Case-series evaluating a transdiagnostic cognitive-behavioral treatment for co-occurring anxiety disorders.

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Abstract

Background. Patients with anxiety disorder diagnoses commonly have more than one anxiety diagnosis. While cognitive-behavioral interventions have proven efficacy in treating single anxiety disorder diagnoses, there has been little investigation of their efficacy in treating co-occurring anxiety disorders.

Aims. To evaluate the efficacy of a transdiagnostic cognitive-behavioral intervention for treating co-occurring anxiety disorders.

Methods. An A-B single case study design (N = 6) was used to evaluate the efficacy of a 12 to 13 session modular transdiagnostic cognitive-behavioral intervention for treating co-occurring anxiety disorders across patients with at least two of the following diagnoses: GAD, Social Phobia, Panic Disorder and/or OCD.

Results. Five of the six participants completed treatment. At post-treatment assessment the five treatment completers achieved diagnostic and symptomatic change with three participants being diagnosis free. All participants who completed treatment no longer met criteria for any *DSM-IV-TR* Axis-I diagnosis at the three-month follow-up assessment, and demonstrated reliable and clinically-significant improvements in symptoms. Across the participants, statistically significant improvements from pre- to post-intervention were found on measures of anxiety, depression and general well-being, and all improvements were maintained at three-month follow-up.

Conclusions. Results suggest that transdiagnostic cognitive behavioral interventions can be of benefit to patients with co-occurring anxiety disorders.

Keywords: Anxiety disorder, co-morbid, transdiagnostic, cognitive behavioral treatment, case-series

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1. Introduction

Cognitive-behavioural therapy (CBT) has demonstrated efficacy in treating the major anxiety disorder diagnoses (for a meta-analysis see Hofmann & Smits, 2008). These treatments have arisen from first specifying a cognitive-behavioral model explaining the maintenance mechanisms and then developing and evaluating diagnosis-specific cognitive-behavioral protocols to address the putative maintaining mechanisms (Clark, 2004). Such protocols have been developed with reference to patients fitting the diagnostic criteria of a specific anxiety disorder, rather than for patients with more than one anxiety disorder. This is a significant limitation since 40% - 80% of patients with an anxiety disorder meet criteria for two or more anxiety disorders (Brown, Campbell, Lehman, Grisham, & Mancill, 2001; Kessler, Chiu, Delmer, & Walters, 2005). There is evidence to suggest that diagnosis-specific protocols are not being delivered in routine care as frequently or optimally as might be ideal (Baker, McFall, & Shoham, 2009; Stobie, Taylor, Quigley, Ewing & Salkovskis, 2007) and clinicians' attempts to address the high level of co-occurrence amongst disorders may be a partial explanation for this (Shafran et al., 2009). Collectively, the results of studies investigating the impact of diagnosis-specific CBT on comorbid anxiety disorders would suggest that approximately half of patients will achieve remission of co-occurring diagnoses following treatment (Norton et al., 2013). This indicates that, despite being beneficial, many patients will continue to present with high levels of co-occurring anxiety disorder symptoms following diagnosis-specific CBT for their primary difficulty. Although a clinically intuitive response to co-occurring anxiety disorders is to administer sequential interventions to address the difficulties concurrently or in turn, findings suggest that adopting this approach may negatively impact upon efficacy as compared to an equivalent duration of a single diagnosis-specific treatments (e.g. Craske et al., 2007).

In response to the limitations of single disorder-specific approaches, researchers have begun exploring transdiagnostic CBT approaches to anxiety disorders which aim to address co-occurring anxiety disorders by identifying and reversing common maintaining mechanisms. The rationale for this approach is lent weight by the fact that many of the cognitive, behavioral and affective processes hypothesized to contribute to the maintenance of anxiety occur across diagnostic categories (Harvey, Watkins, Mansell, & Shafran, 2004) and there is evidence to suggest that anxiety disorders may have a common core pathology (Clark & Watson, 1991; Barlow, Allen, & Choate, 2004). Indeed, if diagnostic categories represent variations in a general syndrome, with common maintaining mechanisms, then treatments addressing the commonalities may demonstrate greater efficiency and effectiveness in treating co-occurring anxiety disorders than diagnosis-specific approaches (McEvoy & Nathan, 2007).

