

Cognitive-behavioral therapy in panic disorder

Terapia cognitivo-comportamental no transtorno de pânico

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Abstract

Objective: Panic disorder is a chronic and recurrent condition that impairs an individual's psychosocial functioning and quality of life. Despite the efficacy of psychopharmacological treatment in reducing panic attacks, many patients fail to respond adequately to these interventions. Cognitive behavioral therapy provides an alternative and efficacious method for treating panic disorder and agoraphobic avoidance. The objective of the study is to describe the use of cognitive behavioral therapy for panic disorder. **Method:** Narrative review of data collected from Medline, SciELO and PsycInfo and specialized textbooks. **Results:** We describe the cognitive-behavioral model for the treatment of panic disorder, and review both short and long-term efficacy findings. We also discuss the role of combined treatment (cognitive behavioral therapy and psychopharmacology). **Conclusions:** Cognitive behavioral therapy, either individual or in group, can be used as first-line therapy for panic disorder. This treatment modality can also be indicated as a next step for patients failing to respond to other treatments.

Descriptors: Panic disorder; Cognitive-behavior therapy; Evidenced-based efficacy; Treatment; Review

Resumo

Objetivo: O transtorno de pânico é uma condição crônica e recorrente que prejudica a qualidade de vida e o funcionamento psicossocial dos portadores. Embora os medicamentos sejam efetivos na redução dos ataques de pânico, muitos pacientes não respondem adequadamente a essas intervenções. A terapia cognitivo-comportamental fornece um método alternativo eficaz para tratar transtorno de pânico e evitação agorafóbica. O objetivo do estudo é o de descrever o uso de técnicas cognitivo-comportamentais no tratamento do transtorno de pânico. **Método:** Revisão narrativa a partir dos bancos de dados do Medline, SciELO e PsycInfo e de livros-texto especializados. **Resultados:** Foram descritos os fundamentos da terapia cognitivo-comportamental no tratamento do transtorno de pânico e revisadas as evidências de eficácia em curto e longo prazos. O uso de medicação concomitante a terapia cognitivo-comportamental foi também discutido. **Conclusões:** A terapia cognitivo-comportamental individual ou em grupo é eficaz para pacientes com transtorno de pânico, seja como tratamento de primeira linha ou como um próximo passo para pacientes com resposta parcial a outros tratamentos.

Descritores: Transtorno de pânico; Terapia cognitivo-comportamental; Evidências de eficácia; Tratamento; Revisão

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Introduction

Panic disorder (PD) is characterized by the presence of sudden anxiety attacks, followed by physical and affective symptoms, fear of having a new attack and avoidance of events or situations in which panic attacks have occurred.¹ The course of PD tends to be chronic in the majority of patients,^{2,3} and PD is associated with a reduced quality of life and impaired psychosocial functioning.⁴⁻⁶

As compared to the other anxiety disorders, the onset of PD is frequently later, occurring in the late twenties on average.⁷ PD affects two to three times more women than men, and may affect up to 3.5% of the population throughout life.⁷ The disorder is associated with a high social cost; patients with PD have reduced productivity and often use public health services, such as emergency rooms, medical visits and evaluations.⁸ Patients frequently report PD onset after a period of stress.⁹

Numerous studies have confirmed the effectiveness of drug therapy for PD.¹⁰⁻¹² Among the pharmacological options used in the treatment of PD are selective serotonin reuptake inhibitors (SSRI), tricyclic antidepressants (TAD), monoamine oxidase inhibitors (MAOI), serotonin and noradrenaline reuptake inhibitors (SNRI), and benzodiazepines.¹³ However, many patients, although being under drug therapy, remain symptomatic and have recurrence of symptoms. Studies have shown that after 4 years on drug therapy about 30% of patients are asymptomatic, 40-50% are better, but still symptomatic, and 20-30% remain the same or worse.¹⁴ It is also known that presence of residual symptoms is associated with increased risk of relapses.¹⁵

