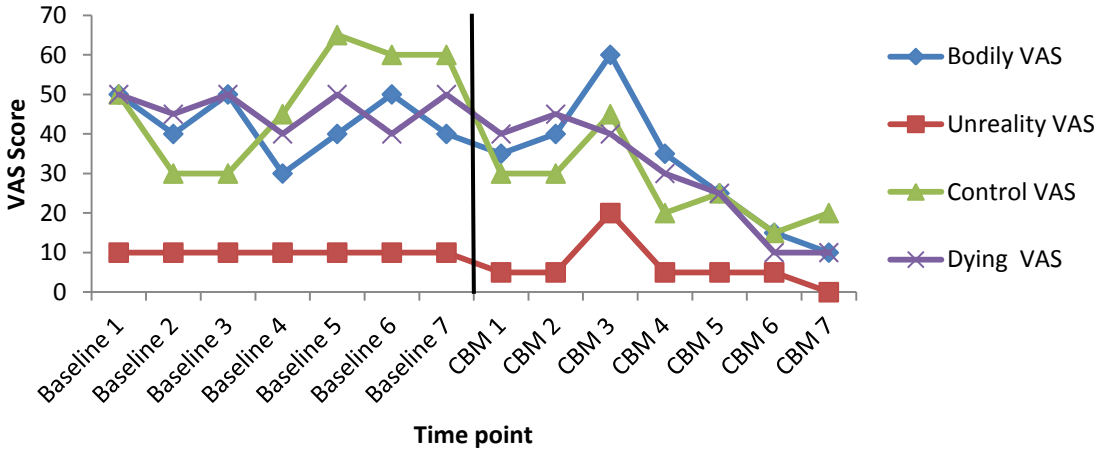


Figure 3.2. VAS scores across time points for Participant 1 (*Responder*).

3.2.2. Visual inspection of data: participant two (*Non-responder*)

Participant two was randomly assigned to the seven-day baseline phase. Baseline stability was confirmed for the PDSS (*tau* = .109, *p*>.05). Additional Kendall's *tau* analyses revealed baseline stability for the bodily VAS (*tau* = -.117, *p*>.05), the unreality VAS (*tau* = .394, *p*>.05), the control VAS (*tau* = -.504, *p*>.05) and the dying VAS (*tau* = .117, *p*>.05). PDSS mean score across baseline and intervention phases is identical (see Figure 3.3). Interestingly, there appears to be a reduction in PDSS score following the second intervention session, with four subsequent scores under the mean of the baseline being recorded. However, this improvement was not maintained with an increasing slope indicating

deterioration evident during the intervention phase. As is the case for the PDSS, a negative change in trend is observable for VAS measures between the second and fifth CBM-I training session (see Figure 3.4). Following this there is a clear positive trend in scores indicating increased distress. Consequently, participant two is judged as being a *non-responder*.

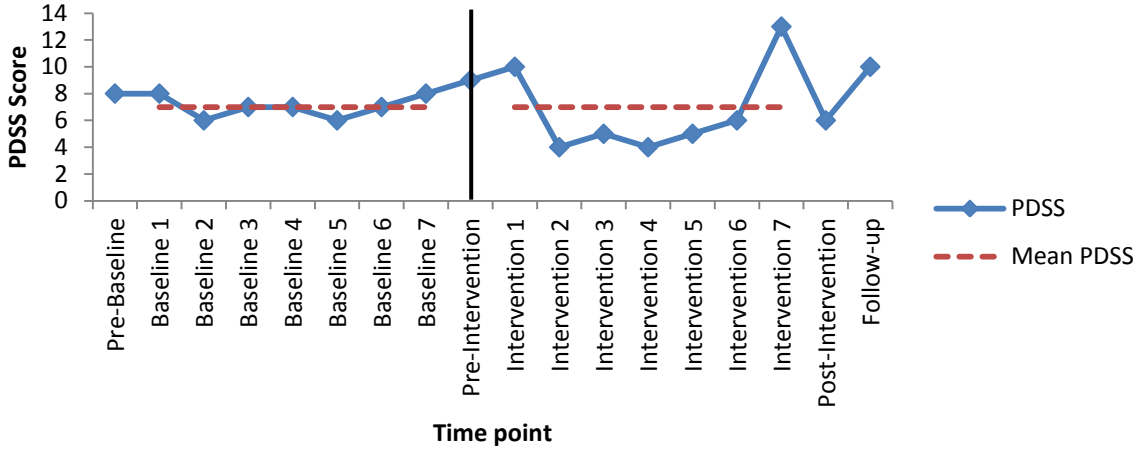


Figure 3.3. PDSS scores across time points for Participant 2 (*Non-responder*).

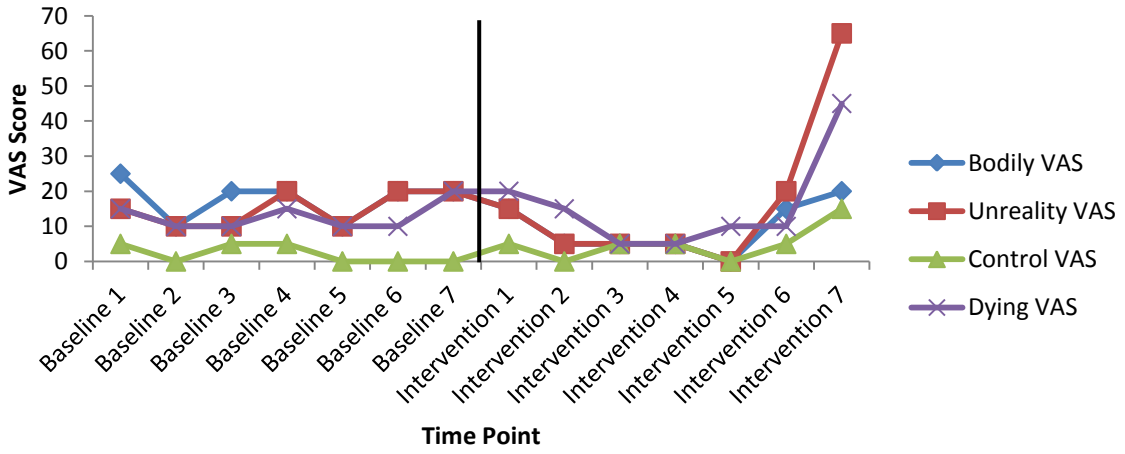


Figure 3.4. VAS scores across time points for Participant 2 (*Non-responder*).

3.2.3. Visual inspection of data: participant three (*Responder*)

Participant three was randomly assigned to the nine-day baseline phase. Baseline stability was confirmed for the PDSS (*tau* = -.382, *p*>.05). Additional Kendall's *tau* analyses revealed baseline stability for the bodily VAS (*tau* = -.031, *p*>.05), the unreality VAS (*tau* = .313, *p*>.05), the control VAS (*tau* = -.382, *p*>.05) and the dying VAS (*tau* = 1.00, *p*>.05).

PDSS mean score decreased from 10.9 to 3.9 during the intervention phase. Additionally, there is a clear and pronounced change in level following the introduction of the intervention phase (see Figure 3.5). This change in level is accompanied by a negative trend during the intervention phase. A clear change in level can be observed for all VAS measures (see Figure 3.6) indicating that participant three responded to the intervention. It should be noted that there was a noticeable increase in scores across all measures at intervention seven time point. Although VAS measures were not recorded post intervention, scores for the PDSS indicate a negative trend suggesting that improvement was maintained. Visual inspection of participant three's data suggests that they are a *responder* to the CBM-I training programme.

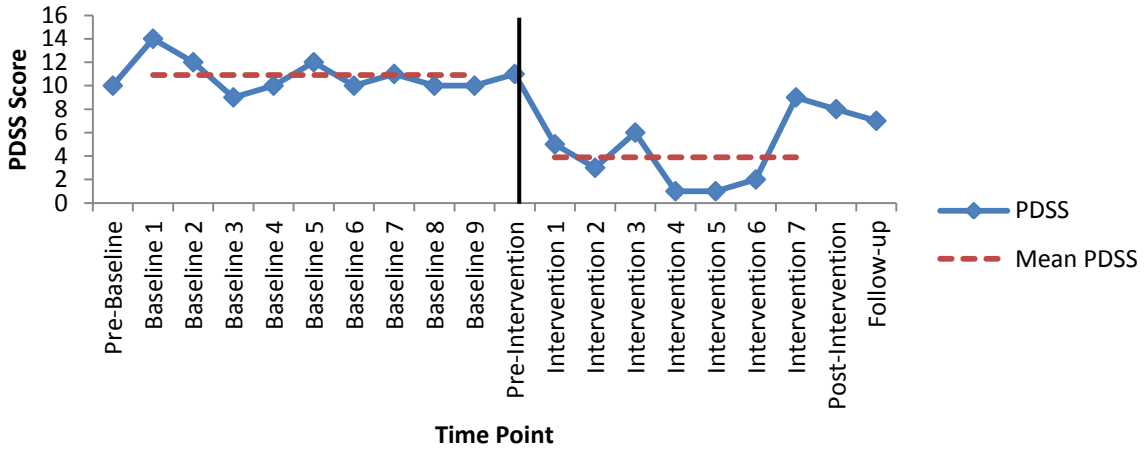


Figure 3.5. PDSS scores across time points for Participant 3 (*Responder*).

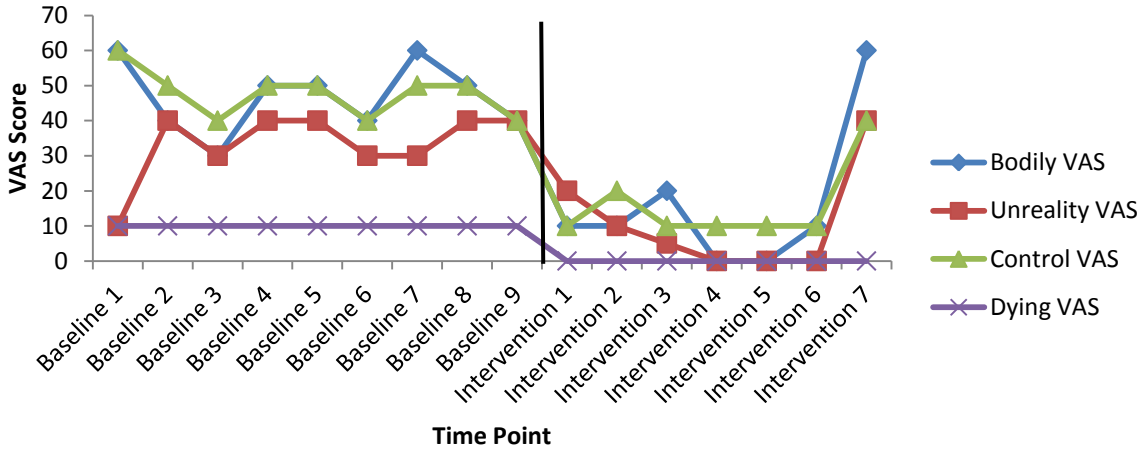


Figure 3.6. VAS scores across time points for Participant 3 (*Responder*).

3.2.4. Visual inspection of data: participant four (*Non-responder*)

Participant four was randomly assigned to the eleven-day baseline phase. Baseline stability was confirmed for the PDSS through Kendall's *tau* analysis (*tau* = -.274, *p*>.05). Additional Kendall's *tau* analyses revealed baseline stability for the bodily VAS (*tau* = .250, *p*>.05), the unreality VAS (*tau* = -.108, *p*>.05), the control VAS (*tau* = .106, *p*>.05) and the dying VAS (*tau* = 1.00, *p*>.05). Participant four's PDSS mean scores marginally decreased in the intervention phase, to 12 from 12.5 in the baseline phase (see Figure 3.7). The introduction of the intervention does not bring about a change in level of PDSS scores. There is little variability of scores during the intervention stage, with no significant trend apparent. No significant differences are noted in scores recorded post-intervention and at a one-week follow up. There is an increase in level following the introduction of the intervention for all VAS measures, which was paired with an initial negative trend which brought scores back in line with the baseline phase (see Figure 3.8). As no improvement is apparent participant four is identified as a *non-responder*.

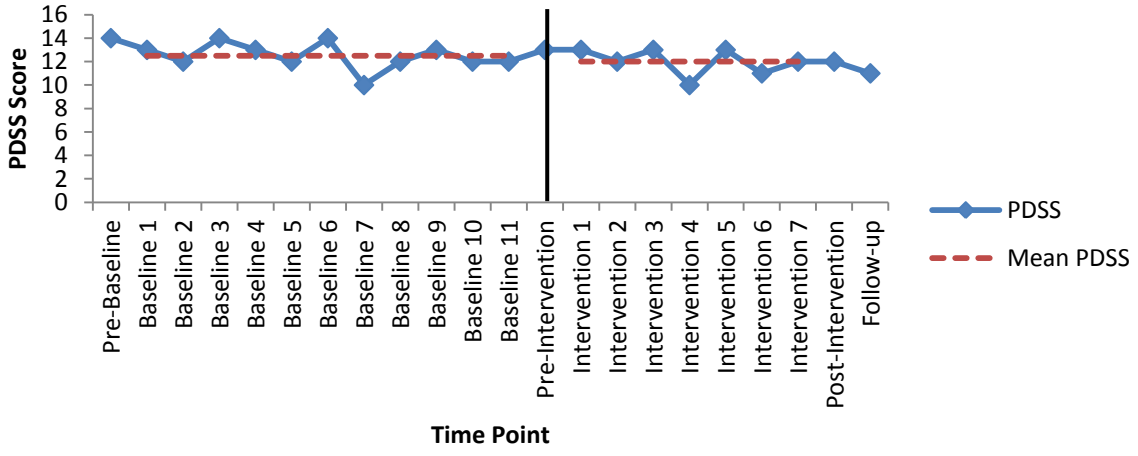


Figure 3.7. PDSS scores across time points for Participant 4 (*Non-responder*).

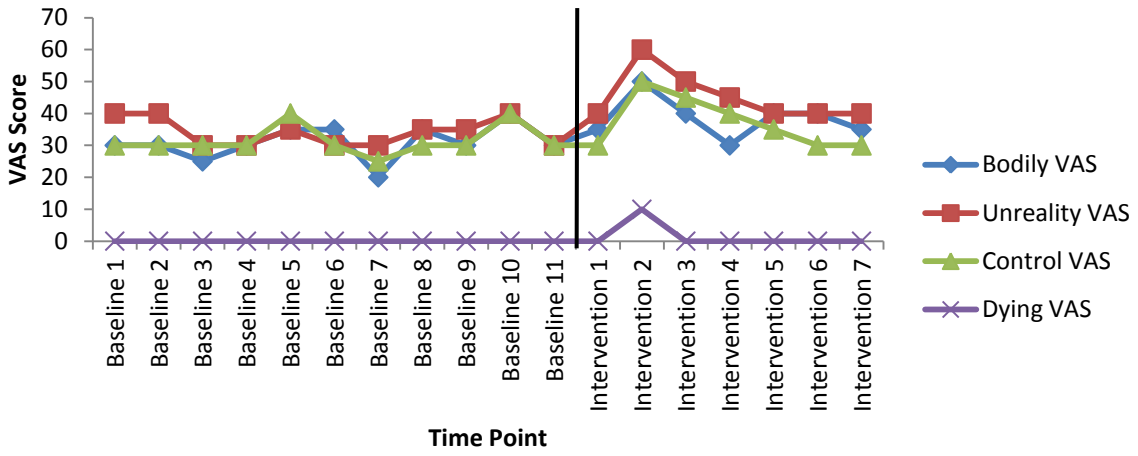


Figure 3.8. VAS scores across time points for Participant 4 (*Non-responder*).

3.2.5. Visual inspection of data: participant five (*Responder*)

Participant five was randomly assigned to the nine-day baseline phase. Baseline stability was confirmed for the PDSS through Kendall's *tau* analysis (*tau* = -.189, $p>.05$). Additional Kendall's *tau* analyses revealed baseline stability for the bodily VAS (*tau* = -.435, $p>.05$), the unreality VAS (*tau* = 1.00, $p>.05$), the control VAS (*tau* = 1.00, $p>.05$) and the dying VAS (*tau* = 1.00, $p>.05$). Participant five demonstrates a clear decrease in mean score on the PDSS, from 9 during the baseline phase to 5.1 during the intervention phase (see Figure 3.9). An immediate latency of change can be observed following the start of the intervention phase, and whilst this initial change is followed by a temporary increase in PDSS score at intervention two time point, there is an overall marked negative trend indicating improvement in mood. This improvement is maintained at one week follow-up. Participant five scored above zero on one VAS only. As with the PDSS there is an initial small decrease in level following the introduction of the intervention phase which is followed by a temporary increase in score (see Figure 3.10). Despite this, there is a clear decreasing trend for the relevant VAS indicating an improvement on that scale. Visual inspection indicates that participant five is a *responder.*

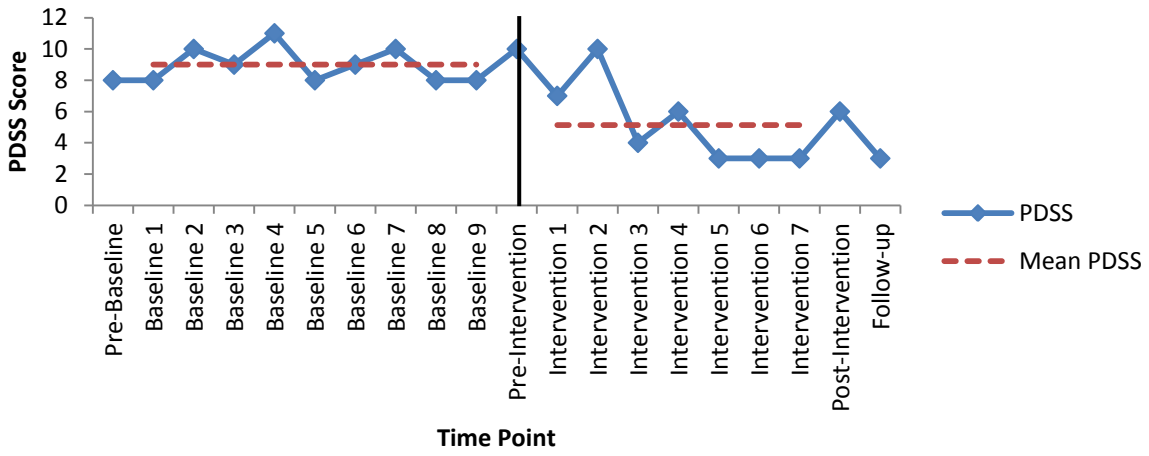


Figure 3.9. PDSS scores across time points for Participant 5 (*Responder*).

