

## COGNITIVE-BEHAVIORAL INTERVENTIONS FOR OCD

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### Summary

The psychological interventions for Obsessive Compulsive Disorder (OCD) are cognitive and behavior therapies. Behavior therapy (BT) is based on Exposure and Response Prevention (ERP), which capitalizes on the fact that anxiety usually diminishes if exposure to the feared stimulus continues for a sufficiently long period of time. In order to achieve adequate exposure it is usually necessary to help the patient block his/her rituals or avoidance behaviors: a process termed response prevention. During ERP therapy, exposure proceeds upwards through the patient's hierarchy of feared situations, starting with the least feared situations in order to facilitate the patient's compliance. Cognitive therapy (CT) is based on a model for treating OCD drawn up by Beck et al. (1985) and developed by Salkovskis (1985, 1989). This model emphasizes the manner in which intrusive thoughts are interpreted through the patient's automatic thoughts. Cognitive strategies for treating OCD are based on the modification of these automatic thoughts and key beliefs. BT and CT have been shown to produce positive results with some OCD patients; however, more studies have been carried out to measure the efficacy of BT than to measure the efficacy of CT. ERP has proved to be a successful form of treatment for OCD, especially for patients with washing and, to a lesser extent, checking rituals. ERP appears to be the most effective treatment currently available (50 - 60% of patients meet criteria for recovery). Cognitive-behavior therapy (CBT) can be carried out individually or in groups. Group therapy has the advantage of increasing the number of patients treated and reducing personnel costs. Compared with the large number of studies into individual CBT, very little research has been carried out into the efficacy of group CBT.

Future research should take into account the recruitment and exclusion of study participants, include more comorbid patients, and focus on longer-term follow up using multiple outcome indices.

**Key Words:** Behavior Therapy – Obsessive Compulsive Disorder – Exposure and Response Prevention – Cognitive Therapy

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### Introduction

Until the 1960s, obsessive-compulsive disorder (OCD) was considered a treatment-refractory and chronic condition. Neither psychodynamic therapy nor the pharmacological treatments available at the time were capable of producing significant improvements in a patient's condition. Today, there is substantial evidence showing that cognitive and behavior therapies, especially behavior therapy, are effective in treating this chronic disorder (Foa et al. 1998). Cognitive-behavior therapy (CBT) combines behavior therapy (BT) and cognitive therapy (CT). After more than a quarter century of research, BT has become the gold standard to which other psychological treatments for OCD, such as CT, are compared (Fisher & Wells 2005, Cottraux et

al. 2001). Although the BT approach is better known and better validated, CT is starting to be the subject of controlled studies. The two approaches can be used either independently or conjointly. They can be carried out individually or in groups of six to ten patients. We describe the two techniques and then present their efficacy for treating OCD.

### 1- Psychological interventions

#### *a) Behavior therapy*

Behavior therapy for OCD is based on exposure with response prevention (ERP). Exposure capitalizes on the fact that anxiety usually diminishes if the subject

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is exposed to the feared stimulus for a sufficiently long period of time. In order to achieve adequate exposure it is usually necessary to help the patient block his/her rituals or avoidance behaviors; a process termed response prevention. Therapy should begin by giving the patient a detailed description of the rationale behind the treatment. This includes carrying out a functional analysis of symptoms and explaining how anxiety-reducing compulsions perpetuate obsessions. It is also necessary to explain the theoretical and practical implications of ERP, focusing on the reduction of anxiety and rituals, and to describe imaginary and in vivo exposure. Information must be gathered about current OCD symptoms and how they manifest themselves, the history of the OCD, previous treatment, the patient's response to that treatment, and the patient's general psychosocial and family history. It is also at this stage that the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) (Goodman et al. 1989a, 1989b) is administered. Information gathering usually requires three sessions. Treatment planning, which involves the construction of a hierarchy of potential anxiety-causing stimuli (including situations the patient currently avoids or overcomes through performing rituals), must be completed in the session preceding the first exposure session. The patient is asked to rate situations on a scale of 0 (no anxiety) to 100 (maximum anxiety), allowing them to be ranked from lowest to highest according to their anxiety rating. Exposure therapy proceeds upward through the hierarchy, beginning with the lower-rated items in order to facilitate patient compliance. The techniques used are in vivo ERP through homework, with assistance from the family whenever the family is involved in the rituals (Foa & Wilson 1991), and therapist-aided ERP with imaginary and/or in vivo exposure. Behavioral homework is discussed and set with the therapist and the patient is asked to record homework completion.