A number of attempts to address multiple co-occurring anxiety disorders are underway which have reported good clinical outcomes in treating patients' primary anxiety disorder along with significant reductions in symptoms of secondary anxiety disorders. These approaches include the 'unified protocol' developed by Barlow and colleagues (Barlow et al, 2004; Farchione et al., 2012), "transdiagnostic" group CBT protocols (Arch et al., 2013; Norton et al., 2013) and internet-delivered transdiagnostic CBT interventions (Johnston, Titov, Andrews, Dear, & Spence, 2013). A number of these interventions incorporate the treatment of mood as well as anxiety disorders with the rationale that mood disorders may share a core pathology with anxiety disorders (Barlow et al., 2004) and frequently co-occur (Brown et al., 2001). However, the commonalities in maintenance processes and shared intervention strategies across diagnosis-specific interventions for anxiety disorders have arguably yet to be established across mood disorders. A limitation of both these approaches is that they do not incorporate the specific interventions developed within evidence-based diagnosis-specific approaches (e.g., manipulating self-focused attention in the treatment of social phobia [Clark et al., 2006] or

identifying and modifying cognitive distortions in trauma memories in the treatment of PTSD [Ehlers et al., 2003]). Ideally, a transdiagnostic approach would address the common maintaining mechanisms across anxiety disorders, whilst also incorporating those specific to a given anxiety disorder. Such an approach should therefore aim to achieve a balance between adopting a standardized approach across patients, whilst ensuring that the intervention remains personalized to the extent where it can address the idiosyncratic presenting difficulties of a given individual (Craske, 2012). This approach has been successfully utilized in the treatment of eating disorders (Fairburn, Cooper, & Shafran, 2003). Within this approach the intervention is guided by a single conceptual model, key transdiagnostic maintenance processes are addressed by core treatment modules, and optional modules are delivered according to individual need.

The primary aim of the study was to advance the evidence-base for treating co-occurring anxiety disorders by evaluating a treatment protocol for conceptualizing and treating co-occurring anxiety disorders transdiagnostically, in individuals with two or more anxiety disorders. The treatment protocol (Shafran, McManus, Cooper & Clark, 2008) was based on a transdiagnostic model of the maintenance of anxiety disorders (McManus & Shafran, 2014) shown below (see Figure 1). The study aimed to evaluate the efficacy of this transdiagnostic CBT protocol against whether it was effective in:

1. ameliorating anxiety disorder diagnoses (*DSM-IV-TR* Axis-I disorders; APA, 2000) for patients with co-occurring anxiety disorders
2. producing clinically significant and reliable reductions in pathology as measured by standardized measures of anxiety, depression and general functioning

FIGURE 1 INSERTED ABOUT HERE

2. Method

2.1 Design

The study utilized an A-B case-series methodology (Barlow & Hersen, 1984) with stability of participant symptoms assessed weekly for a four-week period prior to beginning treatment.

2.2 Participants

Following NHS ethical approval participants were recruited by advertising the study in the local NHS Psychological Therapies service and on the website of a local CBT center. Inclusion criteria were: (i) meeting *DSM-IV-TR* criteria for at least two anxiety disorders (ii) aged 18-70 (iii) fluent in English (iv) agreement to keep any psychotropic medication at a stable dose for the duration of the study. Exclusion criteria were the presence of: (i) psychotic symptoms (ii) active risk of suicide or deliberate self-harm (iii) substance dependence.

Ten people made contact regarding the study and four were excluded for not meeting *DSM-IV-TR* criteria for at least two anxiety disorders. The remaining six participants were included in the study.

2.3 Measures

2.3.1 Diagnoses.

The *Structured Clinical Interview for DSM-IV Axis I disorders* (*SCID-I*; First, Spitzer, Gibbon, & Benjamin, 1997) was administered by an independent assessor, who was not involved in delivering the intervention to establish participant diagnoses. The *SCID-I* is a structured diagnostic interview with demonstrated reliability ($\kappa = 0.65 - 0.83$, Lobbestael, Leurgans, & Arntz, 2011) for anxiety disorder diagnoses. The reliability of diagnostic assessment was established by a second independent assessor re-rating a random selection of 50% of assessment sessions, with 100% agreement on diagnoses. Assessors also rated the

distress and interference caused by the anxiety disorders on a scale from 0 = *Not at all* to 10 = *Extremely.* Reliability of ratings between assessors was calculated using Intra-class Correlation Coefficients (two-way random-effects with absolute agreement on single measures) and was *ICC* = .98 $p < .001$, for both distress and interference ratings.

2.3.2 General measures.

Standard measures were selected based on their use within the evaluation of diagnosis-specific and transdiagnostic CBT interventions (e.g. Clark et al., 2006; Farichione et al., 2012) and their use within NHS outpatient settings. The measures, which all have good psychometric properties, were: The Beck Anxiety Inventory (BAI: Beck, Epstien, Brown, & Steer, 1988), The Beck Depression Inventory (BDIII: Beck, Steer, & Brown, 1996), The Clinical Outcomes in Routine Evaluation– Outcome Measure (COREOM: Evans et al., 2000).