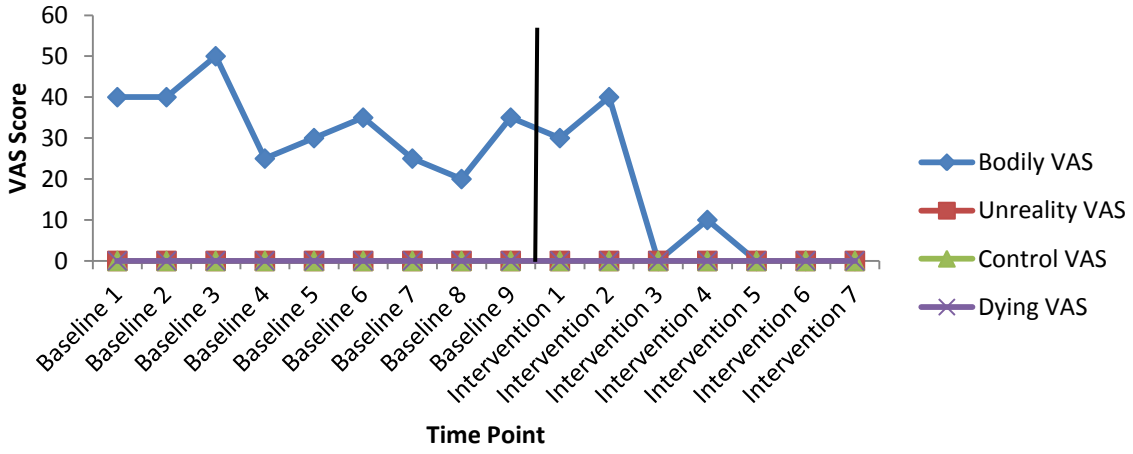


Figure 3.10. VAS scores across time points for Participant 5 (*Responder*).

3.2.6. Visual inspection of data: participant six (*Responder*)

Participant six was randomly assigned to the eleven-day baseline phase. Baseline stability for the PDSS was confirmed by Kendall's *tau analysis* (*tau* = -0.458, *p*>.05). Additional Kendall's *tau* analyses revealed baseline stability for the bodily VAS (*tau* = -.449, *p*>.05), the unreality VAS (*tau* = -.315, *p*>.05), the control VAS (*tau* = -.330, *p*>.05) and the dying VAS (*tau* = 1.00, *p*>.05). It should be noted that for all daily measures there is a large amount of variation of scores during the baseline phase. Despite this variability, during the intervention phase there is a marked decrease in mean PDSS score compared to the baseline phase, with a reduction to 15 to 10.3 evident (see Figure 3.11). Following the

introduction of the intervention phase there is no change in level which suggests no immediate effect of the CBM-I training. Despite this lack of immediate response, there is a clear negative trend from 'intervention two' time point indicating a reduction in levels of panic. This reduction is also maintained at one week follow-up. It is also notable that the variability that is apparent in the baseline phase is replaced by a relatively stable reduction in PDSS scores during the intervention phase. Unlike the PDSS, an immediate change in level can be seen for all relevant VAS measures (see Figure 3.12). This immediate change in level is paired with a stable and consistent negative slope indicating an improvement in symptoms. As with the PDSS, this stable and consistent slope is not reflective of a fluctuating baseline phase. Despite the variability of the baseline phase, participant 6 is considered a *responder*.

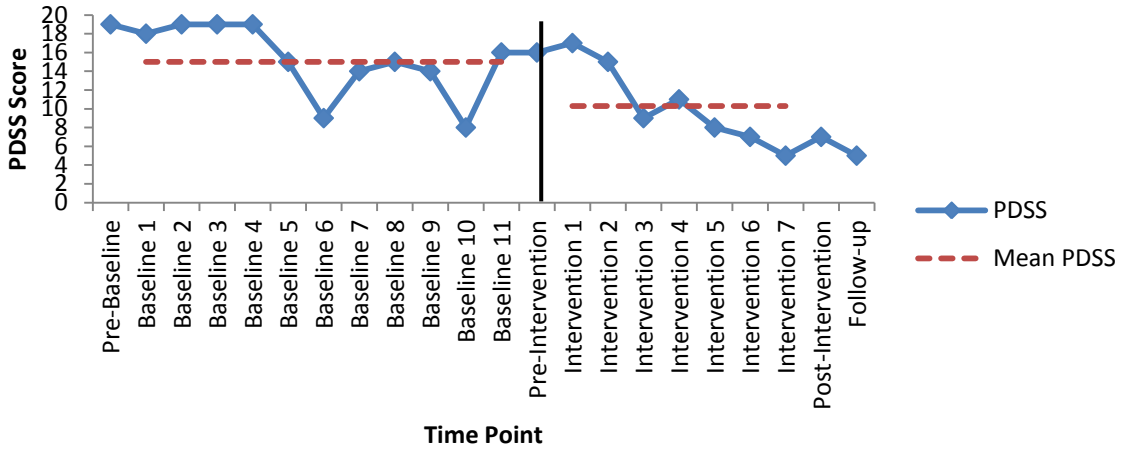


Figure 3.11. PDSS scores across time points for Participant 6 (*Responder*).

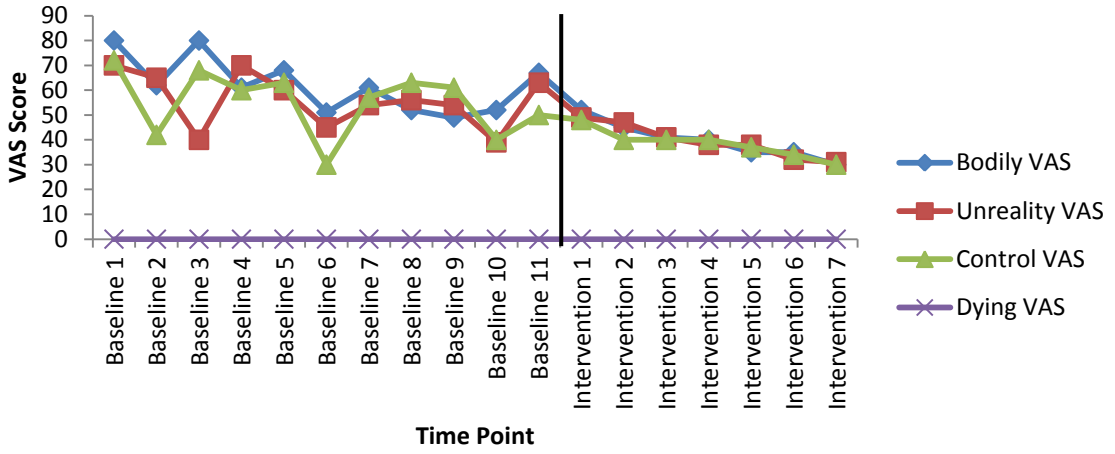


Figure 3.12. VAS scores across time points for Participant 6 (*Responder*).

3.3. Reliable and Clinically Significant Change

As a means of assessing whether observed differences between pre-and-post intervention scores were reflective of clinically significant and reliable change, Reliable Change Index (RCI; Jacobson & Truax, 1991) and Clinically Significant Change (CSC; Jacobson, Follette & Revenstorf, 1984) were calculated. In line with the hypotheses of the present study, RCI were computed for the ASI, PDSS, as well as ranking and believability factors of the BBSIQ. CSC was calculated for the ASI and both the ranking and believability factors of the BBSIQ. In line with the methodology used by Blackwell and Holmes (2010), evidence-based clinical cut offs are used to determine CSC where available. With this in mind, clinical change was said to occurred on the PDSS if participants moved from one clinical category to another (e.g. moderately ill to slightly ill) in line with evidence based guidelines (Furukawa et al., 2009).

CSC aims to determine whether an individual's level of functioning post-test is more typical of a non-clinical population rather than a pre-test clinical population (Evans, Margison & Barkham, 1998). That is to say, were the scores recorded on outcome measures at post-intervention and follow-up typical of an individual without clinical levels of panic symptomatology. Calculating CSC results in a cut-off point which an individual needs to

cross in order for clinically significant change to have occurred. The calculation of this cut-off point depends on the availability of normative and clinical data for the outcome measures used. Depending on the availability of suitable norms, Jacobson et al., (1984), cite three criterions for calculating a CSC cut-off. Of these, criterion C has been cited as the most suitable when normative data are available on both clinical and non-clinical populations. As such, criterion C looks to assess whether an individual's post-test score is statistically more likely to be in the non-clinical rather than the clinical population (Wise, 2004). Due to the availability of normative data for clinical and non-clinical populations for the outcome measures adopted by the present study, criterion C was used to calculate CSC. The formula used to calculate criterion C is, [*SD* (normative data) x *M* (clinical data)] + [*SD* (clinical sample) x *M* (normative data)] / *SD* (normative data) + *SD* (clinical data).

The Jacobson-Truax methodology was used to calculate RCI (Jacobson & Truax, 1991). This methodology calculates reliable change using the standard deviation of a matched sample and the reliability co-efficient of a given outcome measure. Calculating reliable change allows for an appreciation of whether any observed changes are statistically reliable (Wise, 2004). The formula to calculate RCI for each of the outcome measures was, 1.96 x SD1 x $\sqrt{}$ 2 x $\sqrt{}$ (1 - r).

When both CSC and RCI have both been calculated, Wise (2004) advocates the use of a classification system outlining the relationship each participant maintains with both CSC and RCI. The classification system as suggested by Wise (2004) identifies individuals who pass both CSC and RCI criteria as *recovered,* individuals who pass RCI criteria exclusively as *improved,* and individuals who do not pass RCI or CSC criteria as *unchanged.* Individuals, who achieved clinically significant change, but where this change was not deemed to be significantly reliable, are reported and discussed. These individuals were considered to have

achieved a score that was consistent with a non-clinical population despite the magnitude of this change not being statically reliable.

3.3.1. Reliable and clinical change on the PDSS

Clinical change was said to occur on the PDSS if participants moved from one clinical category to another as set out by Furukawa et al. (2009). These evidence-based interpretation guidelines suggest a score ranging from 3-7 was consistent with *borderline ill,* 8-10 *slightly ill,* 11-15 *moderately ill* and 16 and above *markedly ill* (Furukawa et al., 2009). An RCI of 5 was calculated using internal consistency data ($\alpha = .917$) reported by Houck et al. (2002). Clinical change was evident in all except one participant (participant 4), indicating a shift from one clinical category to another (see Table 3.1). Of these five participants who achieved clinical significant change, only participant two did not maintain this at follow-up. Reliable change was observable for only participant six post-intervention, but interestingly participants one and five went on to achieve reliable change at follow-up indicating a developing effect from the intervention phase. Using the classification criteria suggested by Wise (2004), only participant six met criteria to be considered *recovered* at both post-intervention and follow-up time points. Additionally, participants one and five met the criteria consistent with a *recovered* classification at follow-up.

Table 3.1.

Participants who Achieved Reliable and Clinically Significant Change on the PDSS at Post CBM-I and at One Week Follow-up

Participant	Pre-intervention PDSS score	Post-intervention PDSS score	Follow-up PDSS score	Reliable change Post	Clinical change Post	Reliable change Follow	Clinical change Follow
1	15	10*	9	No	Yes	Yes	Yes
2	9	6	10	No	Yes	No	No
3	11	8*	7	No	Yes	No	Yes
4	13	12	11	No	No	No	No
5	10	6*	3	No	Yes	Yes	Yes
6	16	7*	5	Yes	Yes	Yes	Yes

Note. PDSS = Panic Disorder Severity Scale

*Indicates participant was considered a responder to the CBM-I paradigm

3.3.2. Reliable and clinical change on the ASI

Standardised data taken from Stewart, Knize, and Pihl (1992) were used to generate a clinically significant change cut-off point of <23. Stewart et al. (1992) reported both the mean and standard deviation of individuals with panic disorder (M=30, SD=12.5) and a non-clinical control group (M=18, SD=8.7). Internal reliability was taken from Peterson and Heilbronner (1987) who reported high levels of internal reliability for the ASI ($\alpha = .88$) giving an RCI of 10. A total of two participants (participants three and six) achieved clinically significant change post-intervention, with this change maintained at follow up (see Table 3.2). For each of these participants clinically significant change was paired with reliable change at both post-intervention and follow-up time points, consistent with a *recovered* classification (Wise, 2004). Of the remaining participants, participant five demonstrated both reliable and clinically significant change at follow-up, highlighting an improvement of symptomatology as measured by the ASI from the post-intervention time-

point. Mirroring this improvement from post-intervention to follow-up, participant one was considered to have made reliable change at follow-up despite not reaching clinically significant change. When an individual passes the RCI criteria, but does not pass the clinically significant cut-off score they are considered to have *improved* (Wise, 2004). Only participants two and four did not achieve clinical or reliable change at any time-point, although it should be noted that participant four scored below the clinically significant cut-off score at all time-points.

Table 3.2.

Participants who Achieved Reliable and Clinically Significant Change on the ASI at Post CBM-I and at One Week Follow-up

Participant	Pre-intervention ASI score	Post-intervention ASI score	Follow-up ASI Score	Reliable change Post	Clinical change Post	Reliable change Follow	Clinical change Follow
1	50	48*	35	No	No	Yes	No
2	34	34	37	No	No	No	No
3	31	10*	8	Yes	Yes	Yes	Yes
4	20	21	19	No	No	No	No
5	33	29*	22	No	No	Yes	Yes
6	27	10*	5	Yes	Yes	Yes	Yes

Note. ASI = Anxiety Sensitivity Index

*Indicates participant was considered a responder to the CBM-I paradigm

3.3.3. Interpretation bias

3.3.3.1. Reliable and clinical change on BBSIQ interpretation ranking task

In order to calculate CSC and RCI for the ranking of panic related negative interpretations, standardised data were taken from the original paper examining the role of catastrophic misinterpretations in panic disorder (Clark et al., 1997). The authors reported both the mean and standard deviation of individuals with panic disorder (M=2.2, SD=0.5) and 'non-patients' (M=1.1, SD=0.2), alongside satisfactory levels of internal consistency (α =

.86). A CSC cut-off point of 1.41 and an RCI of 0.52 were calculated. Using these values, participants four and six did not score above the clinically significant cut-off point off point at any time-point, potentially indicating a lack of panic related interpretation bias (see Table 3.3). Of the remaining participants, only participant three achieved reliable and clinically significant change post-intervention and at follow-up time-points. Additionally, after demonstrating only reliable change post-intervention, participant five showed reliable and clinically significant change at follow-up. This is suggestive of a continuation in improvement following the completion of the intervention phase. Participants one and two achieved reliable change at post-intervention which was maintained at follow-up. Despite this reliable change, it was not sufficient to be clinically significant at either time point.

Table 3.3.

Participants who Achieved Reliable and Clinically Significant Change on the BBSIQ Ranking Task at Post CBM-I and at One Week Follow-up

Participant	Pre-intervention ranking score	Post-intervention ranking score	Follow-up ranking score	Reliable change Post CBM-I	Clinical change Post CBM-I	Reliable change Follow-up	Clinical change Follow-up
1	2.57	1.57*	1.42	Yes	No	Yes	No
2	2.43	1.71	1.86	Yes	No	Yes	No
3	1.71	1*	1	Yes	Yes	Yes	Yes
4	1	1	1.14	No	No	No	No
5	1.57	1.29*	1	No	Yes	Yes	Yes
6	1	1*	1	No	No	No	No

Note. BBSIQ = Brief Bodily Sensations Interpretation Questionnaire

*Indicates participant was considered a responder to the CBM-I paradigm

3.3.3.2. Reliable and clinical change on BBSIQ believability rating task

As with the BBSIQ ranking task, standardised data were taken from Clark et al. (1997) in order to calculate RCI and CSC. The authors reported both the mean and standard

deviation of individuals with panic disorder (M=4.4, SD=1.6) and 'non-patients' (M=1.1, SD=0.7), alongside satisfactory levels of internal consistency (α = .90). Subsequent calculations generated a CSC cut-off point of 2.3 and an RCI of 1.4. Unfortunately, participant six incorrectly recorded their believability ratings for the BBSIQ and consequently their data has been omitted from the current analysis. Of the remaining participants, only participant one achieved reliably significant change post-intervention and at follow-up (see Table 3.4). As with the ranking task, this change did not cross the cut-off to reach clinically significant change. Despite not showing clinically significant change post-intervention, participant three achieved this at follow-up indicating a continued improvement to pass this threshold. Participant three did not achieve reliable change at either time-point. Participants four and five did not score above the clinically significant cut-off for the believability task at any time-point, and despite participant five showing a reduction in scores in line with a number of other participants this was not sufficient to be reliably significant.