In vivo exposure involves exposing the patient to an anxiety stimulus and asking him/her not to perform any rituals (response prevention). Thus, two techniques are used in conjunction: exposure and response prevention (ERP). The exposure to the anxiety stimulus must be sufficiently long for the patient to become aware of a decrease in anxiety, which is measured by the patient noting at regular intervals (every 5 to 10 minutes), and on a scale of 0 to 8, his/her anxiety level. At the beginning of the session, the patient is told not to produce rituals to control anxiety (response prevention), so any decrease in anxiety will be due solely to prolonged exposure to the stimulus.

- The implications of exposure treatment must be discussed in advance and it must only be carried out with the patient's agreement.
- It is important to gain the patient's confidence and to prepare him/her to confront distressing situations.
- In order to avoid treatment dropout, exposure sessions are graduated from easiest to most difficult (construction of a hierarchy).
- Only one anxiety stimulus should be addressed at a time and the anxiety caused by that stimulus must be reduced by at least 50% before moving onto the next situation.

The length of the exposure sessions is an important variable: a criterion for stopping a session is the reduction of the anxiety by at least 50% compared with the maximum level expressed by the patient. Twenty to twenty-five individual sessions are required, usually at a rate of one per week, although this can be increased to two or three per week if necessary. Following treatment, a program of maintenance sessions should be organized (monthly booster sessions for six to twelve months).

The imaginary exposure technique is similar to in-vivo exposure except that the anxiety-inducing stimulus is imagined rather than real. The patient is asked to sit comfortably, to close his/her eyes, and to imagine a scene related to his/her obsessive thoughts. Generally, the therapy program starts with a situation that provokes a moderate level of anxiety according to the hierarchical list. Every 5 to 10 minutes the patient is asked to note his/her anxiety level on a scale of 0 to 8. The scene is repeated until it loses its anxiety-inducing power (reduction of the anxiety by at least half compared to the maximum). Between sessions, homework tasks are prescribed (reproduction of the imagination sessions or work on the reduction of rituals). Two studies (Foa et al. 1980, 1985) have shown that for checkers, who fear catastrophes and check that they haven't carried them out, the long-term (two years) maintenance of results is better for ERP with imaginary exposure associated with in-vivo exposure than for ERP with in-vivo exposure alone.

"Therapist-aided" ERP sessions consist of checking the work the patient does at home and of programming subsequent ERP sessions as a function of the patient's results. Thus, the therapist explains the rationale behind the ERP and the patient (alone or with a member of his/her family) carries out the exposure program. Marks et al. (1987) showed that exposure sessions carried out in the presence of a therapist are just as effective as RP carried out by the patient at home. In a more recent study, Abramowitz et al. (2002) reported that self-controlled exposure resulted in significantly smaller pre-post reductions in OCD symptoms (27%) compared to therapist-assisted exposure (49%).

In the case of ruminators (OCD without overt compulsions), exposure occurs on a cognitive level because it focuses on intrusive thoughts, while response prevention deals with internal mental rituals (neutralization strategies). Adaptations of ERP to treat ruminator OCDs are based on work by Salkovskis and his colleagues (Salkovskis & Warwick 1988, Salkovskis & Westbrook 1989).

### *b) Cognitive therapy*

Cognitive therapy is based on a model for treating OCD drawn up by Beck et al. (1985) and developed by Salkovskis (1985, 1989). This model emphasizes the manner in which intrusive thoughts are interpreted through the patient's automatic thoughts. Cognitive strategies for treating OCD are based on the

modification of these automatic thoughts and key beliefs (Rachman 1998, Salkovskis & Warwick 1985, van Oppen & Emmelkamp 2000, Whittal & McLean 1999).