Cognitive-behavioral therapy (CBT) for PD is a therapeutic alternative that has good short- and long-term response for both core panic symptoms as well as the residual and often persistent symptoms of anticipatory anxiety, phobic avoidance, and agoraphobia.^{10,11,13,16} Studies have confirmed that CBT can change PD course not only for preventing relapses, but also because it prolongs the time interval between them.^{17,18} Brief treatment (often in the range of 12 sessions) with CBT is associated with high (75%) panic free rates among patients. The efficacy demonstrated in studies suggests that CBT outcomes are better than long-term pharmacology: 87% of patients remain without attacks at 1 year, and 75-81% at 2 years after completion of brief CBT.^{10,18} The effect size found for therapeutic response ranges between 0.6-2.3, depending on the dimension being evaluated.^{6,19} CBT for PD is also associated with improvements in comorbid conditions and quality of life.^{20,21} Heldt et al., in a study of 32 patients, demonstrated that reducing the symptoms of anticipatory anxiety and avoidance are more important for improving quality of life than changes in the frequency of panic attacks.⁶

This article aims at describing the use of CBT for patients with PD, focusing on the nature of the disorder, the interventions used in CBT, and the outcome expected with this treatment modality. To do so, a literature review was performed searching Medline, SciELO and PsycInfo databases for references of the main articles found and also for specialized textbooks.

The cognitive-behavioral model in panic disorder

According to cognitive-behavioral models, panic attacks arise from distorted and catastrophic interpretations of bodily symptoms.²² Dizziness or heart palpitations may be interpreted, for example, as an impending heart attack or stroke. Such interpretations increase arousal and intensify bodily sensations, thus confirming a sense of impending "danger" and generating more catastrophic interpretations and more anxiety in a rapid spiral.

According to Barlow's version of this model, an initial panic attack represents a "false alarm" where too much anxiety is signaled, often in response of life stress. Stressors reported by patients include negative life events such as a threatening loss or severe disease to the self or loved one, as well as separations or interpersonal difficulties.²³ Such "alarm reactions" are hypothesized to be more likely in biologically (genetic heritage) or psychologically (sensitivity to anxiety symptoms) vulnerable individuals. After the first attack, the person becomes apprehensive about new attacks, and develops fears of the physical sensations associated with autonomic arousal (Figure 1).

Repetition of attacks is hypothesized to make individuals increasingly more sensitive to internal stimuli and to situations in which the attack occurred, and to heighten surveillance of any physical sensation. Combined with that is anticipatory anxiety, i.e., fear of having another attack and catastrophic interpretations of symptoms when they do occur.^{17,18} Such fear-conditioned behavior leads the individual to avoid somatic symptoms (for example: physical exercises) or places associated with previous attacks (agoraphobia).²³ As a consequence, patients start having limitations in their everyday activities.¹⁷ Accordingly, CBT is used to eliminate the hypervigilance to symptoms, correct distorted interpretations and beliefs, and eliminate the agoraphobia.

Elements of cognitive-behavioral therapy

CBT is typically a brief treatment, between 10 and 20 structured sessions, with clear objectives to be achieved. It aims at correcting catastrophic interpretations and conditioned fears of body sensations and avoidances. It is practical, task-based and the patient's and therapist's roles are active. CBT can be performed individually or in groups.^{24,25} Despite studies suggesting that CBT should be brief, recent data on therapy "dose" have suggested that a higher number of sessions, either in-person or telephone counseling sessions, is associated with better response to CBT in PD.²⁶ Nonetheless, positive outcomes have been reported for the application of very brief treatment (in the range of six sessions) offered in clinic and primary care settings.²⁷⁻²⁹

CBT can be introduced at any stage of treatment, ranging from primary prevention to interventions to individuals refractory to other treatments.¹⁷ It can be started concomitantly with medications^{17,18,30} and uses the following resources as techniques: psychoeducation, anxiety coping techniques (muscle relaxation and abdominal or diaphragmatic breathing), cognitive restructuring, interoceptive and gradual *in vivo* exposure.^{17,24,25}

Results of a study of 76 PD patients with or without agoraphobia have suggested that the combination of cognitive (psychoeducation, cognitive restructuring, problem solving techniques) and behavioral (interoceptive and *in vivo* exposure) techniques has significant efficacy in the improvement of acute symptom remission and in the maintenance of gains in the follow-up until 6 months after CBT.³¹