Table 3.4.

Participants who Achieved Reliable and Clinically Significant Change on the BBSIQ Believability Task at Post CBM-I and at One Week Follow-up

Participant	Pre-intervention believe. Score	Post-intervention believe. Score	Follow-up believe. Score	Reliable change Post CBM-I	Clinical change Post CBM-I	Reliable change Follow-up	Clinical change Follow-up
1	6.00	4.14*	2.85	Yes	No	Yes	No
2	5.86	3.71	3.86	Yes	No	Yes	No
3	3.14	2.43*	2	No	No	No	Yes
4	1.29	1.57	1.86	No	No	No	No
5	1.43	1*	0.14	No	No	No	No

Note. BBSIQ = Brief Bodily Sensations Interpretation Questionnaire

*Indicates participant was considered a responder to the CBM-I paradigm

3.5. Statistical Analyses and Effect Sizes

In keeping with previous CBM-I research that has adopted a single-case series design methodology (Blackwell & Holmes, 2010) sample means for outcome measures were calculated at pre-intervention, post-intervention and follow-up (see Table 3.5). In order to investigate change over time, and in keeping with the hypotheses of the present study, related samples Wilcoxon signed rank tests (Wilcoxon, 1945) were carried out (see Appendix P). Subsequently, Cohen's (1992) *r* effect sizes were computed as a means of assessing the magnitude of change of completing the CBM-I training task at post-intervention and at follow-up. Effect sizes were categorised according to the criteria advocated by Field (2009).

A Wilcoxon signed rank test revealed a significant difference for the PDSS between pre-intervention and post-intervention ($z = -2.21$, p = .014, one-tailed). Subsequent analysis revealed this difference to reflect a large effect size ($r = -0.64$.). A significance difference was also found for the PDSS between pre-intervention and follow-up ($z = -1.99$, p = .023, one-tailed). Again, subsequent analysis revealed this difference to reflect a large effect size ($r = -0.57$). A significant difference between pre-intervention and post-intervention was found for the ASI ($z = -1.75$, p = .04, one-tailed) with a large effect size ($r = -0.51$). This significant difference was mirrored between ASI scores between pre-intervention and follow-up ($z = -1.78$, p = .038, one-tailed). Subsequent analysis revealed a large effect size ($r = -0.51$). Significant reductions were observed between pre-intervention and post-intervention for the ranking task of the BBSIQ ($z = -1.83$, p = .034, one-tailed) with a large effect size ($r = -0.53$). A Wilcoxon signed rank test also revealed a significant differences on the ranking task of the BBSIQ between pre-intervention and follow-up time points ($z = -1.75$, p = .04, one-tailed). A Cohen's effect size was calculated which revealed a large effect size ($r = -0.51$). As with the BBSIQ ranking task, significant differences were found both the BBSIQ believability task between pre-intervention and post-intervention ($z = -1.75$, p = .04, one-tailed), and between

pre-intervention and follow-up (*z = -1.75*, p = .04, one-tailed). Large effect sizes were revealed at post intervention (*r* = -0.55) and at follow-up (*r* = -0.55).

Table 3.5.

Mean Outcome Scores at Pre-and-Post Intervention and Follow-up

Measure	Pre-intervention	Post-intervention	Follow-up
PDSS			
M	12.33	8.17	7.5
SD	2.8	2.4	3.08
ASI			
M	32.5	25.33	21
SD	9.97	14.77	13.28
BBSIQ Ranking			
M	1.71	1.26	1.24
SD	0.68	0.32	0.35
BBSIQ Believability			
M	3.54	2.57	2.14
SD	2.3	1.35	1.38

Note. PDSS = Panic Disorder Severity Scale; ASI = Anxiety Sensitivity Index; BBSIQ = Brief Bodily Sensations Interpretation Questionnaire

3.5. Impact of Imagery

During the intervention phase of the present study, participants were required to rate the vividness of the image they have created of various training scenarios. Participants rated the vividness of five scenarios during each day of CBM-I training. Mean vividness ratings were calculated for each participant (see Table 3.6.) and Spearman correlations computed on observed score differences on the PDSS and ASI at both post-intervention and at follow-up (see Appendix Q). The calculations revealed no significant correlations on the PDSS between pre-intervention and post-intervention (*rs* = -.116, *p* = .413) or between pre-intervention and follow-up (*rs* = -.486, *p* =.164). Likewise, no significant correlations were identified for the ASI between pre-intervention and post-intervention (*rs* = -.314, *p* = .272) or between pre-intervention and follow-up (*rs* = -.486, *p* = .164). This suggests that the ability to create a

vivid image of the scenarios presented in the CBM-I training does not influence reduction of symptoms as measured by the PDSS and ASI.

Table 3.6.

Mean Imagery Ratings for each Participant with changes in PDSS and ASI scores

Participant	Mean Imagery Rating	Change in PDSS score post-intervention	Change in PDSS score at follow-up	Change in ASI score post-intervention	Change in ASI score at follow-up
1*	7.06	-5.00	-6.00	-2.00	-15.00
2	5.23	-3.00	+1.00	0	+3
3*	7.80	-3.00	-4.00	-21.00	-23.00
4	8.47	-1.00	-2.00	+1.00	-2.00
5*	7.49	-4.00	-7.00	-4.00	-11.00
6*	8.77	-9.00	-11.00	-17.00	-22.00

*Indicates participant was considered a responder to the CBM-I paradigm

Chapter Four: Discussion

4.1. Chapter Introduction

This chapter reflects on the research questions set out by the present study, reviewing the extent to which the statistical analyses discussed in the previous chapter answer these research questions. The contribution of the present study to the existing scientific knowledge base is evaluated with reference made to the existing theoretical perspectives outlined in the introduction. The methodological strengths and weaknesses of the study are then considered. The results are then discussed in relation to the clinical implications they raise and future areas for research are suggested.

4.2. Overview of the Study

4.2.1. Aims of the study

The present study sought to investigate the efficacy of a multi-session internet administered CBM-I task with individuals with clinical levels of panic symptomatology. Despite the studies that have identified the role of misinterpretation of bodily sensations in the onset and maintenance of panic disorder (e.g., Clark et al., 1997; Richards et al., 2001; Schneider & Schulte, 2007), to the authors knowledge this is the first time that the efficacy of CBM-I has been investigated with individuals with clinical levels of panic symptomatology. It was hypothesised that completion of the multi-session CBM-I task would result in lower levels of panic symptomatology and a reduction of catastrophic interpretation bias. In addition, anxiety sensitivity was investigated given the links that this construct is thought to maintain with panic symptomatology (Otto & Reilly-Harrington, 1999; Smits et al., 2004).

4.2.2. Summary of results

The findings of the present study will now be discussed in the context of the research hypotheses set out in section 1.6.

4.2.3. Research hypothesis 1: A seven-session internet administered CBM-I training programme will reduce levels of panic in individuals experiencing clinical levels of panic symptomatology, with these changes evidenced at follow up

Visual analysis of the PDSS data for each participant revealed that four of the six participants (participants 1, 3, 5 and 6) were considered to be *responders* to the CBM-I training paradigm. As such, this suggests that the CBM-I programme, as trialled by the present study, is successful in reducing levels of panic in some individuals with clinical levels of panic symptomatology. Promisingly, of the participants who were considered *responders* to the CBM-I programme, three participants (participant 1, 5 and 6) went on to achieve reliable and clinically significant change at the follow-up time point. Of these three participants, only one individual had achieved reliable and clinical change at post-intervention. The remaining participant (participant 3) achieved clinical change at both post-intervention and at follow-up although the magnitude of this change was not sufficient to be considered statistically reliable. Interestingly, despite the lack of reliable significance, the score achieved by participant three at follow up would have meant that they were excluded from the study on the basis of not meeting the clinical cut-off score of 8 on the PDSS.

Furthermore, Wilcoxon signed rank analyses revealed significant group reductions in PDSS scores between both pre-intervention and post intervention, as well as between pre-intervention and follow-up. For each of the reductions a large effect size was calculated enabling the author to conclude that CBM-I training significantly reduced panic symptoms as measured by the PDSS. In doing so this is the first study to highlight the potential efficacy of a multi-session internet administered CBM-I programme in the reduction of panic symptomatology supporting the above hypothesis.

4.2.4. Research hypothesis 2: Individuals with clinical levels of panic symptomatology will demonstrate an increased positive interpretation bias following a seven-session internet administered CBM-I training programme, with these changes evidenced at follow-up

The interpretation bias measure used by the present study contained a ranking and believability measure of interpretation bias. The ranking task contained in the BBSIQ required participants to rank the order of explanations to a given description. Conversely, the believability task required participants to rate the extent to which they felt each explanation as believable. These will be discussed individually below with reference to second research hypothesis.

4.2.4.1. BBSIQ ranking task

Interestingly, only four of the six participants (participants 1, 2, 3 and 5) scored above the clinically significant cut off score of 1.41 on the BBSIQ ranking task at pre-intervention. Of these participants, all went on to demonstrate reliable change at follow-up supporting the suggestion that the CBM-I package adopted by the present study modified interpretive biases in some of the individuals with clinical levels of panic symptomatology. Of the four participants who achieved reliable change at follow-up, two participants (participants 3 and 5) demonstrated a clinically significant change. Interestingly, of the two participants that didn't score above the clinically significant cut-off score pre-intervention, one participant (participant 6) was the only individual to achieve reliable and clinically significant change at both post-intervention and follow-up on the PDSS. Conversely, participant two did not evidence reliable change on the PDSS at any time point but did show reliable change at both time points on the BBSIQ ranking task. However, it should be noted that participant two did not achieve clinically significant change on the BBSIQ ranking task which may have unpinned a lack of change on the PDSS.

Supporting the above hypothesis, Wilcoxon signed rank analyses revealed significant group reductions in BBSIQ ranking scores between both pre-intervention and post intervention, as well as between pre-intervention and follow-up. For each of the reductions a

large effect size was calculated enabling the author to conclude that CBM-I training significantly reduced panic related interpretations as measured by the BBSIQ ranking task.

4.2.4.2. BBSIQ believability task

Unfortunately, data are only available for five of the six participants on the BBSIQ believability task after participant six incorrectly recorded their believability ratings. Participant six only recorded believability ratings for one explanation for each description. Believability ratings are required for each explanation contained within the BBSIQ meaning that their data were not able to be included in the analysis. Of the remaining five participants, only three individuals (participants 1, 2 and 3) scored above the clinically significant cut-off score pre-intervention. Of these, only two (participants 1 and 2) demonstrated reliable change at post-intervention and at follow-up. Despite this, neither participant achieved clinically significant change. It should be noted however, that participants one and two achieved the highest scores on this task pre-intervention. Interestingly, as with the BBSIQ ranking task, participant two demonstrated reliable change post-intervention and at follow-up without any changes evidenced at either time point on the PDSS. Of the remaining participants, only participant three went onto achieve clinically significant change at the follow-up time point although the magnitude of this change was not sufficient to be considered significantly reliable. Based on the low scores recorded for participants four and five it was impossible to achieve significantly reliable change, although participant five showed a clear reduction in the anticipated direction that fell just short of significantly reliable change. However, for those individuals who scored above the clinically significant cut-off score pre-intervention there appears to be a reliable change evident.

In order to examine group effects, Wilcoxon signed rank analyses revealed a significant main effect of CBM-I on BBSIQ believability scores between pre-intervention and post-intervention, as well as between pre-intervention and follow-up. Further analyses revealed the magnitude of these changes to be consistent with a large effect size. This would suggest that completion of the CBM-I training significantly modified interpretation bias as measured by the BBSIQ believability task which is consistent with the research hypothesis. To the authors knowledge this is the first instance a CBM-I task has been able to modify

interpretation biases using this measure. Although not a primary aim of their research, Steinman and Teachman (2010) did not reveal any modification to biases using this measure following a single-session CBM-I task with individuals with high anxiety sensitivity.

4.2.5. Research hypothesis 3: Individuals with clinical levels of panic symptomatology will demonstrate a decrease in anxiety sensitivity following a seven-session internet administered CBM-I training programme, with these changes evidenced at follow-up

Of the six participants used in the present study, only one individual (participant four) scored below the clinically significant cut-off score at pre-intervention. This would seem to suggest the expected overlap of anxiety sensitivity with the presence of clinical levels of panic symptomatology was observable in the sample recruited by the present study. Indicating that completion of the CBM-I task reduced levels of anxiety sensitivity, four of the five participants who met the clinically significant cut-off score for the ASI (participants 1,3,5 and 6) achieved significantly reliable change at follow-up. Of these four participants, only participant one did not achieve clinically significant change at this time point. As with the PDSS, significantly reliable changes in scores were not initially evidenced at post-intervention for a number of these participants (participants 1 and 5).

Offering further support to the role of CBM-I training in the reduction of anxiety sensitivity and supporting the above hypothesis, Wilcoxon signed rank analyses revealed a significant main effect of CBM-I on ASI scores between pre-intervention and post-intervention, as well as between pre-intervention and follow-up. Further analyses revealed the magnitude of these changes to be consistent with a large effect size. The efficacy of the CBM-I training paradigm used in the present study in reducing levels of anxiety sensitivity mirrors those results of Steinman and Teachman (2010). However, unlike Steinman and Teachman, anxiety sensitivity was not the primary target of the CBM-I training task used in the present study. The scenarios used in the present study were based on the DSM-IV diagnostic criteria for panic attacks (APA, 2000), with the observed effects on anxiety sensitivity consistent with the evidence base associating this two clinical construct together (Smits et al., 2004).

4.2.6. Research hypothesis 4: Individuals who are better able to vividly imagine the training scenarios will evidence the greatest decrease in scores across outcome measures.

Previous research has suggested that imagery maintains a positive relationship with improved outcomes associated with CBM-I training tasks (Holmes et al., 2009). That is to say, an individual's ability to vividly imagine training scenarios will positively influence outcomes on the PDSS and the ASI, therefore enhancing the efficacy of the CBM-I paradigm. The results of the present study do not support the above hypothesis. Spearman correlations were calculated between mean imagery ratings and changes in PDSS and ASI scores from pre-intervention to post-intervention and from pre-intervention to follow-up. None of the performed correlations highlighted a significant relationship. Due to the small sample size and the lack of a non-imagery control condition further conclusions regarding the enhancing effect of imagery on CBM-I outcomes cannot be made.

4.3. Theoretical and Empirical Implications

The findings of the present study lend partial support to the catastrophic misinterpretation model of panic disorder (Clark, 1986). This model asserts that an interpretive bias focused on the catastrophic outcome of ambiguous bodily sensations underlies the onset and maintenance of panic disorder. Of the four participants who achieved significantly reliable change on the ranking task of the BBSIQ, three were deemed to have responded to the CBM-I training. Only participant two was not deemed to have responded to the intervention despite achieving a significantly reliable reduction in their interpretation bias as measured by the BBSIQ ranking task. Given the expected reduction in interpretation bias, it is surprising that participant two did not respond to the CBM-I training as this would be expected according to the catastrophic misinterpretation model of panic disorder (Clark, 1986). With this in mind, this lack of observed response is not consistent with the

catastrophic model of panic disorder (Clark, 1986). When looking to understand this unexpected observation, it may be the case that an awareness of the purpose of the study contributed to this finding. That is to say, being aware that the study aimed to positively modify the way individuals interpret bodily sensations impacted on the responses given on the BBSIQ. This potential influence was not reflected in changes on the other outcome measures. Indeed, insight in to the training contingency of CBM-I tasks has been identified as a factor in observed larger effects on interpretation bias measures within CBM-I research (MacLeod & Mathews, 2012).

As mentioned, four of the six participants who completed the present study achieved significantly reliable change on the BBSIQ ranking task. Of those four participants only two individuals (participants 1 and 2) demonstrated a significantly reliable change on interpretation bias when measured by the BBSIQ believability task. Despite this lack of reliable change for two participants (participant 3 and 5) both individuals achieved a reduction in negative bias as expected. Whilst not significantly reliable, participant three achieved clinically significant change at the follow-up time point. It would appear that completion of the CBM-I training programme enabled participants to more readily identify benign explanations in a ranking task, but the believability attributed to individual explanations was more robust. When attempting to better understand this outcome it is useful to consider the cognitive model of selective processing (Mathews & Mackintosh, 1998).

According to this theoretical perspective, completion of CBM-I training facilitates an increase in positive cognitive responses via the positive evaluation system, with this process occurring at an early stage of cognitive processing (Mathews & Mackintosh, 1998). Through repeated practice, the positive evaluation system becomes dominant over the threat evaluation system consequently suppressing a negative interpretation bias (Mathews & Mackintosh, 1998). The accessibility and dominance of positive evaluations seems to be closely aligned to

the BBSIQ ranking task in which individuals rank the likelihood of a given explanation coming to mind. The observation that change was not significantly mirrored for the BBSIQ believability could potentially be explained by this task being representative of a later conscious evaluative process. Indeed, it is this later level processing that is the target of cognitive restructuring techniques used in cognitive therapy for panic disorder (Clark et al., 1994). The results of the present study tentatively suggest that it is the accessibility of positive cognitions at an automatic and reflexive level that is primarily influenced as a consequence of the CBM-I training. As such, this finding is consistent with the cognitive model of selective processing (Mathews and Mackintosh, 1998) and the assertion that CBM-I training impacts upon the reflexive and automatic processing of information. When relating this specifically to panic disorder, Clark et al., (1997) suggest the interpretation bias represented in their catastrophic misinterpretation model of panic disorder is reflexive in nature. Consequently, the findings of the present study lend support to this assertion.