2.3.3 Diagnosis-specific measures.

In addition to the above general measures, standard diagnosis-specific measures were used to assess the severity of symptoms for each of the specific anxiety disorders. Each of the measures have good psychometric properties and have been used to assess symptomatic change across treatment for each relevant disorder. These were: *a) The Obsessive-compulsive Inventory - Revised (OCI-R:* Foa et al., 2002); *b) The Social Phobia and Anxiety Inventory (SPAI:* Turner, Biedel, Dancu, & Stanley, 1989); *c) The Panic Disorder Severity Scale- Self-report* (PDSS-SR: Houck, Spiegel, Shear & Rucci, 2002); *d) The Penn State Worry Questionnaire (PSWQ:* Meyer, Miller, Metzger, & Borkovec, 1990).

2.4 Assessment Schedule and Procedure

The assessment schedule had six phases:

1. pre-baseline assessment

2. weekly completion of self-report measures during a four-week no-treatment baseline period
3. post-baseline /pre-intervention assessment
4. completion of self-report assessments at each treatment session
5. post-intervention assessment
6. three month follow-up assessment.

2.5 Treatment Overview

All treatment sessions were delivered in an individual format by the second author (GC) with close supervision from the first and last authors (FM and RS). For an in-depth discussion of the treatment protocol see McManus and Shafran (2014). The intervention components comprised of core and optional modules that were based on current empirically validated cognitive-behavioural theory and treatment protocols (e.g. NICE, 2011; NICE, 2013). All interventions involved the utilization of core modules that were designed to address common processes across anxiety disorders (Havery et al., 2004) and common components across evidence-based diagnosis-specific approaches. Specifically, core modules focus on the conceptual links between the patient's anxiety disorders and the commonalities between diagnosis-specific approaches to anxiety disorders (e.g. misinterpretations of anxiety sensations as dangerous, the use of safety seeking behaviors to manage threat) and include: individualized transdiagnostic formulation; psychoeducation and information gathering to normalize symptoms; addressing avoidance and counter-productive safety strategies; addressing misinterpretations of danger (using verbal and behavioural techniques); modifying cognitive biases; and relapse-prevention planning. Optional modules were also employed selectively according to the nature of the difficulties identified within the individual's formulation. Optional modules address processes considered diagnosis-specific or idiosyncratic and include: attenuating low self-

esteem; problem-solving; addressing self-focused attention; addressing intrusive memories; and addressing meta-cognitive beliefs. The intervention is distinct from other transdiagnostic approaches such as those of Barlow as (i) it focuses exclusively on the maintenance of anxiety disorders, (ii) it has optional modules as well as core modules, (iii) it does not have a specific emphasis on interoceptive and situation-based emotion focused exposure or on increasing present-focused emotion awareness.

Participants began treatment at different time points over the course of three months. The intervention was intended to be delivered over 12 one-hour treatment sessions according to the following schedule: the first six sessions were twice a week, the following four sessions weekly, and the last two sessions fortnightly, creating a 12-session, 11-week intervention. However, the protocol was designed to meet the idiosyncratic needs of the individual patient and so allowed the flexibility of allowing extra sessions if any aspect of the patient's presenting diagnoses was not fully addressed within 12-sessions. Similarly, if it was not possible to schedule sessions according to the planned 11-week schedule (due to participants' availability to attend sessions), then treatment duration was extended. The schedule of sessions reflects the structure and length of existing evidence-based diagnosis-specific treatments.

2.6 Data Analysis

A number of approaches have been suggested for identifying observable and clinically meaningful effects within single case research (Borckardt, et al., 2008). This study utilized two of the most widely reported methods, the assessment of the graphical display of change over time (Parsonson & Baer, 1992), and the more conservative method of identification of statistically reliable and clinically significant change (Jacobson & Truax, 1991). Pairing these methods allows the evaluation of whether observed changes are clinically meaningful and establishing whether significant change can be attributed to the intervention or to a general trend in participant scores. Whether each participant achieved reliable change was assessed by calculating a reliable change index (RCI) and clinically significant change (CSC) cut-off for each

measure (Evans, Margison, & Barkham, 1998). CSC cut-off points were calculated under criterion C (Evans et al., 1998), which reflects the minimum movement away from the clinical mean and towards the mean of a non-clinical population to be confident of a clinically significant change – where criterion C falls midway between the two population means. For measures that were completed by four or more participants (BAI, BDI, CORE, SPAI-SP, PSWQ) clinical means and *SD*'s from the current study were used to calculate the RCI and CSC criterion, with published clinical means utilized to calculate these criterion for the remaining questionnaires (PDSS-SR, OCI-R).