Psychoeducation

Psychoeducation for PD breaks the rapid cascade of anxiety and panic into component elements, and provides a rationale for treatment interventions to follow. Emphasis is placed on defining and clarifying the source of anxiety and panic symptoms, introducing the role of thoughts in maintaining fear and anxiety, and the role of avoidance and escape behaviors in maintaining fears and perpetuating the disorder. The diagram presented below is used to provide a better understanding of the cognitive model of panic (Figure 2), adapted from Barlow's model.²³ Psychoeducation is performed in initial sessions and repeated at any time during the treatment.

It is crucial to motivate the patient to perform exposure exercises that inevitably involve increase in anxiety levels.

Anxiety coping techniques

Improper breathing patterns lead to hyperventilation and physiological symptoms resulting from significant increase in blood oxygenation: dizziness, suffocation, and tachycardia. Muscle tension also plays a role in increasing anxiety and may also cause physical reactions such as pains and paresthesias. These sensations are much similar to a panic attack and can be reduced using proper breathing techniques and muscle relaxation. Diaphragmatic breathing is a technique that uses abdominal muscles for respiratory control. Progressive muscle relaxation is an exercise involving practice of tension and relaxation of the main muscle groups. Both techniques (relaxation and abdominal breathing) can be practiced in sequence or independently, especially in situations in which there is anticipatory anxiety.^{24,25} Nonetheless, there is evidence that these anxiety coping techniques are not a necessary element of treatment³² and there is concern that, at times, these techniques may lead individuals into desperate attempts to control anxiety rather than helping patients eliminate fears of these symptoms. It is the elimination of these fears that is the central focus of both cognitive and interoceptive exposure interventions.

Cognitive techniques

Distorted and catastrophic interpretations of physical sensations of anxiety are common in PD, as well as patient's beliefs about hopelessness and inability to manage anxiety and panic. Cognitive

therapy aims at restructuring such catastrophic thoughts. To do so, it is important for the patient to know the basic assumptions of the cognitive model and cognitive therapy: that thoughts influence emotions and behavior, and that, in the case of PD, anxiety and panic can be a consequence of distorted interpretations of physical sensations. In treatment, patients are asked to treat their thoughts as hypotheses or "guesses" about the world. Training is given in identifying overlearned ("automatic") catastrophic thoughts linked to anxiety and panic.²⁴ After identifying these thoughts in session, patients are asked to monitor their thoughts, identify logical errors inherent to catastrophic interpretations, and generate more accurate thoughts. In the anxiety disorders, attention is given to overestimation of the probability of negative outcomes ("if my dizziness gets worse, I will faint") as well as overestimation of the degree of catastrophe of those outcomes ("if I ever fainted it would be simply unbearable"). These negative thoughts are frequently challenged through logical Socratic Questioning, or, in the form of specific behavioral experiments designed to help patients examine the accuracy of their anxiogenic predictions in actual performance situations.²⁴ It is this lattermost approach that is most similar to the type of learning targeted in the stepwise experience provided by exposure interventions.

Exposure techniques

1. Interoceptive exposure

Interoceptive exposure aims to correct the catastrophic interpretation of physical symptoms felt by the patient as part of anticipatory anxiety or panic attack. With interoceptive exposure,