When further reflecting on the catastrophic misinterpretation model of panic (Clark, 1986), it is important to consider the significance of anxiety sensitivity in this theoretical perspective (Taylor, 1994). Anxiety sensitivity can be defined as fear of anxiety related symptoms (Reiss, 1987). The vicious cycle outlined by Clark (1986) in the model of panic disorder is thought to be driven by the fear of anxiety related bodily sensations. That is to say these individuals are typified by elevated anxiety sensitivity (Taylor, 1994). The notion that the vicious cycle of panic is driven by anxiety sensitivity (Reiss, 1991) has clear implications when considered in the context of the present study. If the CBM-I training is successful in reducing levels of panic, then one would expect an observable reduction in levels of anxiety sensitivity.

The findings of the present study generally support this theoretical viewpoint as all participants who achieved significantly reliable change on the PDSS also achieved

significantly reliable change on the ASI. Interestingly, only one participant (participant three) did not achieve significantly reliable change on both the ASI and the PDSS. Despite achieving reliable change on the ASI, this participant did not achieve significantly reliable change on the PDSS. It should be noted however that based on their score at follow-up participant three would not have been included in the present study as a consequence of not meeting the clinical cut-off score of 8 on the PDSS. Overall, it would seem that the assertion that anxiety sensitivity is a key factor in the vicious cycle of panic (Clark, 1994) is supported by the results of the present study.

To date, this is the second study to demonstrate the efficacy of a CBM-I training task in reducing anxiety sensitivity following the study of Steinman and Teachman (2010). Unlike the aforementioned research, the main aim of the present study was to reduce panic related symptomatology as measured by the PDSS. As such, the training scenarios that were constructed and used in the present study primarily related to the panic disorder diagnostic criteria as set out in the DSM-IV (APA, 2000). The training scenarios adopted by Steinman and Teachman were based on the items contained within the ASI as this related to the primary aim of their research. As mentioned, whilst able to evidence reductions in anxiety sensitivity, Steinman and Teachman did not observe a significant change in interpretation bias on the BBSIQ. A suggestion offered by the authors was the similarity of the training scenarios to the main outcome measure potentially impacting upon the generalisability of the training to different measures. The findings of the present research study identify that the panic orientated CBM-I training programme used was generalisable to a different, albeit related, measure of anxiety sensitivity. Whilst of interest, the finding of the present study is not unexpected given the evidence base that anxiety sensitivity and panic disorder share (McNally, 2002).

As previously discussed, there is a growing body of evidence which has highlighted the enhancing impact of mental imagery on the observed effects of CBM-I training tasks (Holmes et al., 2009). Within the present study mental imagery was investigated for both the PDSS and ASI at post-intervention and at follow-up time points. No positive significant correlations were found for either measure. Despite this lack of significant correlation it is important to note a number of factors which limit the theoretical relevance of these findings. Firstly, a significant proportion of the research studies exploring the role of imagery in CBM-I have employed variations on the CBM-I training paradigm which have included presenting information using an auditory platform to promote imagery (e.g. Blackwell & Holmes, 2010). Whilst the present study recorded the perceived ability of participants to imagine themselves in each scenario, the paradigm used was not optimised for imagery focused training. Secondly, given that this analysis fell outside of the single-case series design the theoretical impact of this finding is somewhat limited by the small sample size recruited by the study. Consequently, the subsequent power of the analysis to identify a significant correlation is compromised. As such theoretical conclusions regarding the role of imagery in CBM-I paradigms cannot be made with any confidence.

4.4. Critique of the Study

4.4.1. Strengths

This is the first study to explore the efficacy of a CBM-I training package in those with clinical levels of panic symptomatology. As discussed, individuals experiencing clinical levels of panic symptomatology face significant challenges across various aspects of their lives, as well as being at an increased risk of suicide (Borden, 1994; Johnson et al., 1990; Weissman et al., 1989). With this point in mind, the potential development of future clinical interventions which are effective as well as being amenable to dissemination on a large scale is clearly important (Yiend et al., 2014). The finding of the present study that four out of the

six participants were classed as responders to the CBM-I package is clearly encouraging. Whilst not all of these participants achieved reliable or clinical change across all measures, the findings of the present study are suggestive of a potential clinical utility for panic orientated CBM-I. Indeed, when appreciating the proportion of individuals who demonstrated reliable and clinically significant change (three out of six), this is comparable with internet administered cognitive behavioural treatment packages for panic disorder (Klein, Richards & Austin, 2006). As such, the focus of the present study to develop the CBM-I evidence base with a previously untested population is considered to be a strength.

Previous research exploring the efficacy of CBM-I packages have identified the exclusion of an interpretation measure at follow-up as a limiting factor in their methodologies (e.g., Beard & Amir, 2008; Steinman & Teachman, 2010). The omission of an interpretation bias measure at follow-up doesn't allow for the durability of any observed effects to be evaluated. In administering the BBSIQ at one-week follow-up, the present study enables this analysis to take place. In order for the clinical potential of CBM-I to be developed and realised, it is important that changes consequent to CBM-I training are durable and evident at follow-up. Indeed, it may be beneficial for future studies to include longer follow-up time points to shed further light on the durability of the consequences of completing CBM-I tasks.

The utilisation of the internet to administer the CBM-I package investigated in the present study represents a clear and obvious strength of the study. To date a significant proportion of CBM-I research has been laboratory based (e.g., Hirsch et al., 2009, Murphy et al., 2007; Steinman & Teachman, 2010). Consequently, the ability to generalise these findings to more naturalistic settings is restricted. If CBM-I is to be considered an effective intervention for various psychological presentations, then there is a need for research to explore likely platforms that CBM-I programmes would adopt in real-world contexts (MacLeod et al, 2009). Indeed, there are a number of advantages of delivering therapeutic

interventions via the internet. Internet administered interventions can reduce waiting-lists, save travelling time, reduce stigma and conform to the daily schedules of individuals (Marks, Cavanagh & Gega, 2007). In administering the CBM-I task online, the present research study offers results which one can generalise to more naturalistic settings, This is something which is of importance when aiming to advance the body of research exploring CBM-I. Furthermore, researching the efficacy of CBM-I using a platform that is clearly advantageous to mental health services, given the current context of the NHS, helps to position CBM-I demonstrate its clinical utility.

A further strength of the study relates to the general acceptability of the CBM-I programme reported by participants. Anecdotal feedback provided by participants rated the CBM-I training programme as simple and easy to use which was considered advantageous. Equally being able to access the CBM-I programme online allowed participants to fit their participation around their day to day schedules. Previous research has highlighted the potential for CBM-I paradigms to be considered arduous due to their repetitive nature (Beard, Weisberg, & Primack, 2012). Informal feedback received from participants relating to the present study suggested that this was not consistent with their experiences and as such this acceptability is considered to be a strength of the study.

4.4.2. Limitations

4.4.2.1. Methodological limitations

Single-case series design methodology has long been advocated as a suitable approach to evaluate the efficacy of novel interventions at an early stage in their development (Kazdin, 2010). The suitability of this experimental approach in determining the potential clinical utility of CBM-I has been reflected in a number of studies adopting this methodology in their research (e.g., Blackwell & Holmes, 2010; Turner et al., 2011). Despite the suitability of a single-case series design methodology in this context, it should be noted that this

approach has been criticised due to extent to which results can be generalised to a wider population (Platt, 1992; Wilson, 2000). Whilst this has long been a concern with this methodology, advocates of single-case series design methodology have countered that this criticism is somewhat misguided in its theoretical foundations (Kratochwill & Levin, 2010). Indeed, Hayes, Barlow and Nelson-Gray (1999) highlighted single-case series designs as being embedded within a process of *logical generalization* whereby participant and experimental characteristics are appreciated against a backdrop of the wider applied setting. As such, this enables this methodology to be utilised as a pre-cursor to wider ranging controlled trials investigating the efficacy of novel interventions (Kratochwill & Levin, 2010). This apparent misunderstanding is further expanded on by Flyvbjerg (1994) who explained that this criticism is representative of a poor understanding of case series research. Whilst single-case series design methodology clearly has a role to play in the advancing of psychological interventions, it is nevertheless important to interpret the results of the present study with caution. As previously discussed, challenges with recruitment during the present study resulted in a sample size of six individuals with the aim being for nine participants. This small sample size could be considered a potential limitation. Despite this smaller than desired sample size, it should be noted that a sample size of six is in keeping with other CBM-I research utilising a single-case series design methodology (Turner et al., 2011). As such, the present study offers a useful evaluation of the efficacy of a CBM-I training program suggesting that further larger scale trials are warranted.

A limitation of the present study was that a mechanism to measure compliance was not included. Other research studies exploring the efficacy of CBM-I paradigms have used the number of correct responses given to comprehension questions as a means of measuring compliance and adherence to the CBM-I package (Bowler et al., 2012). Should an individual fall within two standard deviations of the sample mean then they were considered to have

been compliant in the CBM-I training (Bowler et al., 2012). As compliance could not be gauged, the extent to which the results are interpreted with confidence is somewhat measured. Specifically, it may be the case that those individuals who were classed as non-responders were not compliant in the intervention phase of the present study. Future studies should look to include a measure of compliance especially if CBM-I training programmes are accessed outside of controlled laboratory settings.

4.4.2.2. Outcome measures

The measures adopted by the present study are well validated and widely used measures both in clinical and research contexts (e.g., Casey et al., 2004, Klein et al., 2006, Steinman & Teachman, 2010). In order to meet the criteria of single-case series design, daily measures were required to ensure stability of symptoms over the baseline phase and to determine change following the introduction of CBM-I training (Kazdin, 2010). In order to measure panic symptomatology daily, participants were requested to complete a revised version of the PDSS, rating their symptoms over the past 24 hours as opposed to the preceding week. It should be noted that the PDSS is not designed to be a daily measure of panic related symptomatology. It was decided that, despite lacking validation as a daily measure, using the PDSS in this way offered a suitable daily measure of panic symptomatology as there was an overlap between the seven indices represented in the PDSS and the constructs measured by a validated daily panic diary (De Beurs, Chambless & Golstein, 1997).

A further limitation of the present study, linked to daily measures, is the lack of a daily interpretation bias measure. In order for single-case research designs to provide evidence of causality between variables, a number of conditions need to be satisfied (Wilson, 2000). Firstly, as a means of controlling against threats to internal validity, the baseline phase of a single-case series design methodology provides a control against which change is

quantified (Horner et al., 2005). This is achieved through evidencing stable symptomatology over a given period. Secondly, visual inspection of this data needs to be able to judge whether there are any changes in mean or level across phases and whether there are any changes in level or trend evident (Kazdin, 2010). Without a daily measure of interpretation bias, baseline stability cannot be assumed, nor can the effects of the introduction of the CBM-I programme be appreciated in relation to this via visual inspection. Consequently, it is not possible to infer the causality of interpretive biases in the reduction of panic symptomatology after completing CBM-I training. Future research should look to include a daily measure of interpretation bias to shed further light on the causality interpretive biases maintain with various psychological presentations. Despite this lack of daily interpretation bias measure, the BBSIQ was an adequate outcome measure of interpretation bias. Indeed the BBSIQ is a widely used measure of interpretation in panic related research (e.g., Steinman & Teachman, 2010).

4.5. Clinical Implications

For a number of reasons, the findings of the present study have potentially important clinical implications that warrant discussion. Firstly, it is important to consider the prevalence of panic disorder and the contexts in which this is reflected. The United Kingdom has been identified as having the highest prevalence of panic disorder in Europe (King et al., 2008). Additionally, it has been suggested that the prevalence of panic disorder is as high as 13% across primary care settings placing considerable pressures on these systems (Craske et al., 2002). It is clear that there is a need for evidence based effective interventions that can support these high levels of individuals with clinical levels of panic symptomatology. The results of the present study highlight the potential clinical efficacy of CBM-I, suggesting its potential as a clinical intervention. Research exploring the effectiveness of cognitive, behavioural and a combination of cognitive and behaviour treatment components in panic disorder indicated a clear superiority in treatment outcomes when cognitive therapy was

combined with behavioural exposure (Clark, 1999). The potential for CBM-I to be used alongside other treatment strategies in those with clinical levels of panic symptomatology is an interesting notion, and one which deserves future research. Indeed, the concept of CBM-I being adopted into clinical services is not implausible with the potential to form 'therapeutic synergies' with other treatment approaches a distinct possibility (MacLeod et al., 2009).

Secondly, it would be implausible to consider the clinical implications of a task which may have a clinical utility without making reference to the current ethos evident within mental health services and the ways in which this ethos is reflected. Currently, there is a pressure on mental health services to reduce costs whilst maintaining effective and safe treatment packages. Alongside this, there has been an increasing appreciation regarding the need to make psychological interventions accessible, with this need forming a core ideal within IAPT services. These two drivers have contributed to the increase of internet administered cognitive behavioural treatment packages which involve minimal therapist contact (Barak, Hen, Boniel-Nissim & Shapira, 2008). Interventions which are less dependent on therapist contact are more easily accessible by people, often identifying internet administered treatment packages as useful waiting-list control strategies (Marks et al., 2007). In one study of an internet administered cognitive behavioural treatment package for panic disorder, 53% of participants did not meet diagnostic criteria for panic disorder post-intervention (Klein et al., 2006). The results of the present study are comparable to this research as 50% of participants achieved reliable and clinically significant change. However, it is important for these results to be replicated using a larger sample.

Despite the small sample size of the present study, it offers an important insight into the potential clinical utility of panic orientated CBM-I and in doing so justifies further research into this area. Additionally, the benefit of having an evidence based therapeutic intervention that can be widely disseminated is seen to take on further value when

considering the suggestion that panic disorder is an risk factor in other psychological presentations such as depression and generalised anxiety (Skapinakis et al., 2011; Tull, Stipelman, Salters-Pedneault & Gratz, 2009).

An interesting clinical implication raised by the present study resides in the relationship panic symptomatology maintains with anxiety sensitivity. Despite anxiety sensitivity not constituting a primary aim of the study, four of the six participants who completed the study achieved significantly reliable change on the ASI. The clinical relevance of this finding relates to the role that anxiety sensitivity is thought to hold as a risk factor in the onset of panic disorder (McNally, 2002; Plehn & Peterson, 2002). When further expanding this point, there is a large body of evidence highlighting the role of anxiety sensitivity in individuals with non-clinical levels of panic symptomatology (Cox et al., 1991; Donnell & McNally, 1990; Tull et al., 2009). As such, it has been suggested that non-clinical panickers are more likely to develop panic disorder than controls (Ehlers, 1995). For the basis of this discussion, non-clinical panickers are representative of individuals with infrequent panic attacks but who do not meet diagnostic criteria for panic disorder (Richards et al., 2001). The results of the present study indicate that panic focused CBM-I may have a clinical benefit with those individuals who are considered non-clinical panickers. As mentioned, these individuals are at a heightened risk of developing panic disorder and subsequently engaging with services (Rob-Byrne et al., 1999). This distress is not only costly in terms of impacting the quality of life of the individual concerned but it is also results in a financial cost to the NHS. The idea that CBM-I could be utilised as a preventative intervention is a novel concept and one which would require further research.

4.6. Suggestions for Future Research

As previously discussed, to the authors knowledge this is the first time that a CBM-I training task has been investigated with individuals with clinical levels of panic

symptomatology. Unfortunately, due to recruitment issues only six participants successfully completed their participation in the study. Whilst this is in keeping with other research exploring the efficacy of CBM-I training tasks (Turner et al., 2011), future research should look to replicate the results of the present study with a larger sample. Equally, whilst all the participants were help-seeking at the time of their participation in the study, whether that was from mental health services or via their GP, future research may benefit from recruiting from a more closely matched sample. In aiding this process, future research may wish to utilise a diagnostic interview such as the SCID in order to confirm diagnoses (SCID; First et al., 2002).

There are a number of methodological improvements that would offer additional opportunities for discussion in future research. As mentioned, compliance to the CBM-I training was not measured in the present study. As the CBM-I package was accessed online, having an insight into the level of compliance would have enabled an added element of control from which to evaluate data. Equally, future research may benefit from the inclusion of a daily measure of interpretation bias as a means of inferring causality. As interpretation bias was only measured at pre-intervention, post-intervention and at follow-up, data collection did not conform to the criteria of single-case research design (Kazdin, 2010). When reflecting further on the measurement of interpretation bias in panic related CBM-I research, future studies should consider the inclusion of an open-ended interpretation task. This would position future research more in line with research exploring the role of catastrophic misinterpretations of bodily sensations in panic disorder (Austin & Kiropoulos, 2008; Richards et al., 2001), enabling more theoretical implications to be drawn.

Whilst the need to replicate the results of the present study are clear given the small sample size, there are a number of future directions for panic focused CBM-I which warrant discussion. Building on the prediction that the future of CBM-I resides in ‘therapeutic

synergies' (MacLeod, 2009), future research may look to ascertain how this is best reflected with individuals with panic disorder. As discussed, pure cognitive restructuring has demonstrated efficacy in the reduction of panic symptomatology (Arntz et al., 1993; Salkovskis et al., 1991) However, superior reductions in panic symptomatology have been observed when cognitive restructuring was combined with exposure to feared situations (Clark, 1999; Margraf, Barlow, Clark & Telch, 1993). Given the finding of the present study that CBM-I can significantly alter the interpretation bias presented by individuals with clinical levels of panic, future research could investigate whether CBM-I combined with an element of guided exposure results in greater reductions in panic symptomatology than CBM-I alone.

