Nonpharmacological treatments for anxiety disorders

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An evidence-based review of nonpharmacological treatments for anxiety disorders is presented. The vast majority of the controlled research is devoted to cognitive behavior therapy (CBT) and shows its efficiency and effectiveness in all the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) anxiety disorders in meta-analyses. Relaxation, psychoanalytic therapies, Rogerian nondirective therapy, hypnotherapy, and supportive therapy were examined in a few controlled studies, which preclude any definite conclusion about their effectiveness in specific phobias, agoraphobia, panic disorder, obsessive-compulsive disorder (OCD), and posttraumatic stress disorder (PTSD). CBT was clearly better than psychoanalytic therapy in generalized anxiety disorder (GAD) and performance anxiety. Psychological debriefing for PTSD appeared detrimental to the patients in one high-quality meta-analysis. Uncontrolled studies of psychosurgery techniques for intractable OCD demonstrated a limited success and detrimental side effects. The same was true for sympathectomy in ereutophobia. Transcranial neurostimulation for OCD is under preliminary study. The theoretical and practical problems of CBT dissemination are discussed.

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onpharmacological treatments for anxiety disorders—although of varied orientations—are unequally represented in the literature. The bulk of the research is devoted to behavior therapy (BT) and, more recently, to cognitive therapy (CT) methods. Both CT and BT techniques are used in combination by the vast majority of clinicians and researchers under the label of cognitive behavior therapy (CBT). Relaxation methods have been used as the main technique in anxiety disorders or studied as a control condition in some randomized controlled trials (RCTs). Some relaxation techniques, such as Ost's applied relaxation,1-3 are in fact made of several cognitive and behavioral techniques. Psychoanalytic (or psychodynamic) therapies, hypnotherapy, Rogerian nondirective therapy, supportive therapy (ST), and psychological debriefing for posttraumatic stress disorder (PTSD) have been evaluated in RCTs and meta-analyses. Transcranial neurostimulation and psychosurgery techniques have been studied in obsessive-compulsive disorders (OCDs). Some preliminary data exist for sympathectomy in ereutophobia. Hence an evidence-based review of all these nonpharmacological methods is possible.

Panic disorder and agoraphobia

CBT in panic disorder and agoraphobia

Panic disorder and agoraphobia are treated using two basic strategies: exposure (in imagination and in vivo or interoceptive exposure) and cognitive restructuring.

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Selected abbreviations and acronyms

BDZ benzodiazepine BT behavior therapy

CBT cognitive behavior therapy

CT cognitive therapy

EMDR eye movement desensitization and reprocessing

GAD generalized anxiety disorder
OCD obsessive-compulsive disorder
PTSD posttraumatic stress disorder
RCT randomized controlled trial

SSRI selective serotonin reuptake inhibitor

SST social skills training ST supportive therapy

Exposure principle

Exposure in vivo represents the final common pathway of many techniques described by several schools of psychotherapy. The first person to write a report on successful exposure in agoraphobia was a French author, Perroud⁴ who was working at the Hôpital de la Charité, in Lyon. Janet⁵ used the exposure principle in several cases of obsessions or phobias. Later, Freud⁶ made a forgotten contribution to CBT with the straightforward judgement that for resistant agoraphobia "one succeeds only when one can induce them by the influence of the analysis to go into the street and to struggle with their anxiety." In this respect, cognitive behavior therapists are more Freudian than modern psychoanalysts, who continue to treat agoraphobia with classic psychoanalysis, while its effectiveness remains to be demonstrated.

Wolpe⁷ and Marks,⁸ a fervent reader of Janet, systematically developed the exposure paradigm in anxiety disorders and put this principle under systematic scientific inquiry, in several controlled trials, which were replicated all over the world.

Exposure consists in habituating degree by degree the patient to the feared situations in imagination and then in vivo. The aim is to obtain a habituation of emotional responses and the extinction of avoidance behaviors, which are reinforced by anxiety. Generally, the therapy starts with exposure in imagination confronting the patient step by step to the feared situations until habituation occurs. Graded in vivo exposure is then carried out. Each session of exposure in vivo or in imagination

may last up to 45 minutes, which is, in general, the maximum length of time required to habituate the anxiety responses.

Cognitive restructuring

CT implements two main strategies: (i) cognitive restructuring on misinterpretations of bodily sensations; and (ii) breathing retraining in order to control the physiological effects of hyperventilation and tachycardia. Treatment typically includes 15 to 20 sessions, which can be summarized as follows:

- Modifying panic attacks. (i) Breathing retraining to control the sensations resulting from hyperventilation frequently involved in panic attacks; (ii) Valsalva technique through abdominal breathing to control tachycardia; and (iii) cognitive restructuring to modify misinterpretations of bodily sensations and challenge the danger cognitive schemata.
- *Modifying agoraphobia*. Behavioral experiments consist in modifying avoidance behaviors through graded exposure followed by cognitive restructuring through self-talk and written disputing on appropriate forms.

Interoceptive exposure for panic attacks

Some researchers designed specific techniques for the bodily symptoms. Panic control treatment⁹ consists of three major strategies: (i) cognitive restructuring; (ii) breathing retraining; and (iii) interoceptive or structured exposure to bodily sensations that have become associated with panic attacks.

