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ScienceDirect
Behaviour Research and Therapy 45 (2007) 1435–1447
BEHAVIOUR RESEARCH AND THERAPY
www.elsevier.com/locate/brat

Implications of naturalistic use of pharmacotherapy in CBT treatment for panic disorder

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Received 6 July 2006; received in revised form 19 December 2006; accepted 4 January 2007

Abstract

This study examined naturalistic medication use and cognitive behavioral therapy (CBT) treatment outcomes in 105 patients meeting DSM-IV criteria for panic disorder (PD), assessed by structured clinical interview. The association between pre- and post-treatment use of SSRIs, benzodiazepines (BZs), and any anti-anxiety or anti-depressant (A/D) medication were investigated for three indicators of treatment outcome (PD severity, presence of agoraphobia (AG), anxiety sensitivity) at post-treatment and 6-month follow-up. Controlling for pre-treatment severity, pre-treatment SSRI use was associated with worse outcomes for AG ($p = .04$) and anxiety sensitivity ($p = .047$); post-treatment SSRI use was associated with delayed improvements in PD severity ($p = .05$). Pre-treatment use of A/D was associated with poorer PD severity outcomes ($p = .04$). Post-treatment use of A/D was associated with higher anxiety sensitivity scores across post-treatment and 6-month follow-up ($p = .03$). BZ use was not associated with significantly worse outcomes. However, there was a decrease in the number of patients using BZs from pre-treatment to post-treatment ($p = .06$) and follow-up ($p = .006$). In conclusion, controlling for pre-treatment severity, pre- and post-treatment use of SSRIs and A/D was associated with poorer outcomes, particularly for PD severity and anxiety sensitivity.

Keywords: CBT; Panic disorder; Medication; Treatment outcome; SSRI; Benzodiazepine

Introduction

A number of panic disorder (PD) treatment studies have examined randomized clinical trials of pharmacotherapy versus cognitive behavioral therapy (CBT) alone or in combination (e.g. Barlow, Gorman, Shear, & Woods, 2000); fewer have followed naturalistic use of pharmacotherapy in CBT for PD. Among the latter studies, naturalistic medication use typically is associated with poorer treatment outcomes. For example, Brown and Barlow (1995) showed that naturalistic use of anti-anxiety or anti-depressant (A/D) medication during CBT treatment of PD was associated with less favorable outcomes at 24-month follow-up across four measures, including independent clinical severity ratings (CSR) and scores on the Anxiety Sensitivity Index (ASI; Reiss, Peterson, Gursky, & McNally, 1986). Similarly, Otto, Pollack, and Sabatino (1996) reported that

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0005-7967/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.brat.2007.01.005

remaining on medication at initial remission predicted relapse over the course of a 2-year follow-up following CBT for PD. Another study (van Balkom, de Beurs, Koele, Lange, & van Dyck, 1996) demonstrated negative associations between long-term benzodiazepine (BZ) use and CBT outcomes for agoraphobia (AG). For behavioral treatment of PD with AG, Fava et al. (2001) demonstrated that use of anti-depressant drugs at pre-treatment and BZs at post-treatment was associated with worse treatment outcomes. Westra, Stewart, and Conrad (2002) presented evidence that naturalistic, as needed use of BZs was associated with fewer reductions in anxiety sensitivity and anxious arousal from pre- to post-CBT treatment for PD with AG, compared with non- or regular use. Only one study (Oei, Llamas, & Evans, 1997) showed no differences for pre-existing A/D medication use and PD outcomes at long-term CBT follow-up.

The above studies measured different medication classes (BZ use versus any A/D) at different treatment points (pre versus post-treatment) across slightly different therapies (behavioral versus CBT) with various outcome measures at different measurement time points. Nevertheless, they converge upon the finding that naturalistic, concurrent use of pharmacotherapy generally is associated with less favorable outcomes following CBT treatment for PD and AG.

In addition to associations between naturalistic medication use and PD outcomes, Brown and Barlow (1995) reported on changes in medication use during therapy and follow-up. Despite requirements for stabilization of medication use during active CBT treatment, Brown and Barlow (1995) found that the percentage of patients using psychotropic medications dropped by nearly 50% (from 44.4% to 23.8%) from baseline to 3-month follow-up. However, closer examination of medication use over a 2-year follow-up revealed a complex picture in which the number of patients who withdrew from medication between 3- and 24-month follow-up matched the number initiating medication use during the same period (Brown & Barlow, 1995). The extent to which CBT treatment for PD facilitates successful medication withdrawal has important clinical implications, particularly given research documenting difficulties in withdrawal from anti-anxiety medications such as BZs (see Otto, Hong, & Safren, 2002).

The current study aimed to replicate and extend previous findings by exploring in greater detail the relationship between naturalistic use of specific medication classes and treatment outcomes in CBT treatment for PD (with or without AG). We separately investigated use of three classes of medication: (a) BZ, (b) SSRI/SNRIs (SSRI), and (c) any A/D medications, which included BZ, SSRI, tricyclic anti-depressants, buspirone, and others. Our analysis examined combined data from two CBT treatment studies for PD (Craske, DeCola, Sachs, & Pontillo, 2003; Craske, Farchionne, Allen, & Barrios, in press). Five major questions were examined: (1) Do pre-treatment demographic and clinical differences exist between medication users and non-users? Relatedly, are there significant pre-treatment differences to be controlled in treatment outcome analyses? (2) How does use of medication change over the course of CBT treatment and follow-up? (3) What clinical or demographic characteristics are associated with significant changes in medication use? (4) Is use of medication at pre-treatment associated with different treatment outcomes than non-use at pre-treatment? (5) Is use of medication at post-treatment associated with different treatment outcomes than non-use?

Method

Patient sample

Data from two CBT treatment studies for PD (Craske et al., 2003, $n = 53$; Craske et al., in press, $n = 52$) were combined to increase statistical power, total $n = 105$. Inclusion criteria were determined through screening and an independent diagnostic evaluation using the Anxiety Disorder Interview Schedules for DSM-IV (ADIS-IV; Brown, DiNardo, & Barlow, 1994). For the Craske et al. (in press) sample, patients were required to have a principal diagnosis of PD with or without AG and at least one comorbid anxiety or mood disorder. For the Craske et al. (2003) sample, patients were required to meet criteria for PD with AG. Hence, all patients met DSM-IV criteria for PD.

Patients were excluded for presence of psychosis, current substance abuse or dependence, bipolar disorder, organic brain damage, pregnancy, severe medical conditions (e.g. neurological, cardiovascular, thyroid disease), and asthma.