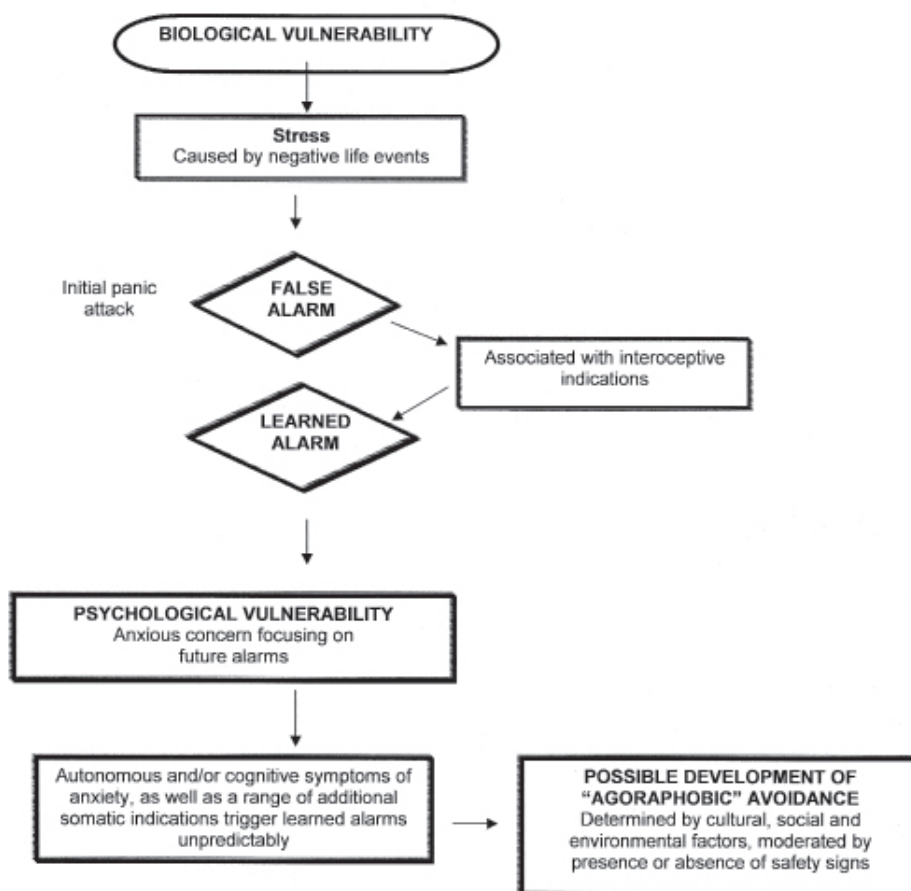


Figure 1 - Etiology of Panic Disorder - Barlow's Model, 1988

patients are provided with stepwise experience to become comfortable with sensations. Such exposure is performed through intentional provocation of symptoms using physical exercises. For example, feelings of dizziness might be induced by spinning in a swivel chair, or paresthesias, derealization and dizziness might be induced with a minute of overbreathing. In addition to direct training to become comfortable with these sensations (where patients learn to experience the sensations as odd or uncomfortable rather than frightening), interoceptive exposure also allows patients to identify automatic thoughts and catastrophic interpretations associated with physical sensations and correct them. Interoceptive exposure exercises can work as a preparation for *in vivo* exposure.²⁴ Interoceptive exposure interventions are typically introduced in the session, completed at least twice by the therapist and patient together, with attention to helping the patient “do nothing” to try to control or minimize the sensations. Home practice with the exercises is then assigned, with the goal of having the patient “get bored” with sensations by the time of the next weekly session. Finally, patients are asked to complete interoceptive exposure in sessions where they fear panic, so that comfort with the sensations can be learned in that context. This out-of-session interoceptive exposure practice provides a useful segue to *in vivo* exposure.

2. *In vivo* exposure

In vivo exposure is the main intervention applied to overcome agoraphobic avoidance. To plan *in vivo* exposure, the patient should make a list of the places or situations they have avoided due to fears, also record the anxiety level and automatic thoughts that arise in these situations.²⁴

That list should be arranged in a hierarchy according to the difficulty level to confront places and situations. *In vivo* exposure exercises are started by situations considered less anxiogenic and that the patient is willing to confront.

To be effective, exposure should be prolonged in time (remain in a given situation for approximately twice as long as it takes to become comfortable in that situation), frequently repeated, and the anxiety level should be felt during the task, monitored by both the patient and the therapist.³³