3. Results

3.1 Participant Characteristics

Six Caucasian participants (four female) participated in the case series. All participants reported the onset of their anxiety difficulties to be more than five years previously, indicating that their difficulties were long-standing and unlikely to be subject to spontaneous remission (Bruce et al*.,* 2005). Participants mean age was 34.33 years (*SD* = 5.72, range 26-41). All participants were married apart from P6. All participants had been educated to degree level and all were employed apart from P2 who was a student and P5 who was unemployed. At the pre-intervention assessment participants met criteria for a mean of 3.17 (*SD* = 0.98) *DSM-IV-TR* Axis I diagnoses, the details of which can be seen in Table 1. None had previously received CBT, but three (P2, P3, P4) had received a previous psychological intervention (counseling or Jungian psychoanalysis) which had not focused on their anxiety disorders. Participants three and four were already taking antidepressant medication prior to joining the trial (Sertraline 100mg and Fluoxetine 20mg respectively) and remained on this dose throughout their participation in the study. One participant (P2) discontinued treatment after six sessions, citing

relationship difficulties and work commitments as the reason for being unable to schedule further appointments.

3.2 Stability of Pre-treatment Baseline

There were no changes in participants' diagnoses, as assessed by the *SCID*, across the four-week baseline period. Similarly Wilcoxen tests comparing scores from the beginning and end of the baseline period showed no significant change on the BAI $Z = -0.21$, $p = .83$, BDI $Z = -0.31$, $p = .75$ or CORE $Z = -0.52$, $p = .60$ across all participants ($N = 6$).

3.3 Post-intervention Outcomes

3.3.1 Change in diagnoses.

Table 1 shows participants' diagnoses, and the distress and interference ratings at pre-intervention, post-intervention and follow-up assessments.

INSERT TABLE 1 ABOUT HERE

For participants who completed treatment ($n = 5$) the mean number of diagnoses reduced from 3.00 ($SD = 1.00$) at the pre-intervention assessment to 0.40 ($SD = 0.55$) at the post-intervention assessment and by the 3-month follow-up assessment no participants met criteria for any diagnosis. For participants who completed treatment, there were also significant reductions in the pre-intervention and follow-up assessor ratings of "distress" (means [*SD*] 8.60 [0.89] vs. 2.8 [0.83] $z = -2.03$, $p = 0.04$) and "interference" (means [*SD*] 8.20 [0.84] vs. 2.0 [0.72] $z = -2.12$, $p = 0.03$).

3.3.2 Changes standardized measures of anxiety, depression and general functioning.

3.3.2.1 Visual analysis.

Participants' baseline, pre- and post-intervention, and follow-up scores are shown graphically in Figures 2 and 3. All participants for whom there is post-intervention data displayed generally stable baselines across global and diagnosis-specific measures. Four of these five participants (P1, P3, P4, P5) show a pattern of decreasing scores on general and diagnosis specific measures across treatment with gains being maintained or improved upon at follow-up. The fifth treatment completing participant, P6, shows less clear decreases in general or diagnosis-specific measures, despite no longer meeting criteria for any diagnosis by follow-up. This may be partially explained by the fact that his pre-intervention questionnaire scores would be considered of relatively low clinical severity, making it harder to detect change. P2 (who did not complete treatment) demonstrated base-line decreases and post-baseline increases in symptoms prior to drop-out. She attributed this change in symptoms to temporary relief from increasing situational pressures (described above) which ultimately led to her discontinuing treatment.

FIGURE 2 & 3 INSERTED ABOUT HERE

3.3.2.2 Clinically significant change (CSC) and reliable change (RC)

Individual participants' scores on self-report measures at the pre-intervention (i.e. post-baseline), post-intervention and follow-up assessments can be seen in Table 2. P1 achieved CSC and RC on the BDI, CORE, SPAI-SP and PSWQ by follow-up. P1 also achieved CSC on the BAI and CSC and RC on the OCR-R at the post- intervention assessment but slipped back slightly on this measure at follow-up so no longer met criteria for CSC. P2 demonstrated RC and CSC during the baseline period only for her scores to return to pre-baseline levels prior to drop-out. P3 scored below the CSC cut-off at pre-assessment so could not meet CSC criteria for any measure. However P3 did show RC on the SPAI-SP at post-intervention and follow up and scores on all measures were reduced to non-clinical levels. P4 showed RC and CSC on the