When considering the role of future research in enhancing the effects of CBM-I training it is important to consider to idiosyncratic nature of panic disorder. Indeed, the highly individualised nature of panic disorder has been cited as a potential explanation under-pinning the ambiguity discussed in research exploring the role of the catastrophic misinterpretation of bodily sensations in panic disorder (Schneider & Schulte, 2007). The CBM-I package adopted by the present study utilised the DSM-IV criteria for panic attack (APA, 2000) to develop the individual training scenarios. This diagnostic criteria requires that individuals demonstrate four or more bodily sensations from a possible thirteen. Consequently, it is feasible to suggest that a significant proportion of the training scenarios were not directly relevant for all participants. Literature exploring the reflexive nature of catastrophic misinterpretations of bodily sensations has previously found that only when stimuli were idiosyncratically selected was a facilitated effect evident on a timed response task for participants with clinical levels of panic disorder comparable to controls (Schneider & Schulte, 2007). As such, future research should look to develop a way of screening relevant bodily sensations so that the proportion of training material is more relevant.

Potentially, a computer platform that allows a researcher to construct CBM-I packages by adding and removing blocks of relevant training stimuli would facilitate this research.

The present study offers an exciting and novel option for future research centred on the suggestion that CBM-I for panic has the potential to not only reduce panic symptoms in individuals with clinical levels of panic symptomatology, but also the potential for the CBM-I package to serve a preventative function for those with non-clinical panic. This future area of research is underpinned by the findings of the present study in reducing levels of anxiety sensitivity alongside panic symptomatology. As mentioned anxiety sensitivity is a known risk factor in individuals with non-clinical panic (McNally, 2002). To the author's knowledge, this would be the first CBM-I package that serves a dual function. When explaining this point further, panic orientated CBM-I may reduce panic symptoms in those with clinical levels of panic symptomatology, whilst also serving a preventative function for those at risk of developing panic disorder. This is an exciting area that could have a significant impact on the quality of life of many individuals, whilst at the same time representing a significant saving for mental health services. Looking to investigate the ability of the CBM-I package used by the present study to reduce levels of anxiety sensitivity in non-clinical panickers with an extended follow-up period would help to shed light on the ability of CBM-I to serve a preventative function.

4.7. Conclusions

The results of the present study suggest that an online multi-session CBM-I package can reduce levels of panic and catastrophic misinterpretations in individuals with clinical levels of panic symptomatology. Interestingly, although not the primary focus of the training material contained within the CBM-I package, levels of anxiety sensitivity were also reduced post-CBM-I. Despite a growing evidence base detailing the enhancing impact of mental imagery of CBM-I procedures, imagery was not found to significantly improve outcomes on

the PDSS or the ASI. As only four of the six participants responded to the CBM-I training, the results of the present study lend partial support to the catastrophic misinterpretation model of panic disorder (Clark, 1986). Discussion of observed differences between interpretation bias as measured by the ranking and believability tasks support the cognitive model of selective processing (Mathews & Mackintosh, 1998). In doing so the reflexive nature of catastrophic cognitions (Clark et al., 1997) in those with clinical levels of panic is also supported. An interesting finding of the present study was the reduction of levels of anxiety sensitivity post CBM-I. This finding highlights a novel option for future research focused on the ability of CBM-I for panic to serve a preventative function for those with non-clinical levels of panic. With this in mind, it would highlight the exciting potential of CBM-I for panic disorder to serve a dual therapeutic-preventative function in individuals with clinical and non-clinical levels of panic.

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Appendices

Appendix A: Newcastle and North Tyneside 2 Ethical Approval

NHS
Health Research Authority
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21 May 2013

Mr James Peter Hampson
Trainee Clinical Psychologist
Clinical Psychology Dept
Cambridge and Peterborough Mental Health Foundation Trust
University of East Anglia
Norwich, Norfolk
NR4 7TJ

Dear Mr Hampson

Study title:	**A single case series investigation of the efficacy of an internet delivered multi-session cognitive bias modification - interpretation task in a clinical population with Panic Disorder**
REC reference:	**13/NE/0171**
Protocol number:	**N/A**
IRAS project ID:	**124494**

The Proportionate Review Sub-committee of the NRES Committee North East - Newcastle & North Tyneside 2 reviewed the above application by Correspondence.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the Co-ordinator Gillian Mayer, nrescommittee.northeast-newcastleandnorthtyneside2@nhs.net.

Ethical opinion

The following issues were raised by the sub-committee and as chief investigator you responded accordingly as follows –

1. Clarification was requested why there are three baseline groups of one, two or three weeks before the actual intervention.

   You explained that the three baselines are in effect a 'control' period to which the outcome of completing the computer task will be compared against. Using three baselines is in keeping with other studies looking at Cognitive Bias Modification. The inclusion of three baselines allows the inference that completing the task had an impact on levels of panic or interpretation bias.

2. It was noted that participants may complete the computer interventions at a time of their choosing but should be drug free when completing the package. It was not

clear how this can be monitored. Help or support to upset patients is not always available. It would be better to have recommended times for the patients to complete the packages when immediate help from the research team or a clinician is available rather than asking them to contact their GP if upset. This research has not been completed with this clinical population so the outcomes cannot be predicted.

You noted that in relation to participants being drug free when completing the package, this is no longer the case and this was an error which should not have been included. Participants may be taking medication in relation to their mood and still meet the inclusion criteria. It is intended that participants will negotiate a time to complete the computer task which will correspond with the availability of the researcher.

3. The participant information sheet needs to state that this research is for an educational qualification.

   You provided a revised information sheet accordingly.

4. The consent form needs to note a section regarding the use of quotes to be included.

   You provided a revised consent for accordingly.

5. Participants are to be entered for a prize draw for a voucher and in view of the time spent by participants it was considered that each participant should have a voucher. There are only nine participants and no travel expenses are being provided.

   You explained that no travel expenses are being provided as the participants are not expected to travel. The researcher will meet participants at their home to complete outcome measures and the computer task is internet based. Ideally, all participants would be given a voucher, however due to the financial restrictions placed on the researcher by the University this has not been possible.

6. Clarification was requested if patients' medical records will show that patients have been screened for physical causes of their symptoms.

   You informed that patients will be taken from a mental health service and as such it is understood that participants will have been screened for physical causes of their symptoms at point of referral. Point of referral into the service is via their GP.

7. Clarify what training the PhD student has had/will have in terms of consent and one to one patient support for this type of research.

   It was clarified that the researcher has completed the good clinical practice training. Supervision will be provided by a member of staff at the University of East Anglia. This member of staff will be a qualified clinical psychologist who has research experience. The researcher also works clinically as part of their doctorate and manages obtains consent for various aspects of treatment on a regular basis.

8. The PDSS asks about "during the last week" and "in the past week" but patients are being asked to complete these instruments daily and this does not match up – clarification was requested if this should instrument be used daily in this way.

   You explained that the PDSS is a widely used measure of panic disorder in both clinical and research settings. Participants are required to complete this measure daily as the data this brings will allow for visual analysis of the data. It

will be explained to patients that they consider their mood over the past seven days when completing the measure. These results will be supplemented with data taken from the visual analogue scales that participants will complete daily.

9. The follow-up is immediately after the seven day intervention and then on a single occasion one week later and this seems unusual to require several baseline measures but then only a single follow up measure - further explanation was requested.

   You informed that the researcher will meet participants immediately after the completion of the final computer task to complete outcome measures to see whether the task has impacted on interpretation bias or levels of panic disorder. The varying baseline conditions allow a more robust level of evidence that it is the computer task that has brought about an effect. The final follow up session, is to see whether the impact of the computer task has been maintained after one week. This is not staggered as it does not impact on the ability of the research design to measure change.

The sub-committee was satisfied with the responses given to the issues raised and the revised documentation provided.

On behalf of the Committee, the sub-committee gave a **Favourable** ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.
Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

You should notify the REC in writing once all conditions have been met (except for

site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which can be made available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Approved documents

The documents reviewed and approved were:

Document	*Version*	*Date*
Evidence of insurance or indemnity	Zurich Municipal (for UEA)	15 May 2012
GP/Consultant Information Sheets	3	25 April 2013
Interview Schedules/Topic Guides	2	15 February 2013
Investigator CV	James Hampson	10 May 2013
Letter from Sponsor		03 May 2013
Other: Letter re indemnity (UEA)		03 May 2013
Other: CV for academic supervisor M Ononaiye		10 May 2013
Other: CV for academic supervisor J Hodgekins		
Participant Consent Form	4	20 May 2013
Participant Information Sheet	4	20 May 2013
Protocol	3	25 April 2013
Questionnaire: GAD-7 Patient Questionnaire		
Questionnaire: Panic Disorder Severity Scale - Self-Report Form		
Questionnaire: PHQ-9 Patient Questionnaire		
Questionnaire: Brief Bodily Sensations Interpretation		
Questionnaire: Visual Analogue Scales		
REC application	IRAS 3.5	10 May 2013
Referees or other scientific critique report	University East Anglia	22 February 2013
Summary/Synopsis	2 (Flow Diagram)	15 February 2013

Membership of the Proportionate Review Sub-Committee

The members of the Sub-Committee who took part in the review are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.
information is available at National Research Ethics Service website > After Review

13/NE/0171 **Please quote this number on all correspondence**

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

With the Committee's best wishes for the success of this project.

Yours sincerely
pp

Professor Philip M Preshaw
Chair

Email: nrescommittee.northeast-newcastleandnorthtyneside2@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

"After ethical review – guidance for researchers"

Copy to: Mrs Sue Steel – Research & Enterprise Services, University of East Anglia

Mr Stephen Kelleher – R&D Office, Cambridgeshire and Peterborough NHS Foundation Trust

NHS
Health Research Authority

NRES Committee North East - Newcastle & North Tyneside 2
Room 002
TEDCO Business Centre
Rolling Mill Road
Jarrow
NE32 3DT

Tel: 0191 428 3561

18 March 2014

Mr James Peter Hampson
Trainee Clinical Psychologist
Cambridge and Peterborough Mental Health Foundation Trust
University of East Anglia
Clinical Psychology Course
Norwich
Norfolk
NR4 7TJ

Dear Mr Hampson

Study title:	**A single case series investigation of the efficacy of an internet delivered multi-session cognitive bias modification - interpretation task in a clinical population with Panic Disorder.**
REC reference:	**13/NE/0171**
Protocol number:	**N/A**
Amendment number:	**Substantial Amendment 2**
Amendment date:	**13 February 2014**
IRAS project ID:	**124494**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The committee requested clarification / further information on the following points:

1. The title of the study was now incorrect as the sample was no longer a clinical population with Panic Disorder. Please clarify the new title of the study.

   You responded that the title of the study was still accurate as it refers to 'clinical levels' of panic and all participants would still be experiencing 'clinical levels' of panic disorder as measured by the PDSS. Individuals could experience clinical levels of panic disorder without seeking support. The PDSS was used within Improving Access to Psychological Services to measure panic disorder. The only change was that participants may not be help-seeking. In essence these individuals would not be in too dissimilar position as individuals recruited from NHS services as they were individuals predominantly who would be on waiting lists and so not receiving on-going support.

2. Clarification on what upper score on the PDSS would be considered concerning for an individual who was not in the care of a clinical service or seeking help. If there was no upper score then clarification on how this scale was used and interpreted. There was no information on what actions would be taken, or if no actions would be taken how that is justified, if any individual was recruited whose score on that scale would indicate a cause for concern.

   You explained that the PDSS was used to measure responses to the cognitive training programme. For all participants who responded to poster/email advertisements you would include in the protocol that would suggest participants visit their GP to seek support. However, some people do not wish to, or do not feel in a position to access support. If their symptomatology is so severe that this GP care was not sufficient, the current information contained in the information sheet referred to contacting the emergency services was applicable.

3. What actions would be taken (other than exclusion), or if no actions would be taken how was that justified, if any individual was recruited whose score on the PHQ 9 was above 19, and/or, who was considered to abuse substances. How, when and by whom would the latter be determined. When, how and by whom would individuals excluded on this criterion be informed of that. What additional advice would they be given, by whom and when and if no advice would be given how was that justified.

   You replied that should an individual score above 19 on the PHQ9 or be deemed to be abusing substances then you would suggest that they contact their GP to initiate support. As in the point above, individuals may not feel that they were ready to access support and this point needed to be respected. Should pressure be applied to an individual to seek help, if they were not ready, then it may impact on the extent to which they seek support in the future.

4. In the application you stated it was proposed to recruit from counselling and well-being services at the University; the PIS also refer to this. The committee requested clarification on how that could be achieved with this amendment. At present there were no details given as to how eligible potential participants would be identified from those services, contacted, given information and consented to the study.

   You included a tracked change copy of the protocol to make this explicit, to this response. Referral from UEA wellbeing and counselling services would be made in the exact same way as in NHS services, with participants being identified by clinicians embedded within these teams.

5. The Protocol states that should a person responding to the Poster or bulletin invitation meet the eligibility criterion they would be given an information sheet. Given the stated eligibility criterion this would not appear possible as the Protocol stated that baseline data collection (and hence participation which should not normally proceed informed consent in ethical research) was required to identify eligibility.

   You explained that the procedure for participants responding to poster/email advertisements mirrored the procedure for other participants from the point of contact with yourself onwards, as approved in the original submission. Completing screening measures was separate from baseline data and was not used in this way. The only difference in recruiting participants in this way was that in essence they were self-referring and had not been identified by clinicians. It was important to note that the baseline data collection phase and screening were separate. Screening measures were not included in data analysis. Baseline data collection followed informed consent being obtained.

6. If this change were applied (above point 5) the study would contain a non-homogenous sample, the sample, including both clinical and non-clinical participants would be likely to be non-homogenous on several parameters which may well affect response to the intervention. How would this be accounted for in the analysis models and how would the results be reported. Given the already extremely small proposed total sample of nine participants how could the sub-group analyse - clinical and non-clinical samples which would be required - be conducted with any degree of objectivity or rigour.

   You replied that the case series design methodology adopted by the study was well suited to small scale research, and was often employed as a pre-cursor to larger scale trials. In this methodology the baseline phase completed by each participant was in effect their individual control period against which change was measured. Therefore, recruiting form different populations does not impact on homogeneity in the same way that it would if participants were being compared against one another. Case series designs usually recruit between 6 and 9 participants and as such recruiting 6 participants was in line with the suggested sample size for the methodology used and therefore appropriate. Other studies investigating CBM-I have recruited between 6 and 9 participants, with articles being published in peer reviewed journals using 6 participants.

7. There was no information on if people must be experiencing symptoms and how severe or long lasting those symptoms must be for them to be eligible in the Protocol or PIS. If it was proposed that asymptomatic people were to now be eligible it was unclear what scientific value data collected from them could have in an intervention study. If only symptomatic people were to be eligible (as the Poster suggests) it must be clearly explained how potential participants will be made aware of that and information given in the PIS on how severe or long lasting those symptoms must be for them to be eligible.

   You advised that the PDSS measures panic symptomatology and measures symptoms over the past 7 days. This measure was used within NHS services and was well established. The purpose of the baseline phase for each participant was to allow for the stability of symptoms to be measured. You were slightly unsure as to where the suggestion asymptomatic individuals would be recruited to the study has come from and you apologised if that was unclear in the amendment. The inclusion criterion stated that participants must score above 8 which was the clinical cut off point for panic disorder as identified by the PDSS. In line with the procedure approved in your original submission, the information sheet was given to participants if they met inclusion criterion. For people who make contact with yourself after responding to the poster/email this screening would be completed at that point. That mirrored the procedure as outlined and approved in the original submission for participants recruited from the NHS. As each participant acted as their own 'control' severity and duration was not important in relation to the aims of the study, nor does it impact its clinical rigour.

8. It was unclear how, given that the original study required nine clinical participants, for adequate power, the study aims could be achieved with less than that and a new sub-sample of non-clinical participants introduced. Clarification was requested on how many clinical participants had been recruited and completed the study. What is the target number for recruitment of the non-clinical sample proposed here and how could the scientific integrity and rigour of the study be preserved.

   You answered that to date one participant had completed the study. It was important to stress that the study did not compare groups, it was not comparing a non-clinical group against a clinical group. All participants would meet the clinical cut off for panic disorder as measured by the PDSS. Whether participants are help-seeking or not does not impact on the scientific integrity of the study as all participants will still meet a clinical cut

off for panic disorder. The effectiveness of the CBM-I programme was being measured by the PDSS. As mentioned above, studies utilising single case series design have been published in peer reviewed journals using 6 participants. This number was considered the norm with this methodology.

9. The following points needed to be amended / added to the PIS, along with the version number and date:
   - The study title, researcher's name and names of academic supervisor(s) should be given at the top of the first page as the text refers to these people.
   - There was no information in the PIS on the screening tools that would be used, the eligibility criterion and in particular the potential exclusion on the basis of clinical/symptom related measures and the discovery of substance abuse.
   - There was no indication in the PIS that people must be symptomatic to be eligible.
   - If there was an incentive/reward for participation this must be determined in advance and stated in the PIS.
   - The section on possible disadvantages was neither appropriate nor relevant to a person who was not in receipt of care and/or who was asymptomatic.

   You explained that the changes were made to the document and one by tracked changes. Using a prize-draw was approved in the original submission. As one participant had already completed the study changing this was not feasible. You were slightly unsure as to a number of changes such as the need to include the study title and researcher/supervisor name as this was not highlighted in the original approval.

10. Clause five (in the consent form) would not appear appropriate nor relevant to a person who was not in receipt of care and/or who was asymptomatic.

    You felt that individuals who were not help-seeking should still have the option to inform their GP of their participation.