3. Dependence on relatives

Dependence on relatives is a very common problem in PD, and

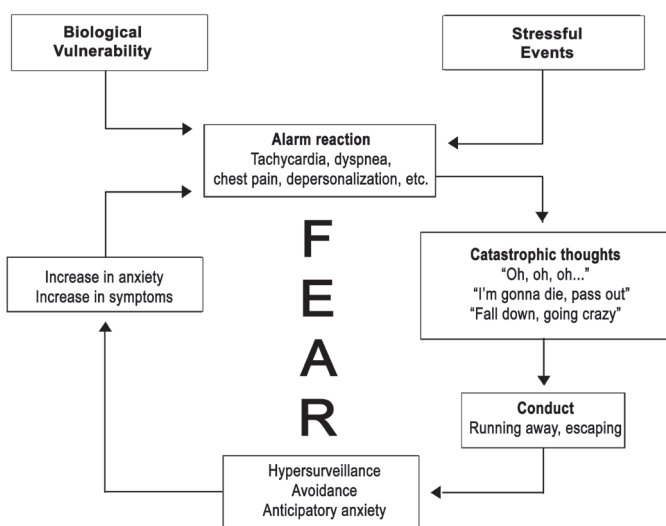


Figure 2 - Cognitive cycle of fear for panic disorder

its consequences are loss of autonomy by the patient, besides performance impairment and reduced self-esteem. Relatives can often be involved at some treatment stage to help exposure tasks. However, the treatment should encourage the patients to go to places they did not use to go alone to restore lost autonomy.

Cognitive-behavioral therapy sessions

CBT sessions in PD are structured, following the basic model proposed by Beck.³⁴ Initial sessions are dedicated to patient assessment, psychoeducation, and training of techniques to cope with anxiety (muscle relaxation and abdominal breathing) if these techniques are used. As sessions progress, greater attention is given to cognitive, interoceptive, and *in vivo* exposure interventions. Final sessions are devoted to the consolidation of gains and to relapse prevention efforts. Relapse prevention is aided by full practice of interoceptive exposure in a wide variety of situations, assuring that patients do not “leave well enough alone” and avoid full exposures in feared situations. Also, rehearsal of likely future difficulties (e.g., special events where anxiety may arise) and appropriate coping techniques, along with a review of the strategies that the patient found helpful in the past, provided additional elements of relapse prevention efforts.^{23,24} According to Wade et al., chronic stress was a predictor of worse outcome in patients with agoraphobia 12 weeks after CBT,³⁵ as well as in a 2-year follow-up assessment.³⁶ Therefore, it is important to identify situations that predispose to a higher psychological vulnerability to prevent relapses and chronicity.^{36,37}

Cognitive-behavioral therapy and medication

CBT is an excellent choice as a first-line treatment. It has good acceptability to patients,^{13,17,38} a relatively fast onset of action,³⁹ strong acute efficacy and strong maintenance of treatment gains,^{10,16} and strong cost-efficacy.⁴⁰ There is also evidence that CBT can be effective for PD patients refractory to drug treatment (i.e., failure to respond adequately following treatment with the recommended dose and duration of pharmacotherapy, or intolerance to higher dose). CBT offered in either an individual or group setting has been shown to benefit these patients for both short- and long-term outcomes.^{6,41}

Treatment outcome studies of PD have provided a complex picture regarding the value of combination treatment.¹⁶ Some researches suggest at least minimal additive treatment effects when CBT and medications are combined.^{42,43} However, there is also evidence that upon medication discontinuation, there is a loss of efficacy in combined treatment conditions that is not found in CBT alone conditions.⁴⁴ As such, whereas the addition of medications to CBT may enhance shorter-term outcomes, longer-term maintenance of treatment gains and the cost-efficacy of treatment⁴⁰ may be compromised with this approach. However, if patients have been started on medication and are subsequently offered CBT, there is evidence that medication can be tapered successfully during the course of CBT, with strong maintenance of treatment gains.^{32,45,46} For example, studies performed in our country have demonstrated that patients significantly reduced use of AD: of 61 (95%) patients using it before CBT, 45 (75%) remained under use at 1 year after the therapy. On the other hand, a follow-up of 48 patients for 5 years has demonstrated that 44 (93%) were using AD before CBT, and only 26 (55%) remained using the medication during the follow-up.³⁶ As to benzodiazepines, 49% of patients were using it before CBT and only 22% still used the drug after a 1-year follow-up.³⁰

