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Psychological treatment of panic disorder with or without agoraphobia: A meta-analysis ☆

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ABSTRACT

Although the efficacy of psychological treatment for panic disorder (PD) with or without agoraphobia has been the subject of a great deal of research, the specific contribution of techniques such as exposure, cognitive therapy, relaxation training and breathing retraining has not yet been clearly established. This paper presents a meta-analysis applying random- and mixed-effects models to a total of 65 comparisons between a treated and a control group, obtained from 42 studies published between 1980 and 2006. The results showed that, after controlling for the methodological quality of the studies and the type of control group, the combination of exposure, relaxation training, and breathing retraining gives the most consistent evidence for treating PD. Other factors that improve the effectiveness of treatments are the inclusion of homework during the intervention and a follow-up program after it has finished. Furthermore, the treatment is more effective when the patients have no comorbid disorders and the shorter the time they have been suffering from the illness. Publication bias and several methodological factors were discarded as a threat against the validity of our results. Finally the implications of the results for clinical practice and for future research are discussed.

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1. Introduction

Initially called agoraphobia with panic attacks (American Psychiatric Association, 1980), and later renamed panic disorder (PD) with or without agoraphobia (American Psychiatric Association, 1987, 1994, 2004), PD is one of the most researched anxiety disorders due to its high rate of lifetime prevalence (about 5.1% of adults in USA; Bienvenu, 2006). PD is characterized by its resistance to spontaneous remission, its comorbidity with other disorders (e.g., depression, alcohol or substance disorders), and the decrease in quality of life. Additionally, PD can have serious social and economic consequences, since a large percentage of individuals with PD suffer social isolation and many of them have to give up work (Klerman et al., 1991; Mitte, 2005; Tsao, Mystowski, Zucker, & Craske, 2005).

In order to be diagnosed with PD a patient must have suffered recurrent and unexpected panic attacks over a minimum period of a month, followed by persistent concern about having additional attacks. Panic attacks are commonly accompanied by uncontrollable fear, worry about the implications of the attacks (e.g., losing control, having a heart attack), or a significant change in behavior relating to these symptoms. Furthermore, the attacks are not due to the direct effects of substance abuse or to a medical condition, and they cannot be explained by the presence of another mental illness. On the other hand, panic attacks often come together with agoraphobia, that is, an uncontrollable fear of having a panic attack in a setting from which it may be difficult to escape or receive help. About one in three people with PD develops agoraphobia, but agoraphobia without a history of panic attacks is very uncommon, with a lifetime prevalence of about 0.17% (Bienvenu, 2006).

1.1. The treatment of panic disorder

Since the recognition of PD as a separate diagnostic entity in the *Diagnostic and Statistical Manual of Mental Disorders*, DSM-III-R (American Psychiatric Association, 1980), much research has been devoted to examining the efficacy of different psychological and pharmacological interventions in ameliorating panic symptoms. Particular attention has been paid to cognitive–behavioral and pharmacological type interventions, alone or in combination (Barlow, Gorman, Shear, & Woods, 2000). Prior to 1980, the study of the etiology and treatment of PD was focused on biological theories, which enable the development of pharmacological treatments. Since 1980, the understanding of PD from the psychological perspective has advanced, as has the development of efficacious psychological treatments.

According to the criteria of the *Task Force on Promotion and Dissemination of Psychological Procedures* (1995), and in agreement with Barlow, Raffa, and Cohen (2002), the treatments for PD that have received empirical support are those based on the cognitive–behavioral model. Of particular notability are the panic control treatment developed by Barlow and his colleagues (Barlow & Craske, 1989; Craske & Barlow, 2006) and cognitive therapy by Clark's research group (Clark, 1997; Clark & Salkovskis, 1989).

In the treatment model developed by Barlow's group the exposure of the patient to interoceptive sensations plays a central role. Interoceptive exposure consists of inducing the feared sensations through exercises such as visualization of anxiety scenes, overbreathing and spinning. The treatment includes an educational component which teaches the patient about panic and the factors that influence its origin and recurrence. Cognitive therapy procedures are also included, with the objective of modifying erroneous beliefs about panic and anxiety, as well as cognitions that overestimate the threat and the danger that the attacks represent. The program includes progressive muscle relaxation training, which involves systematically constricting and relaxing various muscle groups paying attention to the sensations as well as suggestions to induce relaxation and warmth. Finally, the program also includes homework exercises, which vary according to the phase of therapy.

The cognitive therapy developed by Clark's group includes both an educational and a cognitive component. As with Barlow's approach, the educational component aims to demystify panic attacks by explaining their causes and triggering mechanisms. The cognitive component helps to identify and challenge the patient's erroneous interpretations of their symptoms. The program includes breathing retraining to influence dysfunctional habitual breathing patterns through the direct or indirect control of respiratory muscles, in order to alleviate fearful sensations. The program also introduces behavioral procedures, such as the generation of feared sensations by carrying out small experiments (e.g., hyper-ventilation, attentional focus, etc.), which have a twofold effect on the patient. Firstly, these exercises show him/her the possible causes of the sensations. Secondly, they help to give up the safety behaviors, disproving any catastrophic thoughts about the consequences of the symptoms. Finally, the program incorporates a series of homework exercises, in addition to a daily record of attacks, negative thoughts and rational interpretations of fearful symptoms.

In practice the most obvious difference between the approaches by Barlow and Clark is that in the former the emphasis is on exposure to interoceptive sensations, while the latter is more focused on the cognitive component.

Other psychological treatments for PD have been examined, but have not provided such clear benefits in terms of a statistically significant reduction of panic and agoraphobia symptoms. These include 'Eye Movement Desensitization and Reprocessing' (EMDR; Feske & Goldstein, 1997; Goldstein, de Beurs, Chambless, & Wilson, 2000), emotion regulation therapy (Shear, Houck, Greeno, & Masters, 2001), and Gestalt therapy (Chambless, Goldstein, Gallagher, & Bright, 1986).

PD with or without agoraphobia has been the focus of various meta-analytic studies to examine the differential efficacy of psychological and/or pharmacological interventions (Bakker et al., 1998; Chambless & Gillis, 1993; Clum, Clum, & Surls, 1993; Cox, Endler, Lee, & Swinson, 1992; Gould, Otto, & Pollack, 1995; Mattick, Andrews, Hadzi-Pavlovic, & Christensen, 1990; Mitte, 2005; Oei et al., 1999; Trull, Nietzel, & Main, 1988; van Balkom et al., 1997; van Balkom, Nauta, & Bakker, 1995; Westen & Morrison, 2001; Wilkinson, Balestrieri, Ruggeri, & Bellantuono, 1991). The results of these studies clearly prove the efficacy of cognitive therapy, *in vivo* exposure, and both techniques combined. *In vivo* exposure is a cognitive–behavioral technique consisting of gradually exposing the patient to feared situations. There is evidence that the main component in treating PD is *in vivo* exposure, with an effect size ranging between $d=0.78$ and $d=1.34$ in terms of the standardized mean difference. Furthermore, the effects increase over the course of time (between $d=1.09$ and $d=1.53$), although the follow-up periods were short, not exceeding 12 months on average. Meta-analyses that have addressed the differential efficacy of psychological and pharmacological treatments have shown good results for both cognitive–behavioral and pharmacological interventions, alone or in combination (cf. e.g., Cox et al., 1992; Mitte, 2005; van Balkom et al., 1997; Wilkinson et al., 1991).

Other relevant treatment characteristics have been empirically examined. One of these is the application format of the therapy,

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