The sub committee was satisfied with the responses given to the issues raised along with the revised documentation.

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Notice of Substantial Amendment (non-CTIMPs)	Substantial Amendment 2	13 February 2014
Advertisement	Advertisement Poster / Version 1	10 February 2014
Participant Consent Form	Version 5 (Tracked Changes)	06 March 2014
Protocol	Version 6	06 March 2014
Participant Information Sheet	Version 5 (Tracked Change)	06 March 2014
Email Staff and Student Bulletin Content		
Covering Letter	Email from James Hampson	

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

13/NE/0171:	Please quote this number on all correspondence

Yours sincerely

pp

Dr Alasdair MacSween
Chair

E-mail: nrescommittee.northeast-newcastleandnorthtyneside2@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Mr Stephen Kelleher, Cambridgeshire and Peterborough NHS Foundation Trust*
Mrs Sue Steel, University of East Anglia

Appendix C: Recruitment Timeline

- 22/03/2013 – Meeting with CPFT service lead, agreed to allow recruitment from IAPT services within CPFT
- 01/05/2013 – 01/08/13 – Ongoing difficulties with computer platform used to deliver CBM-I
- 10/05/2013 – Apply for NHS ethical approval (proportionate review)
- 21/05/2013 – Receive ethical approval from REC
- 22/05/2013 – Apply for ethical approval from CPFT research and development department
- 13/06/2013 – Receive approval from CPFT research and development department
- 10/09/2013 – Email sent out to IAPT team leaders to arrange to present research to team
- 11/09/2013 – Meeting arrange to present at joint Cambridge IAPT meeting on the 29/10/2013
- 20/09/2013 – Email received back from Huntingdon IAPT team leader, appointment arranged to present to team on 04/10/2013
- 30/09/2013 – Email received back from Fenland IAPT team leader, appointment arrange to present to team on 14/10/2013
- 04/10/2013 – Huntingdon IAPT team meeting attended
- 14/10/13 – Fenland IAPT team meeting attended
- 29/10/2013 – Attended Cambridge IAPT meeting, presentation cut to five minutes due to full agenda
- 30/10/2013 – Email sent to service lead requesting information regarding study to be forwarded to various teams
- 30/10/2013 – Extension request submitted for thesis
- 10/11/2013 – Approached Adult ADHD service to discuss potential to use as a recruitment site
- 11/11/2013 – Minor amendment made to clarify role of secondary mental health teams in recruitment
- 11/11/2013 – Email send to Peterborough IAPT service lead to request to meet
- 15/11/2013 – Arranged appointment to present to Peterborough IAPT team on 29/11/2013
- 25/11/2013 – Email sent to speciality service lead to add ADHD team as recruitment site
- 25/11/2013 – Permission received to recruit from adult ADHD team
- 29/11/2013 – Attended Peterborough IAPT team meeting
- 17/12/2013 – Extension granted, new hand in date 06/05/2014
- 08/01/2014 – Email sent to IAPT lead requesting research kept in mind and email is forwarded to teams
- 10/02/2014 – NHS ethics committee contacted requesting clarification regarding potential amendment
- 13/02/2014 – Response received from ethics committee noting substantial amendment needed to recruit from UEA
- 03/03/2014 – Email sent to IAPT service lead requesting further meetings with Cambridge IAPT teams
- 06/03/2014 – Substantial amendment documentation submitted
- 10/03/2014 – Emails sent to Cambridge IAPT team leads
- 14/03/2014 – Second extension request submitted
- 18/03/2014 – Substantial amendment approval received

- 20/03/2014 – Arranged to attend Cambridge IAPT team meetings on the 01/04/2014 and 02/04/2014
- 25/03/2014 – Research advertisement included in UEA staff and student e-Bulletin
- 01/04/2014 – Attended Cambridge North IAPT team meeting
- 02/04/2014 – Attended Cambridge South IAPT team meeting
- 10/04/2014 – Extension request granted, new hand in date 30/06/2014
- 27/05/2014 – Recruitment completed (6 participants)

Appendix D: Patient Health Questionnaire (PHQ-9)

PHQ-9 Patient Questionnaire

Participant Identification Number: _____ Date: _____

Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1 Little interest or pleasure in doing things	0	1	2	3
2 Feeling down, depressed, or hopeless	0	1	2	3
3 Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4 Feeling tired or having little energy	0	1	2	3
5 Poor appetite or overeating	0	1	2	3
6 Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7 Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8 Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9 Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

PHQ9 total score

Appendix E: Brief Symptom Inventory (BSI)

Brief Symptom Inventory

"Here I have a list of problems people sometimes have. As I read each one to you, I want you to tell me HOW MUCH THAT PROBLEM HAS DISTRESSED OR BOTHERED YOU <u>DURING THE PAST 7 DAYS INCLUDING TODAY</u>. These are the answers I want you to use. *[Hand card and read answers.]* **Do you have any questions?"**

0 = Not at all
1 = A little bit
2 = Moderately
3 = Quite a bit
4 = Extremely
R = Refused

<u>DURING THE PAST 7 DAYS, how much were you distressed by:</u>
1. Nervousness or shakiness inside 0 1 2 3 4 R
2. Faintness or dizziness 0 1 2 3 4 R
3. The idea that someone else can control your thoughts 0 1 2 3 4 R
4. Feeling others are to blame for most of your troubles 0 1 2 3 4 R
5. Trouble remembering things 0 1 2 3 4 R
6. Feeling easily annoyed or irritated 0 1 2 3 4 R
7. Pains in the heart or chest 0 1 2 3 4 R
8. Feeling afraid in open spaces 0 1 2 3 4 R
9. Thoughts of ending your life 0 1 2 3 4 R

<u>DURING THE PAST 7 DAYS, how much were you distressed by:</u>
10. Feeling that most people cannot be trusted 0 1 2 3 4 R
11. Poor appetite 0 1 2 3 4 R
12. Suddenly scared for no reason 0 1 2 3 4 R
13. Temper outbursts that you could not control 0 1 2 3 4 R
14. Feeling lonely even when you are with people 0 1 2 3 4 R
15. Feeling blocked in getting things done 0 1 2 3 4 R
16. Feeling lonely 0 1 2 3 4 R
17. Feeling blue 0 1 2 3 4 R
18. Feeling no interest in things 0 1 2 3 4 R

<u>DURING THE PAST 7 DAYS, how much were you distressed by:</u>
19. Feeling fearful 0 1 2 3 4 R
20. Your feelings being easily hurt 0 1 2 3 4 R
21. Feeling that people are unfriendly or dislike you 0 1 2 3 4 R
22. Feeling inferior to others 0 1 2 3 4 R
23. Nausea or upset stomach 0 1 2 3 4 R
24. Feeling that you are watched or talked about by others 0 1 2 3 4 R
25. Trouble falling asleep 0 1 2 3 4 R
26. Having to check and double check what you do 0 1 2 3 4 R
27. Difficulty making decisions 0 1 2 3 4 R

<u>DURING THE PAST 7 DAYS, how much were you distressed by:</u>
28. Feeling afraid to travel on buses, subways, or trains 0 1 2 3 4 R
29. Trouble getting your breath 0 1 2 3 4 R
30. Hot or cold spells 0 1 2 3 4 R
31. Having to avoid certain things, places, or activities because they frighten you 0 1 2 3 4 R
32. Your mind going blank 0 1 2 3 4 R
33. Numbness or tingling in parts of your body 0 1 2 3 4 R
34. The idea that you should be punished for your sins 0 1 2 3 4 R
35. Feeling hopeless about the future 0 1 2 3 4 R
36. Trouble concentrating 0 1 2 3 4 R

DURING THE PAST 7 DAYS, how much were you distressed by:

37. Feeling weak in parts of your body 0 1 2 3 4 R
38. Feeling tense or keyed up 0 1 2 3 4 R
39. Thoughts of death or dying 0 1 2 3 4 R
40. Having urges to beat, injure, or harm someone 0 1 2 3 4 R
41. Having urges to break or smash things 0 1 2 3 4 R
42. Feeling very self-conscious with others 0 1 2 3 4 R
43. Feeling uneasy in crowds 0 1 2 3 4 R
44. Never feeling close to another person 0 1 2 3 4 R
45. Spells of terror or panic 0 1 2 3 4 R

DURING THE PAST 7 DAYS, how much were you distressed by:

46. Getting into frequent arguments 0 1 2 3 4 R
47. Feeling nervous when you are left alone 0 1 2 3 4 R
48. Others not giving you proper credit for your achievements 0 1 2 3 4 R
49. Feeling so restless you couldn't sit still 0 1 2 3 4 R
50. Feelings of worthlessness 0 1 2 3 4 R
51. Feeling that people will take advantage of you if you let them 0 1 2 3 4 R
52. Feeling of guilt 0 1 2 3 4 R
53. The idea that something is wrong with your mind 0 1 2 3 4 R

Appendix F: Panic Disorder Severity Scale (PDSS)

PDSS

Participant Identification Number: Date:

Several of the following questions refer to panic attacks and limited symptom attacks. For this questionnaire we define a panic attack as a sudden rush of fear or discomfort accompanied by at least 4 of the symptoms listed below. In order to qualify as a sudden rush, the symptoms must peak within 10 minutes. Episodes like panic attacks but having fewer than 4 of the listed symptoms are called limited symptom attacks. Here are the symptoms to count:

□ Rapid or pounding heartbeat □ Chest pain or discomfort □ Chills or hot flushes □ Sweating

□ Nausea □ Fear of losing control or going crazy □ Trembling or shaking □ Dizziness or faintness

□ Breathlessness □ Feelings of unreality □ Fear of dying □ Feeling of choking □ Numbness or tingling

1. How many panic and limited symptoms attacks did you have during the week?

0 No panic or limited symptom episodes

1 Mild: no full panic attacks and no more than 1 limited symptom attack/day

2 Moderate: 1 or 2 full panic attacks and/or multiple limited symptom attacks/day

3 Severe: more than 2 full attacks but not more than 1/day on average

4 Extreme: full panic attacks occurred more than once a day, more days than not

2. If you had any panic attacks during the past week, how distressing (uncomfortable, frightening) were they while they were happening? (If you had more than one, give an average rating. If you didn't have any panic attacks but did have limited symptom attacks, answer for the limited symptom attacks.)

0 Not at all distressing, or no panic or limited symptom attacks during the past week

1 Mildly distressing (not too intense)

2 Moderately distressing (intense, but still manageable)

3 Severely distressing (very intense)

4 Extremely distressing (extreme distress during all attacks)

3. During the past week, how much have you worried or felt anxious about when your next panic attack would occur or about fears related to the attacks (for example, that they could mean you have physical or mental health problems or could cause you social embarrassment)?

0 Not at all

1 Occasionally or only mildly

2 Frequently or moderately

3 Very often or to a very disturbing degree

4 Nearly constantly and to a disabling extent

4. During the past week were there any places or situations (e.g., public transportation, movie theatres, crowds, bridges, tunnels, shopping malls, being alone) you avoided, or felt afraid of (uncomfortable in, wanted to avoid or leave), because of fear of having a panic attack? Are there any other situations that you would have avoided or been afraid of if they had come up during the week, for the same reason? If yes to either question, please rate your level of fear and avoidance this past week.

0 None: No fear or avoidance

1 Mild: Occasional fear and/or avoidance but I could usually confront or endure the situation. There was little or no modification of my lifestyle due to this.

2 Moderate: Noticeable fear and/or avoidance but still manageable. I avoided some situations, but I could confront them with a companion. There was some modification of my lifestyle because of this, but my overall functioning was not impaired.

3 Severe: extensive avoidance. Substantial modification of my lifestyle was required to accommodate the avoidance making it difficult to manage usual activities.

4 Extreme: pervasive disabling fear and/or avoidance. Extensive modification in my lifestyle was required such that important tasks were not performed.

5. During the past week, were there any activities (e.g., physical exertion, sexual relations, taking a hot shower or bath, drinking coffee, watching an exciting or scary movie) that you avoided, or felt afraid of (uncomfortable doing, wanted to avoid or stop), because they caused physical sensations like those you feel during panic attacks or that you were afraid might trigger a panic attack? Are there any other activities that you would have avoided or been afraid of if they had come up during the week for that reason? If yes to either question, please rate your level of fear and avoidance of those activities this past week.

0 No fear or avoidance of situations or activities because of distressing physical sensations

1 Mild: occasional fear and/or avoidance, but usually I could confront or endure with little distress activities that cause physical sensations. There was little modification of my lifestyle due to this.

2 Moderate: noticeable avoidance but still manageable. There was definite, but limited, modification of my lifestyle such that my overall functioning was not impaired.

3 Severe: extensive avoidance. There was substantial modification of my lifestyle or interference in my functioning.

4 Extreme: pervasive and disabling avoidance. There was extensive modification in my lifestyle due to this such that important tasks or activities were not performed.

6. During the past week, how much did the above symptoms altogether (panic and limited symptom attacks, worry about attacks, and fear of situations and activities because of attacks) interfere with your ability to work or carry out your responsibilities at home? (If your work or home responsibilities were less than usual this past week, answer how you think you would have done if the responsibilities had been usual.)

0 No interference with work or home responsibilities

1 Slight interference with work or home responsibilities, but I could do nearly everything I could if I didn't have these problems.

2 Significant interference with work or home responsibilities, but I still could manage to do the things I

needed to do.

3 Substantial impairment in work or home responsibilities; there were many important things I couldn't do because of these problems.

4 Extreme, incapacitating impairment such that I was essentially unable to manage any work or home

responsibilities.

7. During the past week, how much did panic and limited symptom attacks, worry about attacks and fear of situations and activities because of attacks interfere with your social life? (If you didn't have many opportunities to socialize this past week, answer how you think you would have done if you did have opportunities.)

0 No interference

1 Slight interference with social activities, but I could do nearly everything I could if I didn't have these

problems.

2 Significant interference with social activities but I could manage to do most things if I made the effort.

3 Substantial impairment in social activities; there are many social things I couldn't do because of these problems.

4 Extreme, incapacitating impairment, such that there was hardly anything social I could do.

Appendix G: Anxiety Sensitivity Index (ASI)

Reiss-Epstein-Gursky A.S.I.

Name _____ **Today's Date** _____

Circle the one phrase that best represents the extent to which you agree with the item. If any of the items concern something that is not part of your experience (e.g., "It scares me when I feel shaky" for someone who has never trembled or had the "shakes"), answer on the basis of how you think you might feel *if you had* such an experience. Otherwise, answer all items on the basis of your own experience.

1. It is important to me not to appear nervous.

Very Little A Little Some Much Very Much

2. When I cannot keep my mind on a task, I worry that I might be going crazy.

Very Little A Little Some Much Very Much

3. It scares me when I feel "shaky" (trembling).

Very Little A Little Some Much Very Much

4. It scares me when I feel faint.

Very Little A Little Some Much Very Much

5. It is important to me to stay in control of my emotions.

Very Little A Little Some Much Very Much

6. It scares me when my heart beats rapidly.

Very Little A Little Some Much Very Much

7. It embarrasses me when my stomach growls.

Very Little A Little Some Much Very Much

(Over)

8. It scares me when I am nauseous.

Very Little A Little Some Much Very Much

9. When I notice that my heart is beating rapidly, I worry that I might have a heart attack.

Very Little A Little Some Much Very Much

10. It scares me when I become short of breath.

Very Little A Little Some Much Very Much

11.When my stomach is upset, I worry that I might be seriously ill.

Very Little A Little Some Much Very Much

12. It scares me when I am unable to keep my mind on a task.

Very Little A Little Some Much Very Much

13.Other people notice when I feel shaky.

Very Little A Little Some Much Very Much

14. Unusual body sensations scare me.

Very Little A Little Some Much Very Much

15. When I am nervous, I worry that I might be mentally ill.

Very Little A Little Some Much Very Much

16.It scares me when I am nervous.

Very Little A Little Some Much Very Much

Appendix H: Brief Body Sensations Interpretation Questionnaire (BBSIQ)

Here are some outline descriptions of situations in which it is not quite clear what is happening. Below the descriptions you will see three possible explanations for the situations. After you have read each description arrange the possible explanations in the order in which they would be most likely to come to your mind if you found yourself in a similar situation. So the one that you would consider most likely to be true should come first, and the one that you would consider least likely to be true should come third. Do not think too long before deciding. We want you first impressions, and do not worry if none of them fits with what you actually did.

1. You have visitors round for a meal and they leave sooner than expected, why?

a. They did not wish to outstay their welcome

b. They had another pressing engagement to go to

c. They did not enjoy the visit and were bored with your company

2. You feel short of breath, why?

a. You are developing the flu

b. You are about to suffocate or stop breathing

c. You are physically "out of shape"

3. Your vision has become slightly blurred, why?

a. You have strained your eyes slightly

b. You need to get glasses or change your existing glasses

c. This is the sign of a serious illness

4. You go into a shop and the assistant ignores you, why?

a. They are bored with their job, and this makes them rude

b. They are concentrating very hard on something else

c. They find you irritating and resent your presence

5. You feel light headed and weak, why?

a. You are about to faint

b. You need to get something to eat

c. You didn't get enough sleep last night

6. You smell smoke, why?

a. Your house is on fire

b. Some food is burning

c. Someone is smoking a cigarette

7. A friend suggest that you change the way that you're doing a job in your own house, why?

a. They are trying to be helpful

b. They think that you're incompetent

c. They have done the job more often and know an easier way

8. Your chest feels uncomfortable and tight, why?

a. You have indigestion

b. You have a sore muscle

c. Something is wrong with your heart

9. You wake with a start in the middle of the night, thinking you heard a noise, but all is quiet. What woke you up?

a. You were woken by a dream

b. A burglar broke into your house

c. A door or window rattled in the wind

10. You are introduced to someone at a party who fails to reply to a question you ask them, why?

a. They did not hear the question

b. They think you are uninteresting and boring

c. They are preoccupied with something else at the time

11. You notice your heart is beating quickly and pounding, why?

a. Because you have been physically active

b. Because there is something wrong with your heart

c. Because you are excited

12. You suddenly feel confused and are having difficulty in thinking straight, why?

a. You are going out of your mind

b. You are coming down with a cold

c. You've been working too hard and need a rest

13. A letter marked "URGENT" arrives in the post. What is in the letter?

a. It is a circular designed to attract your attention

b. You forgot to pay a bill

c. News that someone you know has died or is seriously ill

14. You notice that your heart is pounding, you feel breathless, dizzy and unreal, why?

a. You have been overdoing it and are overtired

b. Something you ate disagreed with you

c. You are dangerously ill or going mad

Now that you have answered the preceding questions we would be grateful if you would answer one more question about each of the ambiguous situations. Please return to the start of the questions and then rate the extent to which you think each of the three explanations for a situation would be like to be true if you found yourself in that situation.