BAI, BDI, SPAI-SP, PSWQ and PDSS-SR at follow-up and RC on the CORE (missing the criteria for CSC on this measure by less than one point). P5 achieved RC and CSC on the BDI, CORE, SPAI-SP, PSWQ and OCI-R at post-intervention and follow-up assessments, and RC on the BAI at follow-up. P6 scored below the cut-off for CSC all but one (PSWQ) measure at the pre-intervention assessment so could not achieve CSC on most measures, but P6 did achieve RC and CSC on the PSWQ by follow-up, and scores on other measures were reduced.

INSERT TABLE 2 ABOUT HERE

3. Discussion

This study describes a preliminary investigation of a transdiagnostic CBT approach to co-occurring anxiety disorders, using a single-case experimental design. Six participants, with a range of anxiety disorder diagnoses and severities participated, five of whom completed treatment. The intervention was effective in ameliorating participants' diagnoses, and in significantly reducing the distress and impairment associated with the anxiety disorder diagnoses, for the five participants that completed treatment. In addition, scores on a range of global and diagnosis-specific self-report measures were reduced following the intervention. Consistent with trials of diagnosis-specific CBT treatment for anxiety (Hofmann & Smits, 2008) treatment gains were largely maintained at three month follow-up. In contrast to the general pattern of positive response to the treatment, it is worth noting that one participant (P2) discontinued treatment after receiving no benefit.

Spontaneous recovery from GAD, social phobia, panic disorder and OCD would not be predicted by epidemiological research (Bruce et al*.,* 2005), nor by the fact that the participants' difficulties had been present for a number of years prior to participating in this study, or by their demonstrating little change across the four-week baseline period. Additionally it is interesting to note that participants showed significant improvements in depression, with

three participants achieving reliable and clinically significant change on the BDI (P1, P4, P5), and no longer meeting criteria for Major Depressive Disorder at post-intervention or follow-up. It is notable that this intervention for anxiety disorders also works for MDD, a finding shared with disorder-specific treatments for anxiety which result in significant improvement in depression (e.g. Clark et al., 2006). There are a number of possible explanations for this outcome: the treatment may be targeting shared maintaining mechanisms, there may be a generalization of skills, or the depression may have been secondary to participants' anxiety (i.e. associated with the functional impairment caused by anxiety symptoms). Whilst it has been argued that there is a common core pathology amongst anxiety and mood disorders (e.g. Craske [2012]; Barlow et al., [2004]) the transdiagnostic model and protocol was developed to understand and reverse those maintenance processes involved in the perception of threat. An area for future research may be whether the impact on co-occurring mood disorders can be better understood and whether the transdiagnostic protocol can be updated to be able to address such presentations.

The findings must be interpreted within the study's limitations. The generalizability of the findings is limited by the small sample and the lack of a control group. The nature of the A-B case series methodology means that treatment effects may be attributable to non-specific factors (e.g. impact of assessment procedure, non-specific therapeutic effects) and cannot necessarily be ascribed to the purported active-ingredients of treatment (Barlow & Hersen, 1984). Similarly, lack of data regarding the timing and content of previous psychological intervention that participants had received means that the potential impact of this on treatment outcome is unknown. The lack of a comparison to an alternative evidence-based intervention means that it cannot be determined what benefit the transdiagnostic model and protocol created, over and above generic or diagnosis-specific CBT interventions. Additionally, whilst the assessments and reliability checks were carried out by individuals who were not involved in the delivery or supervision of the intervention, it was not possible to blind the assessors to the stage

of assessment. Consequently, the possibility of overestimating treatment effects exists. A further consideration in interpreting the results is that the general symptom measures utilised (e.g. BAI) may not equitably detect change across anxiety disorder diagnoses (Cox, Cohen, Direnfeld & Swinson, 1996). Finally, the treatment being delivered by only one therapist also limits generalizability. However, the fact that the intervention was carried out by a relatively inexperienced therapist, with patients from NHS referral pathways, suggests that the protocol may be able to generalize to outpatient clinical settings and be disseminated to relatively novice clinicians.

Collectively the results provide a provisional indication that the transdiagnostic CBT intervention can successfully treat co-occurring anxiety disorders, bringing about significant symptomatic change as well as effecting change in diagnostic status, with treatment gains being maintained or improved upon in the three months following treatment. Thus the results of this study provide provisional validation of a transdiagnostic CBT protocol for treating co-occurring anxiety disorder.

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