The theoretical models underlying CT treatments for OCD postulate that the appraisal of thoughts plays a key role in the onset and maintenance of OCD symptoms and should therefore be addressed directly. The general strategies are: first, to consider the intrusions as stimuli; second, to identify the distressing thoughts (negative automatic thoughts) that immediately follow the intrusions; third, to challenge these automatic thoughts; fourth, to change these thoughts to non-distressing ones; and, finally, to look for the underlying dysfunctional schemas and modify these. The first step in CT for OCD consists of informing the patient that his/her intrusive thoughts are a normal phenomenon and providing him/her with a list of intrusive thoughts that commonly occur in the general population (for example, the Interpretation of Intrusions Inventory, Obsessive–Compulsive Cognitions Working Group 2001). A negative interpretation occurs most frequently when the intrusive thought contradicts the person's values (Rachman 1997, Salkovskis 1999). The patient then learns that the difference between normal and dysfunctional intrusive thoughts lies in the significance attached to these thoughts. The interpretation of an intrusive thought by a person with obsessions affects the occurrence and/or the content of this thought (Salkovskis 1989). The patient learns to distinguish the intrusive thought (my hands are dirty) from the negative automatic thought (I am going to spread disease and make my children ill) and the associated mental rituals. The second step involves modifying the automatic thought using classic cognitive therapy techniques. One of the general cognitive techniques most frequently used by therapists to challenge automatic thoughts is Socratic dialogue (Beck 1976), which involves encouraging the patient to question the catastrophic significance of the intrusive thought and to construct alternative, less catastrophic interpretations. For example, the patient may identify the pros and cons of his/her interpretation. Overviews of cognitive restructuring that describe these techniques for the appraisal of thoughts have been published (van Oppen & Arntz 1994, Freeston et al. 1996a). The third stage is to replace the automatic negative thought by a more rational thought. Behavioral experiments are commonly used to test the patient's belief in the new interpretation (session 6). The results of these experiments allow the therapist to evaluate the outcome of the cognitive process. Stage four involves recognizing the subject's schemas. Analysis of the different automatic thoughts worked on during the therapy sessions should reveal recurrent themes that the patient is taught to organize into key beliefs (after about session 10). The fifth and final stage consists of relaxing the schema by questioning the central beliefs. Discussions are held to examine the positive and negative consequences of the schema in the short, medium and long terms, and to seek more realistic interpretations. Each belief in the schema is then tested during a "behavioral experiment", such as the ones described above. In general, around twenty, weekly one-hour sessions are needed.

This technique helps OCD patients construct and test an alternative explanation for their problem that is both coherent and less threatening. Many of the dysfunctional beliefs seen in OCD patients, such as the faulty estimation of the importance of thoughts, the exaggerated sense of personal responsibility and perfectionism, can be addressed using CT, either alone or in conjunction with BT. CT may also provide additional benefits by improving compliance with ERP. The cognitive treatment of OCD patients has been described in several articles, for example Freeston et al. (1996b, 1998), Rachman (1998) and Salkovskis (1999).

### *c) Group therapy*

BT and CT can be carried out in groups. Group therapy has the advantage of increasing the number of patients treated while reducing personnel costs (therapist's time). Groups can also allow subjects, who are often socially very isolated due to the time spent carrying out rituals, to create relationships with other people. There are several different types of group: support groups associated with individual therapy sessions, groups for maintaining the therapeutic improvements made during individual sessions, groups run in conjunction with individual sessions and groups run to provide treatment without additional individual sessions. The objective of support groups is to provide OCD patients and their families with information about OCD and possible treatments. They are of short duration – five weeks in the Fals-Stewart and Lucente (1994) program. Marks et al. (1975) were the first to show the benefits to be gained from groups involving members of the family as a complement to individual treatment. Such groups provide information and practical help for carrying out ERP within the family. Programs are described by van Noppen et al (1997a, 1997b). Groups for maintaining results are particularly useful for patients who have had a very long illness (for example, OCD beginning in childhood) and for patients with very severe disorders. The objective of these groups is to help patients continue carrying out ERP to maintain the improvements that have been made (Marks et al. 1975, Hand & Tichatzsky 1979). The treatment of OCD through the use of group therapy alone is mostly based on BT, although some studies have reported the concomitant use of BT and CT (Bouvard 2003). The most common program for group BT is that of Krone et al. (1991). It consists of seven 2-hour sessions with, on average, five or six patients per therapist. Bouvard et al. 2002 described a CBT program consisting of six 3-hour weekly sessions of CT followed by six sessions of BT with six or seven patients per therapist.