Use the scale below for your ratings. Put a number between 0 and 8 next to each of the three explanations in the text. Do not worry if your ratings appear to be different from your previous answers, and please do not change any of your original answers.

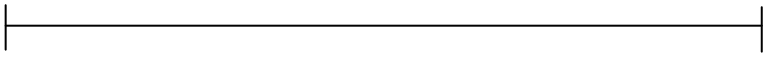
0 - - - - - - 1 - - - - - - 2 - - - - - - 3 - - - - - - 4 - - - - - - 5 - - - - - - 6 - - - - - - 7 - - - - - 8

Not at all likely	A Little	Moderately	Very	Extremely likely

Appendix I: Visual Analogue Scales (VAS)

Please rate the extent to which you have been distressed by the symptoms highlighted below over the past 24 hours. Mark on the line and number the extent of which each statement below is true.

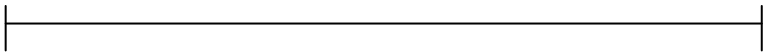
Today bodily sensations have been distressing for me



0 100

Not at all Excessively

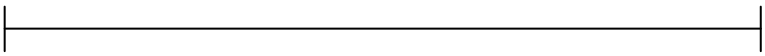
Today feelings of unreality have been distressing for me



0 100

Not at all Excessively

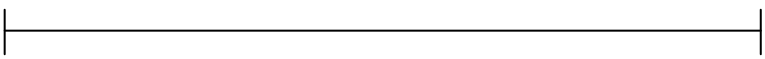
Today feelings of losing control have been distressing for me



0 100

Not at all Excessively

Today feelings that I am going to die have been distressing for me



0 100

Not at all Excessively

Appendix J: Cambridgeshire and Peterborough Research Approval

Cambridgeshire and Peterborough NHS
NHS Foundation Trust

Understanding children, young people and families

Research and Development Department

13 June 2013

R&D Ref: M00550

Mr James Hampson
Trainee Clinical Psychologist
Faculty of Health
University of East Anglia
Norwich, NR4 7TJ

Joint Research Office
Box 277
Addenbrooke's Hospital
Hills Road
Cambridge
CB2 0QQ

Direct Dial: 01223 596472 ext 6472
E-mail: beth.muldrew@cpft.nhs.uk
www.cpft.nhs.uk

Dear James

13/NE/0171: A single case series investigation of the efficacy of an internet-delivered multi-session cognitive bias modification - interpretation task in a clinical population with Panic Disorder

In accordance with the Department of Health's Research Governance Framework for Health and Social Care, all research projects taking place within the Trust must receive a favourable opinion from an ethics committee and approval from the Department of Research and Development (R&D) prior to commencement.

R&D have reviewed the documentation submitted for this project, and has undertaken a **site specific assessment** based on the information provided in the SSI form, and I am pleased to inform you that we have no objection to the research proceeding within CPFT.

Sponsor: University of East Anglia

Funder: University of East Anglia

End date: 03/02/2014

Protocol: Version 3.0 dated 25 April 2013

Conditions of Trust Approval:

- The project must follow the agreed protocol and be conducted in accordance with all Trust Policies and Procedures especially those relating to research and data management. Any mobile devices used must also comply with Trust policies and procedures for encryption.

- You and your research team must ensure that you understand and comply with the requirements of the NHS Confidentiality Code of Practice and the Data Protection Act 1998 and are aware of your responsibilities in relation to the Human Tissue Act 2004, Good Clinical Practice, the NHS Research Governance Framework for Health and

Social Care, Second Edition April 2005 and any further legislation released during the time of this study.

- Members of the research team must have appropriate substantive or honorary contracts with the Trust prior to the study commencing. Any additional researchers who join the study at a later stage must also hold a suitable contract.

- You and your research team must provide to R&D, as soon as available, the date of first patient first visit.

If the project is a clinical trial under the European Union Clinical Trials Directive the following must also be complied with:

- the EU Directive on Clinical Trials (Directive 2001/20/EC) and UK's implementation of the Directive: The Medicines for Human Use (Clinical Trials) Regulations 2004;

- the EU Directive on Principles and Guidelines for Good Clinical Practice (EU Commission Directive 2005/28/EC); and UK's implementation of the Directive: The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006;

Amendments
Please ensure that you submit a copy of any amendments made to this study to the R&D Department.

Annual Report
It is obligatory that an annual report is submitted by the Chief Investigator to the research ethics committee, and we ask that a copy is sent to the R&D Department. The yearly period commences from the date of receiving a favourable opinion from the ethics committee.

Please refer to our website www.cpft.nhs.uk for all information relating to R&D including honorary contract forms, policies and procedures and data protection.

Should you require any further information please do not hesitate to contact us.

Yours sincerely

Stephen Kelleher
Senior R&D Manager

Cc Sue Steel, Contracts Manager, Research and Enterprise Services West Office, University of East Anglia, Norwich Research Park, Norwich NR4 7TJ

Appendix K: Patient Information Sheet

University of East Anglia

Cambridgeshire and Peterborough NHS
NHS Foundation Trust

Understanding mental health, understanding people

Participant Information Sheet

A single case series investigation of the efficacy of an internet delivered multi-session cognitive bias modification – interpretation task in a population with clinical levels of Panic Disorder

Researcher: James Hampson

Research Supervisor: Dr Margo Ononaiye

Invitation Paragraph

You are being invited to take part in a research study, which is being undertaken as part of a Doctorate of Clinical Psychology qualification. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others or the researcher if you wish. Ask the researcher if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

What is the purpose of the study?

People who have frequent reoccurring panic attacks, often for no obvious reason, may have Panic Disorder. People who have Panic Disorder are believed to interpret bodily sensations in a catastrophic manner. People with Panic Disorder may overlook other possible reasons for these bodily symptoms. Research into Panic Disorder has suggested that the catastrophic misinterpretation of bodily sensations contributes to the development and maintenance of Panic Disorder. It is believed that by modifying these misinterpretations to look at bodily sensations in a different way will help reduce symptoms of Panic Disorder. The research aims to better understand how helpful changing these interpretation biases may be.

The aim of the study is to investigate whether Cognitive Bias Modification for Interpretation (CBM-I), an internet delivered computer programme delivered daily over 7 days, helps reduce levels of Panic and negative interpretation biases. The

researchers are trying to find out whether CBM-I might be a useful therapeutic tool to use in the future for other individuals who may have Panic Disorder.

Why have I been invited to take part?

We are approaching people who are experiencing clinical levels of Panic Disorder through NHS teams and through Wellbeing and Counselling services at the University of East Anglia. Equally, you may have responded to a poster or email advertisement or heard about the study through word of mouth and been keen to participate. Individuals referred from NHS and Wellbeing and Counselling services will have been referred by clinicians working within these teams. It is these people that will have first contacted you, to ensure confidentiality.

There will be approximately 9 participants selected in this way for the study.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and will be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive. If you do withdraw or in the unlikely event that you lose capacity to consent, the data collected up until this point may still be used.

What will happen to me if I take part?

If you do agree to take part, you will meet or speak with the researcher who will ask about your current problems. You will be asked to fill in some questionnaires which shouldn't take more than half an hour and the whole session will last about an hour. If you are referred to participate in the study by an NHS team you can choose whether to meet the researcher in your own home or an NHS premises. Should you be referred by the Wellbeing and Counselling services at the University of East Anglia, or respond to a poster or email advertisement, you can choose whether to meet the researcher on campus or in your own home. You will be allocated to a length of assessment period which could be between seven and eleven days. During this time, you will be asked to complete three short measures about Panic Disorder every day; these will take no longer than ten minutes. If you would like, the researcher can email or text you to remind you to fill these out.

Once this assessment phase (seven, nine or eleven days later) is complete and all the measures returned to the researcher, the researcher will arrange to meet with you again to complete the same measures that you did at the start. The researcher will also show you how to access the programme for the intervention phase. The programme is easy to use and you will be provided with clear and concise instructions.

The treatment phase (CBM-I) will last for seven consecutive days, whereby you must try to complete the CBM-I computer programme at home every day at a time that suits you. This should take around 30 minutes. You can have breaks in between the training material if this is needed. The same daily measures that you did before should also be completed. The researcher, if you choose, will send you text messages or emails to remind you to do this. If you get stuck, then you can always contact the researcher on the details given below.

After completing the seven day treatment phase, the researcher will meet with you again to ask you to complete the some more short questionnaires. You will then be contacted by the researcher one week later to see how you are getting on and to complete the same questionnaires again. The researcher will also ask for your feedback on the computer programme and whether you feel it has helped or not. The information taken from this feedback will be used in to write a separate piece of research exploring participants' experience of an internet delivered CBM-I package.

How long will I be involved for?

Participation in this research will last between twenty one to twenty five days. If you are on a waitlist for other therapy you may be asked to wait to begin this until the study completion. This will not affect your place on the waitlist and will be discussed with the appropriate clinician or service. The researcher also asks you to inform them of any anxiety medication you are taking and notify the researcher of any changes in medication during the study.

Expenses and payments

We are not able to offer reimbursements of travel costs or expenses. For the most part however, the researcher is happy to visit you in your home, as long as this okay with you.

As a thank you for taking part in the study you will be entered into a prize draw to win one of three prizes. These prizes are likely to be high street vouchers.

What do I have to do?

As mentioned above, the therapeutic tool we are trialling is called Cognitive Bias Modification for Interpretation (CBM-I). It is a computer programme containing training materials that has proven to help people with high levels of anxiety appraise or interpret situations in a different way. The researcher will show you how to use this programme guiding you through the first session and you will be provided with clear instructions and a troubleshooting guide. The programme is easy to use with on-screen instructions.

You will be presented on the screen with various scenarios and all you have to do is complete the sentence. You are asked to imagine yourself in these situations. There is only one possible solution to complete the sentence. You will be required to repeat

this using different scenarios 50 times during each daily session. The scenarios will be split in to groups of 10 and you are welcome to have a break in between. You are also needed to complete the daily measures, which take around 5-10 minutes to complete. It is really important for you to complete the daily sessions and the daily measures. If you would like reminding, the researcher can send you a daily text or email.

It is important that you do not consume alcohol or recreational drugs when completing the measures or when using the computer programme as not to influence the results of the study. It is also important to complete the tasks at a suitable time, in suitable surroundings and preferably free from distraction.

During your final assessment session you will be asked to take part in a short interview, exploring your experiences of the CBM-I programme and any changes this may have brought. This part of the final session will recorded, so that the researcher can accurately transcribe the feedback you give. You will have the opportunity to read this transcription to make sure it is a true reflection of what was discussed. The recordings will be anonymous, stored in a locked filing cabinet and destroyed at the end of the study. The information obtained during the interview will be used in a separate service based research project that aims to explore participant's experiences of using an internet delivered CBM-I programme.

What is the programme being tested?

The aim of CBM-I for Panic Disorder is to help people interpret ambiguous bodily symptoms in a less negative way. By repeated practice of interpreting panic related scenarios differently it is hoped that this will translate in to real life scenarios, which is why it is really important for you to imagine yourself in the situations. We know that negative interpretation biases are common within those who have Panic Disorder and are a maintaining factor in Panic Disorder. If the CBM-I training materials can help make these more positive, it is hoped that Panic symptomatology may be reduced. As this reflects early stages of clinical research, it is anticipated that CBM-I will be most beneficial alongside other treatments for Panic Disorder and enhance them.

What are the alternatives for treatment?

Cognitive Behavioural Therapy (CBT) is the main therapy available to help people who are experiencing Panic Disorder. CBM-I is being developed to supplement or be an extension of CBT. It may also be beneficial to those people on a waitlist for CBT or other treatments.

What are the possible disadvantages and risks of taking part?

There are few disadvantages to taking part. If you have been referred to participate in the study from a NHS or UEA counselling and wellbeing service, participation may result in delayed onset of alternative treatments if they have been offered to by

between 4 to 5 weeks, however participation will not affect your routine clinical care. There is no suggestion or evidence that completion of CBM-I worsens Panic related symptoms.

The various assessments and completion of questionnaires required may briefly disrupt your day-to-day routine as it may take up to an hour of your day. This is required for only one week. Some people may perceive the repetition of the training materials to be tedious, however it is this aspect of repeated practice that is hoped to change the autonomous way of interpreting information. Much like repeated exercise helps keep the body fit.

What are the possible benefits of taking part?

The aim of CBM-I is to help people to feel less worried and stressed about certain bodily symptoms. We hope that the CBM-I programme will help you. However, this cannot be guaranteed. The information we get from this study may help us treat future patients with Panic Disorder more effectively.

What happens when the research study stops?

When the research study finishes, all participants will receive normal care from the service you have already been in contact with or that referred you to this research. If you chose to delay the onset of any other intervention until study completion, the service offering this will be in contact.

What happens if something goes wrong?

In the unlikely event that you are harmed by taking part in a research project, there are no special compensation arrangements. If you are harmed by someone's negligence you may have grounds for legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of the study, the normal National Health Service complaints procedures should be available to you. Should you not be referred from a NHS team please contact Dr Margo Ononaiye, Research Supervisor. Any complaint about the way you have been dealt with during the study will be addressed.

In the event that you become distressed while participating in the study, please contact the researcher James Hampson in the first instance. If the researcher is not available please contact your GP services or primary care contact. In the event that this outside of normal working hours please contact your out of hours GP service, or the NHS 111 service (telephone: 111).

Will my taking part in this study be kept confidential?

If you consent to take part in the study the researcher will speak with the clinician or team that referred you. All information that is collected about you during the course

of the research will be kept strictly confidential. If the researcher is worried about risk to yourself or others during the course of the research then some information may need to be disclosed to relevant persons. In the unlikely event of this occurring it would be discussed with you first.

Any information about you that leaves or University premises will have your name and address removed so that you cannot be recognised from it, You will be allocated a participant number to help with this. If you consent, the researcher will inform your GP and the team responsible for your care about your involvement in the study. The researcher will send them a very brief summary of our assessment unless you do not wish us to do this.

Results and research data, with personal information removed will be looked at by my research supervisors. Dr Margo Ononaiye (Research Supervisor) will also have access to some personal details such as names, addresses and phone numbers in case a second point of contact is needed by yourself. These details will be kept securely and your name and contact details stored separately using your participant number to help ensure confidentiality.

Where and how long will records be stored?

Data will be stored in locked cabinets in local health care or university premises. It will be kept for 5 years after the completion of the study and then destroyed.

What will happen to the results of the research study?

The results of the study will be reported as anonymous data. The study will be seen by colleagues and supervisors at the University of East Anglia, Doctoral programme in psychology and other members of the research team. Results may also become available more publicly if the research is published, however no identifiable material will be published.

Who is organising and funding the research?

The study has been designed by James Hampson Trainee Clinical Psychologist who is a student from the University of East Anglia and research supervisors. The research is being carried out as part of training for a Doctorate in Clinical Psychology. It is hoped that this research will further the CBM literature and develop the use of CBM as a therapeutic tool.

Who has reviewed the study?

The research has been considered and approved by the NHS Research Ethics Committee. The research has also been reviewed and approved by the University of East Anglia.

Thank you for reading this. If you need further information, please contact the researcher directly. The researcher will give you this information sheet to keep as well as a signed consent form if you agree to take part in the study.

Contact for further information:

If you would like any more information about the study or need to contact the researcher, please feel free to contact James Hampson (Trainee Clinical Psychologist) or Margo Ononaiye (Research Supervisor):

Doctoral Programme in Clinical Psychology

University of East Anglia

Queens Building

Norwich

Norfolk

NR4 7TJ

Tel: 01603 593600 (Mon-Fri, 9am – 5pm)

Email: j.hampson@uea.ac.uk

Participants referred from NHS services: For independent advice on participating in research, you can also contact your local Patient Advice and Liaison Service (PALS) at CPFT, Elizabeth House, Fulbourn Hospital, Cambridge, CB21 5EF or telephone 01223 726789.

Participants not referred from NHS services: Should you have any complaints regarding the conduct of the research please contact Dr Margo Ononaiye, (Research Supervisor).

Version: 5

Date: 06/03/2014

Appendix L: E-Bulletin Content

Volunteers are sought for a psychology study examining a computer program which seeks to reduce levels of panic.

If you choose to take part, you will be asked to complete a number of questionnaires and a complete a computer-based task over seven consecutive days, with each computer task lasting approximately 45 minutes.

Participants will be entered into a prize draw for a £10 high street voucher.