Because exposure assignments appear to enhance the efficacy of medication treatment,⁴⁷ we recommend that elements of CBT, particularly instruction in stepwise exposure, should be offered as

part of medication treatment of PD. However, when state-of-the-art CBT is available to patients, we believe this intervention can be offered alone and achieve results that rival combination treatment in many cases and offer the potential for greater durability of treatment and lower cost.^{40,48} Nonetheless, we do recommend consideration of combination treatment when non-response is encountered in one or the other treatment modalities. There is also evidence suggesting that patients who fail to respond to CBT for PD can achieve benefits from subsequent pharmacotherapy, and as we observed, there are a number of small studies indicating that nonresponders to medication treatment of PD can do well in CBT.^{30,39}

Novel combination treatment – D-cycloserine

In the face of limitations on the benefit of traditional combined treatments (CBT plus antidepressants or benzodiazepines) for PD, there is promising evidence for a new strategy for combined treatment for the anxiety disorders. This strategy is focused on the promotion of better learning in therapy sessions, and grew out of basic research on the neural circuits underlying fear extinction.⁴⁹ These animal studies have indicated that fear extinction is both blocked by antagonists at the glutamatergic N-methyl-d-aspartate (NMDA) receptor. Moreover, d-cycloserine (DCS), a partial NMDA agonist, appears to augment extinction learning in animal studies (for review see^{50,51}). In particular, the retention of extinction learning appears to be facilitated by DCS given in individual doses prior to or soon after extinction (exposure) trials in animals, and may even aid the generalization of extinction to related cues.^{50,51}

After an initial clinical trial by Ressler et al. has indicated that DCS can enhance brief exposure-based CBT for the fear of heights, there has been a surge of interest in this combination treatment strategy.⁵² In these studies, brief exposure-based treatment is offered in conjunction with single doses of DCS; the patient takes a single dose of DCS prior to specific weekly sessions of exposure-based

treatment. A meta-analysis of the number of small trials completed to date indicates large effect sizes for this strategy as has been applied to social anxiety disorder, obsessive-compulsive disorder, and most relevant to the current paper, PD.⁵³ These findings, albeit in need of replication, encourage a new approach to combination treatment strategies – where CBT is used to provide the core treatment and a medication like DCS is used to enhance the retention of this therapeutic learning. If the trend of positive treatment trials continues, this novel approach to combining medication and CBT may provide additional benefit and perhaps more efficient treatment for patients with PD and other anxiety disorders.

Final considerations

In conclusion, CBT is an efficacious treatment modality for PD patients, whether as first-line therapy¹⁷ or as a strategy for patients who do not respond to medication,^{26,30,33} or even, as a combined treatment with drug therapy, as seen before.³²

This treatment presupposes correction of automatic catastrophic thoughts that worsen anxiety symptoms and fear, anticipatory anxiety, and predispose to avoidances. Through strategies to relieve anxiety (diaphragmatic breathing and muscle relaxation), cognitive changes and interoceptive exposures, the patients are more able to be exposed to avoided situations and, therefore, improve their quality of life, overcoming agoraphobia and dependence on relatives, which account for a major impairment in daily activities, often reaching the level of disability.

New approaches, such as Internet-based CBT⁵⁴ and intensive CBT (2 days), have been tested in PD with favorable outcomes.⁵⁵ Moreover, new combination treatment strategies using putative memory enhancers for extinction learning offer promise for extending treatment gains. Further studies should better evaluate the efficacy of this approach to combined treatments, and the role of comorbidities and stressful life events in the nonresponse and relapses in PD patients submitted to CBT.

Disclosures

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Gisele Gus Manfro	UFRGS	CNPq* FIPE-HCPA*	---	Boheringer* Ely-Lilly*	---	---	Roche*
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* Modest

** Significant

*** Significant. Amounts given to the author's institution or to a colleague for research in which the author has participation, not directly to the author.

Note: UFRGS = Universidade Federal do Rio Grande do Sul; HCPA = Hospital de Clínicas de Porto Alegre; CNPq = Conselho Nacional de Desenvolvimento Científico e Tecnológico; FIPE = Fundo de Incentivo à Pesquisa.

For more information, see Instructions for authors.

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