## **2 - Efficacy**

### *a) Efficacy of behavior therapy*

Behavior therapy by exposure and response prevention (ERP) is considered the most efficacious treatment for OCD (Nathan & Gorman 1998). Its therapeutic efficacy has been shown by numerous

controlled studies carried out in several centers in different countries and on a large population of patients. On average, 80% of patients undergoing ERP BT show some improvement and at least 50% of patients make considerable progress (Steketee 1993, Steketee & Shapiro 1993). Follow up studies show that these results persist for up to six years after treatment stops and booster sessions can be offered to patients who relapse. ERP has proved to be a successful form of treatment for OCD, especially for patients with washing and, to a lesser extent, checking rituals. In a meta-analysis of 24 outcome studies, Abramowitz (1996) reported that ERP gave large effect sizes, indicating that most patients experienced substantial reductions in OCD symptoms.

However, these studies of BT efficacy have certain limits. For example, they usually concern patients without comorbid pathologies (depression or personality disorders), although it has been shown that 75 to 82% of OCD patients will one day show symptoms of depression (DeVaugh-Geiss 1993, Crino & Andrews 1996). Consequently, the results of these studies cannot be generalized to the entire OCD population. Franklin et al. (2000) evaluated the effectiveness of ERP amongst a large population of patients with a primary diagnosis of OCD; however, unlike most randomized controlled trials, no subjects were excluded because of comorbid diagnoses (Axis I and II), concurrent medication, other medical problems or past treatment. To achieve recovery, patients had to show sufficient improvement and cross a cut-off point of 16 on the Y-BOCS (Goodman et al. 1989a, 1989b). Recovery status was achieved by 86% of treatment completers. This study suggests that the manualized treatments delivered in randomized controlled trials are applicable to a general clinical population and that the results of those randomized trials can be generalized. In contrast, Abramowitz and Foa (2000) examined the outcome of ERP treatment for 15 OCD patients with comorbid major depressive disorder (MDD) and 33 OCD patients without MDD. Improvements in OCD symptoms were observed in both patient groups, and treatment gains were maintained at follow up (three to six months). Although there was no relationship between the presence of a comorbid MDD diagnosis in OCD and treatment failure, non-depressed patients had significantly lower post-treatment and follow up OCD severity scores. In addition, Steketee et al. (2001) examined the impact of concurrent axis I diagnoses and axis II traits on the efficacy of a 22-session exposure-based treatment program for 63 outpatients with OCD. Only GAD comorbidity predicted dropout, whereas MDD and all three personality cluster traits (anxious, dramatic and odd) predicted post-treatment outcomes. Follow up (six months) analyses showed significant effects of MDD and GAD, but axis II cluster criteria were not predictive. Major depression appeared to have the most consistent adverse effect on immediate and six-month outcome.

Furthermore, symptom reduction does not signify total recovery: in general, patients showing the biggest improvements only reduce their symptoms by half (Bouvard 2003). At least 25% of OCD patients are not able to tolerate BT due to the stress of being exposed to feared stimuli, and a further 20 to 30% show little or no improvement (Pallanti & Quercioli 2006). Therefore, it is

necessary to consider patients who refuse treatment or who dropout prematurely. On average, approximately 75% of OCD patients are considered likely to benefit from BT, although this figure does not take into account the nature of the benefit expected or the difficulties patients have in volunteering for and completing a program of treatment. People who refuse the treatment proposed, severely depressive OCD sufferers and OCD sufferers with overvalued ideas account for the 25% of patients resistant to the classic behavioral approach. The rate of patient dropout from classic treatment programs can be quite high (up to 10% of patients), as can post-treatment relapse rates (up to 20%). Relapse is particularly common among patients who have made limited progress at the end of the treatment. In conclusion, one in two OCD sufferers requesting treatment and considered likely to benefit from BT will not overcome his/her problem (Salkovskis & Warnick 1988, Salkovskis & Kirk 1997, Ladouceur et al. 1999) - effective treatment of OCD remains a real challenge for behavior therapists.