To express interest, email James Hampson (Trainee Clinical Psychologist) at j.hampson@uea.ac.uk

Version: 1

Date: 10/02/2014

Appendix M: Consent Form

Patient Identification Number for this study: …….

CONSENT FORM

Title of Project: Modifying Interpretation Biases in Panic Disorder

Name of Researcher: James Hampson

Please initial box

1. I confirm that I have read and understand the information sheet for the above study. I have had the opportunity to consider the information, ask questions and had these answered satisfactorily. ☐
2. I understand that participation is voluntary and that I am free to withdraw at any time, without giving reason, without my medical care or legal rights being affected. ☐
3. If I withdraw from the study, I am willing for information that I have provided during the course of the study to be used for research purposes, as stated in the information sheet. ☐
4. I will inform the researcher of any changes in medication during my involvement in the study, including dates of the change, dose and name of the medication. ☐
5. I am willing for my GP and/or care team/clinician involved to be informed of my participation and completion of this project, and for assessment information to be shared with my GP and/or care team. ☐
6. I give my consent for a qualitative semi-structured interview and for a recording of this to be made. I understand that this is for the purposes of transcribing information that will be used as data in a separate service based research project. ☐
7. I understand that I can choose to withdraw from the study or delay any other therapy or intervention, if offered during my participation. I understand that if this occurs it will be negotiated with the relevant care team/clinician and therapy will commence at the earliest opportunity after my participation in the above study. ☐
8. I agree to take part in the above study. ☐

_____	_____	_____
Name of Patient	Date	Signature
_____	_____	_____
Name of Person taking consent	Date	Signature
_____	_____	_____
Researcher	Date	Signature

Version: 5

Date: 06/03/2014

Appendix N: Acknowledgement of Receipt of End of Study Form

NHS
Health Research Authority
NRES Committee North East - Newcastle & North Tyneside 2
Room 002
JARROW Business Centre
Rolling Mill Road
Jarrow
NE32 3DT

Tel: 0191 428 3561

07 July 2014

Mr James Peter Hampson
Trainee Clinical Psychologist
Cambridge and Peterborough Mental Health Foundation Trust
University of East Anglia
Clinical Psychology Course
Norwich
Norfolk
NR4 7TJ

Dear Mr Hampson

Study title:	**A single case series investigation of the efficacy of an internet delivered multi-session cognitive bias modification - interpretation task in a clinical population with Panic Disorder.**
REC reference:	**13/NE/0171**
Protocol number:	**N/A**
IRAS project ID:	**124494**

Thank you for sending the declaration of end of study form and final report (abstract), notifying the Research Ethics Committee that the above study concluded on 27 May 2014. I will arrange for the Committee to be notified.

13/NE/0171:	**Please quote this number on all correspondence**

Yours sincerely

Miss Kerry Dunbar
REC Assistant

E-mail: nrescommittee.northeast-newcastleandnorthtyneside2@nhs.net

Copy to: *Mrs Sue Steel, University of East Anglia*
Mr Stephen Kelleher, Cambridgeshire and Peterborough NHS Foundation Trust

A Research Ethics Committee established by the Health Research Authority

Appendix O: Kendall's Tau Statistical Output

Nonparametric Correlations - PDSS

			Baseline7	Participant1
Kendall's tau_b	Baseline7	Correlation Coefficient	1.000	.651*
		Sig. (2-tailed)	.	.046
		N	7	7
	Participant1	Correlation Coefficient	.651*	1.000
		Sig. (2-tailed)	.046	.
		N	7	7

*. Correlation is significant at the 0.05 level (2-tailed).

			Baseline7	Participant2
Kendall's tau_b	Baseline7	Correlation Coefficient	1.000	.109
		Sig. (2-tailed)	.	.748
		N	7	7
	Participant2	Correlation Coefficient	.109	1.000
		Sig. (2-tailed)	.748	.
		N	7	7

			Baseline9	Participant3
Kendall's tau_b	Baseline9	Correlation Coefficient	1.000	-.340
		Sig. (2-tailed)	.	.225
		N	9	9
	Participant3	Correlation Coefficient	-.340	1.000
		Sig. (2-tailed)	.225	.
		N	9	9

			Baseline11	Participant4
Kendall's tau_b	Baseline11	Correlation Coefficient	1.000	-.274
		Sig. (2-tailed)	.	.278
		N	11	11
	Participant4	Correlation Coefficient	-.274	1.000
		Sig. (2-tailed)	.278	.
		N	11	11

			Baseline9	Participant5
Kendall's tau_b	Baseline9	Correlation Coefficient	1.000	-.189
		Sig. (2-tailed)	.	.506
		N	9	9
	Participant5	Correlation Coefficient	-.189	1.000
		Sig. (2-tailed)	.506	.
		N	9	9

			Baseline11	Participant6
Kendall's tau_b	Baseline11	Correlation Coefficient	1.000	-.458
		Sig. (2-tailed)	.	.057
		N	11	11
	Participant6	Correlation Coefficient	-.458	1.000
		Sig. (2-tailed)	.057	.
		N	11	11

Nonparametric Correlations - Participant 1

			VASbaseline7	BodilyVAS
Kendall's tau_b	VASbaseline7	Correlation Coefficient	1.000	-.169
		Sig. (2-tailed)	.	.622
		N	7	7
	BodilyVAS	Correlation Coefficient	-.169	1.000
		Sig. (2-tailed)	.622	.
		N	7	7

			VASbaseline7	UnrealityVAS
Kendall's tau_b	VASbaseline7	Correlation Coefficient	1.000	.
		Sig. (2-tailed)	.	.
		N	7	7
	UnrealityVAS	Correlation Coefficient	.	.
		Sig. (2-tailed)	.	.
		N	7	7

			VASbaseline7	ControlVAS
Kendall's tau_b	VASbaseline7	Correlation Coefficient	1.000	.451
		Sig. (2-tailed)	.	.167
		N	7	7
	ControlVAS	Correlation Coefficient	.451	1.000
		Sig. (2-tailed)	.167	.
		N	7	7

			VASbaseline7	DyingVAS
Kendall's tau_b	VASbaseline7	Correlation Coefficient	1.000	-.117
		Sig. (2-tailed)	.	.734
		N	7	7
	DyingVAS	Correlation Coefficient	-.117	1.000
		Sig. (2-tailed)	.734	.
		N	7	7

Nonparametric Correlations - Participant 2

			VASbaseline7	BodilyVAS
Kendall's tau_b	VASbaseline7	Correlation Coefficient	1.000	-.117
		Sig. (2-tailed)	.	.734
		N	7	7
	BodilyVAS	Correlation Coefficient	-.117	1.000
		Sig. (2-tailed)	.734	.
		N	7	7

			VASbaseline7	UnrealityVAS
Kendall's tau_b	VASbaseline7	Correlation Coefficient	1.000	.394
		Sig. (2-tailed)	.	.250
		N	7	7
	UnrealityVAS	Correlation Coefficient	.394	1.000
		Sig. (2-tailed)	.250	.
		N	7	7

			VASbaseline7	ControlVAS
Kendall's tau_b	VASbaseline7	Correlation Coefficient	1.000	-.504
		Sig. (2-tailed)	.	.157
		N	7	7
	ControlVAS	Correlation Coefficient	-.504	1.000
		Sig. (2-tailed)	.157	.
		N	7	7

			VASbaseline7	DyingVAS
Kendall's tau_b	VASbaseline7	Correlation Coefficient	1.000	.117
		Sig. (2-tailed)	.	.734
		N	7	7
	DyingVAS	Correlation Coefficient	.117	1.000
		Sig. (2-tailed)	.734	.
		N	7	7

Nonparametric Correlations - Participant 3

			VASbaseline9	BodilyVAS
Kendall's tau_b	VASbaseline9	Correlation Coefficient	1.000	-.031
		Sig. (2-tailed)	.	.913
		N	9	9
	BodilyVAS	Correlation Coefficient	-.031	1.000
		Sig. (2-tailed)	.913	.
		N	9	9

			VASbaseline9	UnrealityVAS
Kendall's tau_b	VASbaseline9	Correlation Coefficient	1.000	.313
		Sig. (2-tailed)	.	.288
		N	9	9
	UnrealityVAS	Correlation Coefficient	.313	1.000
		Sig. (2-tailed)	.288	.
		N	9	9

			VASbaseline9	ControlVAS
Kendall's tau_b	VASbaseline9	Correlation Coefficient	1.000	-.382
		Sig. (2-tailed)	.	.194
		N	9	9
	ControlVAS	Correlation Coefficient	-.382	1.000
		Sig. (2-tailed)	.194	.
		N	9	9

			VASbaseline9	DyingVAS
Kendall's tau_b	VASbaseline9	Correlation Coefficient	1.000	.
		Sig. (2-tailed)	.	.
		N	9	9
	DyingVAS	Correlation Coefficient	.	.
		Sig. (2-tailed)	.	.
		N	9	9

Nonparametric Correlations - Participant 4

			VASbaseline11	BodilyVAS
Kendall's tau_b	VASbaseline11	Correlation Coefficient	1.000	.250
		Sig. (2-tailed)	.	.318
		N	11	11
	BodilyVAS	Correlation Coefficient	.250	1.000
		Sig. (2-tailed)	.318	.
		N	11	11

			VASbaseline11	UnrealityVAS
Kendall's tau_b	VASbaseline11	Correlation Coefficient	1.000	-.108
		Sig. (2-tailed)	.	.674
		N	11	11
	UnrealityVAS	Correlation Coefficient	-.108	1.000
		Sig. (2-tailed)	.674	.
		N	11	11

			VASbaseline11	ControlVAS
Kendall's tau_b	VASbaseline11	Correlation Coefficient	1.000	.106
		Sig. (2-tailed)	.	.687
		N	11	11
	ControlVAS	Correlation Coefficient	.106	1.000
		Sig. (2-tailed)	.687	.
		N	11	11

			VASbaseline11	DyingVAS
Kendall's tau_b	VASbaseline11	Correlation Coefficient	1.000	.
		Sig. (2-tailed)	.	.
		N	11	11
	DyingVAS	Correlation Coefficient	.	.
		Sig. (2-tailed)	.	.
		N	11	11

Nonparametric Correlations - Participant 5

			VASbaseline9	BodilyVAS
Kendall's tau_b	VASbaseline9	Correlation Coefficient	1.000	-.435
		Sig. (2-tailed)	.	.112
		N	9	9
	BodilyVAS	Correlation Coefficient	-.435	1.000
		Sig. (2-tailed)	.112	.
		N	9	9

			VASbaseline9	UnrealityVAS
Kendall's tau_b	VASbaseline9	Correlation Coefficient	1.000	.
		Sig. (2-tailed)	.	.
		N	9	9
	UnrealityVAS	Correlation Coefficient	.	.
		Sig. (2-tailed)	.	.
		N	9	9

			VASbaseline9	ControlVAS
Kendall's tau_b	VASbaseline9	Correlation Coefficient	1.000	.
		Sig. (2-tailed)	.	.
		N	9	9
	ControlVAS	Correlation Coefficient	.	.
		Sig. (2-tailed)	.	.
		N	9	9

			VASbaseline9	DyingVAS
Kendall's tau_b	VASbaseline9	Correlation Coefficient	1.000	.
		Sig. (2-tailed)	.	.
		N	9	9
	DyingVAS	Correlation Coefficient	.	.
		Sig. (2-tailed)	.	.
		N	9	9

Nonparametric Correlations - Participant 6

			VASbaseline11	BodilyVAS
Kendall's tau_b	VASbaseline11	Correlation Coefficient	1.000	-.449
		Sig. (2-tailed)	.	.059
		N	11	11
	BodilyVAS	Correlation Coefficient	-.449	1.000
		Sig. (2-tailed)	.059	.
		N	11	11

			VASbaseline11	UnrealityVAS
Kendall's tau_b	VASbaseline11	Correlation Coefficient	1.000	-.315
		Sig. (2-tailed)	.	.183
		N	11	11
	UnrealityVAS	Correlation Coefficient	-.315	1.000
		Sig. (2-tailed)	.183	.
		N	11	11

			VASbaseline11	ControlVAS
Kendall's tau_b	VASbaseline11	Correlation Coefficient	1.000	-.330
		Sig. (2-tailed)	.	.160
		N	11	11
	ControlVAS	Correlation Coefficient	-.330	1.000
		Sig. (2-tailed)	.160	.
		N	11	11

			VASbaseline11	DyingVAS
Kendall's tau_b	VASbaseline11	Correlation Coefficient	1.000	.
		Sig. (2-tailed)	.	.
		N	11	11
	DyingVAS	Correlation Coefficient	.	.
		Sig. (2-tailed)	.	.
		N	11	11

Appendix P: Wilcoxon Signed Rank Statistical Output

Wilcoxon Signed Ranks Test - Group Effects

Ranks

		N	Mean Rank	Sum of Ranks
ASIint - ASIpre	Negative Ranks	4[a]	3.50	14.00
	Positive Ranks	1[b]	1.00	1.00
	Ties	1[c]		
	Total	6		

a. ASIint < ASIpre
b. ASIint > ASIpre
c. ASIint = ASIpre

Test Statistics[b]

	ASIint – ASIpre
Z	-1.753[a]
Asymp. Sig. (2-tailed)	.080

a. Based on positive ranks.
b. Wilcoxon Signed Ranks Test

Ranks

		N	Mean Rank	Sum of Ranks
ASIfu - ASIpre	Negative Ranks	5[a]	3.80	19.00
	Positive Ranks	1[b]	2.00	2.00
	Ties	0[c]		
	Total	6		

a. ASIfu < ASIpre
b. ASIfu > ASIpre
c. ASIfu = ASIpre

Test Statistics[b]

	ASIfu - ASIpre
Z	-1.782[a]
Asymp. Sig. (2-tailed)	.075

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

		N	Mean Rank	Sum of Ranks
PDSSpost - PDSSpre	Negative Ranks	6[a]	3.50	21.00
	Positive Ranks	0[b]	.00	.00
	Ties	0[c]		
	Total	6		
PDSSfu - PDSSpre	Negative Ranks	5[d]	4.00	20.00
	Positive Ranks	1[e]	1.00	1.00
	Ties	0[f]		
	Total	6		
RANKpost - RANKpre	Negative Ranks	4[g]	2.50	10.00
	Positive Ranks	0[h]	.00	.00
	Ties	2[i]		
	Total	6		
RANKfu - RANKpre	Negative Ranks	4[j]	3.50	14.00
	Positive Ranks	1[k]	1.00	1.00
	Ties	1[l]		
	Total	6		
BELIEVEpost - BELIEVEpre	Negative Ranks	4[m]	3.50	14.00
	Positive Ranks	1[n]	1.00	1.00
	Ties	0[o]		
	Total	5		
BELIEVEfu - BELIEVEpre	Negative Ranks	4[p]	3.50	14.00
	Positive Ranks	1[q]	1.00	1.00
	Ties	0[r]		
	Total	5		

a. PDSSpost < PDSSpre
b. PDSSpost > PDSSpre
c. PDSSpost = PDSSpre
d. PDSSfu < PDSSpre
e. PDSSfu > PDSSpre
f. PDSSfu = PDSSpre
g. RANKpost < RANKpre
h. RANKpost > RANKpre
i. RANKpost = RANKpre
j. RANKfu < RANKpre
k. RANKfu > RANKpre
l. RANKfu = RANKpre
m. BELIEVEpost < BELIEVEpre
n. BELIEVEpost > BELIEVEpre
o. BELIEVEpost = BELIEVEpre
p. BELIEVEfu < BELIEVEpre
q. BELIEVEfu > BELIEVEpre
r. BELIEVEfu = BELIEVEpre

Test Statistics[b]

	PDSSpost – PDSSpre	PDSSfu - PDSSpre	RANKpost - RANKpre	RANKfu - RANKpre
Z	-2.207[a]	-1.992[a]	-1.826[a]	-1.753[a]
Asymp. Sig. (2-tailed)	.027	.046	.068	.080

a. Based on positive ranks.
b. Wilcoxon Signed Ranks Test

	BELIEVEpost – BELIEVEpre	BELIEVEfu - BELIEVEpre
Z	-1.753[a]	-1.753[a]
Asymp. Sig. (2-tailed)	.080	.080

a. Based on positive ranks.

b. Wilcoxon Signed Ranks Test

Appendix Q: Imagery Correlation Output

Nonparametric Correlations - Imagery

Correlations

			MeanImagery	PDSSprePost
Spearman's rho	MeanImagery	Correlation Coefficient	1.000	-.116
		Sig. (1-tailed)	.	.413
		N	6	6
	PDSSprePost	Correlation Coefficient	-.116	1.000
		Sig. (1-tailed)	.413	.
		N	6	6

Correlations

			MeanImagery	PDSSpreFU
Spearman's rho	MeanImagery	Correlation Coefficient	1.000	-.486
		Sig. (1-tailed)	.	.164
		N	6	6
	PDSSpreFU	Correlation Coefficient	-.486	1.000
		Sig. (1-tailed)	.164	.
		N	6	6

Correlations

			MeanImagery	ASIprePost
Spearman's rho	MeanImagery	Correlation Coefficient	1.000	-.314
		Sig. (1-tailed)	.	.272
		N	6	6
	ASIprePost	Correlation Coefficient	-.314	1.000
		Sig. (1-tailed)	.272	.
		N	6	6

Correlations

			MeanImagery	ASIpreFU
Spearman's rho	MeanImagery	Correlation Coefficient	1.000	-.486
		Sig. (1-tailed)	.	.164
		N	6	6
	ASIpreFU	Correlation Coefficient	-.486	1.000
		Sig. (1-tailed)	.164	.
		N	6	6