### *b) Efficacy of cognitive therapy for OCD*

Four studies of protocols of individual cases have shown the efficacy of cognitive therapy used in conjunction with behavioral methods of the type "exposure to a thought that is distressing for the subject" (Salkovskis & Warwick 1985, Simos & Dimitriou 1994, Ladouceur et al. 1995, Hartl & Frost 1999). Two further studies have investigated protocols of single cases of CT without concomitant BT: Ladouceur et al. (1996) worked with checker subjects, and Freeston et al. (2001) worked with ruminator subjects. These studies showed that CT based on cognitive restructuring reduces OCD symptoms for checker and for ruminator OCDs. Ladouceur et al (1996) measured responsibility scores for each of the checker subjects before and after the cognitive correction treatment. They found that the patients' responsibility scores for situations perceived to be problematic decreased following CT. Freeston et al. (2001), however, only assessed their subjects' OCD symptoms. In a more recent study, Wilson and Chambless (2005) tested the efficacy of CT on six patients suffering from OCD. After treatment, the compulsions of three of the six patients had decreased, whereas the compulsions of the other three subjects remained unchanged. Two patients met stringent criteria for Jacobson and Truax's recovered status at post-test according to the Y-BOCS. For all patients, large pre-test-post-test effect sizes were found.

Three controlled studies have compared the results obtained using Beck's CT and those obtained using BT. The earliest study, by Van Oppen et al. (1995), compared CT and BT without revealing any post-treatment differences in OCD symptoms or in the associated symptomology. Freeston et al. (1997) showed the efficacy of both CT and BT with respect to a list of expectations of ruminator subjects, in terms of both the OCD symptoms and the cognitions specific to the OCD patients (estimates of danger and responsibility). These results were maintained at follow up. A more recent study, by Cottraux et al. (2001), confirmed the efficacy



of CT compared with BT, with the two approaches leading to comparable reductions in OCD symptoms. Improvements for depression were much greater with CT than with BT; however a follow-up study one year later found that this difference had disappeared.

In a study of 59 OCD patients, Whittal et al. (2005) compared the efficacy of CT with behavioral experiments with that of BT. They did not find any significant difference in Y-BOCS scores between CT and ERP at post-treatment or at three-month follow up. A higher percentage of CT participants obtained recovered status (a decrease of at least 6 points on the Y-BOCS and a final Y-BOCS score of less than 12) at post-treatment (67%) and at follow up (76%) than ERP participants (59% and 58%, respectively), but the difference was not significant. In addition, the two treatment groups presented significantly similar reductions in OBQ (Obsessive Beliefs Questionnaire) and III (Interpretation of Intrusions Inventory) scores (Obsessive Compulsive Cognitions Working Group 1997) at post-treatment and at follow up. This suggests that CT gave similar changes in interpretations of thoughts and beliefs as ERP, despite such cognitive phenomena being the main focus of treatment in CT. In Whittal et al.'s study, the ERP and CT protocols for OCD yielded similar symptom reduction effects (just over 50%), measured using the Y-BOCS scale. These results were maintained at the three-month follow up.

#### *c) Comparison of different forms of OCD therapy*

Abramowitz et al. (1999) analyzed seventeen controlled studies of BT, CT and combined BT/CT for OCD. Six studies that directly compared BT and CT had an effect size close to zero, revealing no differential efficacy. For the eight studies of BT, the effect size was 1.50 and the average OCD symptom reduction was 48%. For the two studies of CT, the effect size was 1.19 and the average OCD symptom reduction was 30%. For the three studies of combined therapy, the effect size was .99 and the average OCD symptom reduction was 39%. Eddy et al. (2004) reported a multidimensional meta-analysis of studies of psychological and pharmacological treatments for OCD published between 1980 and 2001. Although all psychotherapies show strong effects, the more behaviorally (as opposed to cognitively) oriented psychotherapies tended to be more efficacious. However, OCD symptoms persist at moderate levels, even following adequate treatment, and no replicable data are available on the maintenance of gains for either form of treatment at one year or beyond. Future research should track recruitment and exclusion of study participants, include more comorbid patients, and focus on longer-term follow up using multiple indices of outcome. Finally, Fricke et al. (2005) examined whether comorbidity with personality disorders (PD) affects CBT outcome in OCD patients. In the sample, 44% of the patients had at least one PD, thereby showing the relevance of comorbid Axis II diagnoses in OCD. However, these patients benefited as much from treatment as patients without comorbid PDs, and both groups maintained their improvement at follow up.

The methods used to calculate clinical significance vary considerably between studies and some methods are more stringent than others. When recovery is defined using the Jacobson methodology (Jacobson & Truax 1991), BT appears to be the most effective treatment currently available (50 - 60% of patients met criteria for recovery). However, when the asymptomatic criterion is used as the index of outcome, BT and CT have low and equivalent recovery rates (approximately 25%) (Fisher & Wells 2005).

#### *d) Efficacy of group therapy*

Enright (1991) was the first to study the efficacy of group BT. The behavioral program of Krone et al. (1991) has been the subject of several efficacy studies and the results have been satisfactory (Krone et al. 1991, Himle et al. 2001). Overall, the behavioral technique produces significant improvements in OCD symptoms and in depression. For the subjects studied by Himle et al. (n = 113), the overall Y-BOCS score decreased from 22 in the pre-test to 15 in the post-test, and to 14 at the three-month follow up. The Beck Depression Inventory (BDI) score decreased from 16 in the pre-test to 11 in the post-test, and to 10 at the follow up. Van Noppen et al. (1997a) reported that ten to twelve sessions of group behavioral ERP produced significant improvements in both Y-BOCS and disability scores. The majority of OCD patients showed gains: between 70 and 80% of patients improved by at least 5 points (20% or more) on the Y-BOCS at post-test and at follow up. The only controlled study to have been carried out in this field is that of Fals-Stewart et al. (1993), who compared group BT (n = 30) with individual BT (n = 31) and group relaxation therapy (n = 32). The programs used ERP with either in-vivo exposure or imaginary exposure, depending on the patient. Group BT appeared just as efficacious as individual BT and the results were maintained for a period of six months; however, OCD symptom reduction (Y-BOCS) was faster with individual treatment. The control group (progressive relaxation) only reduced anxiety; it was ineffective in reducing OCD symptoms (Y-BOCS) and depression (BDI).

Bouvard et al. (2002) evaluated three groups of OCD patients (a total of twenty subjects) following the same group CBT program. At the end of the treatment, improvements were noted in OCD symptoms (Y-BOCS and therapeutic objectives) and in the beliefs associated with the OCD (Obsessive Beliefs Questionnaire). There was no improvement in depression or anxiety. A six-month follow up confirmed the maintenance of the results. McLean et al. (2001) examined the efficacy of CT and ERP conducted in small groups and found that both treatments resulted in statistically significant improvements according to most outcome measures. At post-treatment, 16% of group CT patients had achieved recovery, compared with 38% of group ERP patients. The differences in the proportions of recovered patients were not significant. However, at three-month follow up the recovery rate was significantly greater for group ERP patients than for group CT patients (45% and 13%, respectively). O'Connor et al. (2005) compared the efficacy of group and individual CBT

formats for obsessions without compulsions. Both formats produced a significant clinical change, but individual treatment produced a greater change in symptoms and in beliefs. The results of this study suggest that the impact of a group format in ruminators may result from shared social support but at the expense of individual targets.

The efficacy of group CBT for OCD has received relatively little research attention compared with the large number of studies of individual CBT. Anderson and Rees's (2006) work is the latest controlled study to compare an identical CBT protocol delivered individually and in a group. Both the active treatment conditions resulted in significantly greater symptom improvement than the control condition. Individual CBT resulted in a larger percentage of participants meeting the criteria for recovery. However, the percentage of individual CBT participants who met the criteria for recovery dropped from 41% at post-treatment to 23% at short-term follow up. In contrast, the percentage of group CBT participants who met the criteria for recovery increased from 20% at post-treatment to 22% at short-term follow up. Hence, at short-term follow up both individual and group conditions were equivalent in terms of the percentage of participants meeting the criteria for recovery. These results are consistent with previous reports by Fals-Stewart et al. (1993), who found that individual BT led to faster rates of symptom improvement than group BT but that the treatment modes were equally effective over time.

## Conclusion

The efficacy of BT in treating OCD has been established. However, the majority of patients still have some symptoms after treatment. The efficacy of CT is less established but it may be comparable with the efficacy of BT. It allows resistance to ERP to be overcome and facilitates the reduction in anxiety during exposure sessions. The two techniques can be used alone, or, if the results for the patient are not satisfactory, conjointly. Most therapies are still carried out on an individual basis, with the involvement of the family if necessary. Group therapies are starting to be offered but further studies of their efficacy are needed. Better solutions still need to be found for patients who are resistant to therapy and to anti-depressants.

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