Since physical sensations often trigger conditioned anxiety, the procedure of interoceptive exposure attempts to extinguish anxiety connected with these bodily sensations. Identifying "interoceptive avoidance," or avoidance of situations that might provoke specific physical sensations and their catastrophic cognitive appraisal, is implemented during the therapy. These situations are not identical to agoraphobic situations and may include watching frightening movies or driving with the windows closed. All patients are presented with exercises meant to induce physical sensations: running on the spot, being spun in a swivel chair, breathing through a narrow straw, etc. Patients are then encouraged to enter naturalistic situations that might be associated with the elicitation of physical sensations that are particularly anxiety-provoking.

Outcomes of exposure treatments

Meta-analyses on panic disorder¹⁰⁻¹³ found that in vivo exposure was a critical component of treatment, but disagreed on its results in combination with antidepressants, anxiolytic drugs, and cognitive interventions. Van Balkom et al's¹³ meta-analysis and its follow-up study by Bakker et al¹⁴ suggested that the most effective treatment was a combination of exposure in vivo and antidepressants. Another meta-analysis by Gould et al¹⁵ found a higher size effect for CBT than for pharmacotherapy and a combination of medication with therapy, with the lowest dropout rate and the best cost–effectiveness ratio. *Table I* presents the outcomes of Gould et al's¹⁵ meta analysis. Interoceptive exposure appears to be the most effective technique.

Outcomes at follow-up

O'Sullivan and Marks¹⁶ conducted a review of 10 long-term follow-ups (the longest lasted 9 years). Four hundred and forty-seven patients out of a panel of 553 had been followed up in controlled studies for a mean duration of 4 years. They found a 76% improvement in the cumulated samples with residual symptoms as a rule; 15% to 25% of the patients continued to have depressive episodes after treatment. In the longer follow-ups, up to 50% consulted practitioners for their psychological problems and 25% saw psychiatrists for depression and/or agoraphobia. However, the consultation rate decreased.

CBT and medication: combination studies

Combination allows stopping the medication without the very high relapse rate that is found in drug-only studies. However, a positive interaction was found only with certain antidepressant drugs (imipramine, fluvox-

Therapy	Size effect
CT + interoceptive exposure	0.88
CBT	0.68
Pharmacological treatment	0.47
Pharmacological treatment + CBT	0.56
Antidepressants	0.55
Benzodiazepines	0.40

Table I. Panic disorder: meta-analysis of size effects. ¹⁵ CT, cognitive therapy; CBT, cognitive behavior therapy.

amine, and paroxetine) and anxiolytic drugs (buspirone). Moreover, CBT facilitates the withdrawal of benzodiazepines (BDZs). One may summarize the outcomes of the combination studies as follows:

- Positive interactions with antidepressants were reported in seven controlled studies. 17-23
- No interaction with antidepressants was found in five studies.²⁴⁻²⁸
- Short-term positive interaction and long-term *negative* interaction of exposure in vivo with high doses of alprazolam (6 mg) was found by Marks et al²⁹ and Wardle et al.³⁰
- Short-term positive interaction of exposure in vivo with low doses of diazepam (<30 mg) was found in a controlled study. However, there was a transient with-drawal syndrome. No negative long-term effects.³¹
- Short-term positive interaction of CBT with low doses of buspirone (<30 mg) on agoraphobia and generalized anxiety was demonstrated in a controlled study. No withdrawal syndrome and no long-term negative effects appeared. The effect of buspirone on agoraphobia correlated with its effects on depressive cognition. Buspirone's action on agoraphobic behaviors is probably mediated by the reduction of both anxiety and depression.³²
- CBT facilitated BDZ withdrawal in two controlled studies.^{33,34}

Relaxation in panic disorder and agoraphobia

CT appeared to be superior to Jacobson's relaxation in one trial.³⁵ In a 2-year follow-up study, Craske et al³⁵ suggested that Jacobson's relaxation could even impede the positive effects of BT.

Clark et al³⁶ found that CBT (84%) was superior to relaxation (40%), imipramine with a maximum dose of 300 mg/day (42%), and a waiting list. The follow-up of this study was 1 year. At this point, all intention-to-treat groups received self-exposure instructions. This study confirmed the superiority of CBT over relaxation and also suggested that imipramine, the reference drug, was neither the only effective treatment nor the most efficient.

Applied relaxation¹⁻³ has been found to be as effective as CBT in panic disorder with agoraphobia. However, it contains cognitive coping strategies, as well as exposure assignments. Accordingly, the applied relaxation format is more a variant of CBT than a pure relaxation tech-

nique. This is confirmed by the fact that applied relaxation appeared better than Jacobson's relaxation in one controlled trial.³⁷ Nevertheless, applied relaxation was superior to a waiting list, but inferior to CT in another trial dealing with panic disorder *without* agoraphobia.³⁸

ST in panic disorder

In a controlled study, Beck et al³⁹ reported a rate of 71% panic-free patients after 8 weeks of CT versus 25% after 8 weeks of ST. It is worth noting that 94% of the patients who were randomized to ST chose to have CT after ST. At a 1-year follow-up 87% of the patients who had CT were panic-free versus 79% in the group who had ST first and then CT. Beck et al's³⁹ outcomes were at variance with those of Shear et al's⁴⁰ controlled study, which found at a 6-month follow-up that CT and ST demonstrated positive and equivalent effects on panic attacks.

Psychodynamic therapy in panic disorder

To our knowledge, there is only one controlled study concerning panic disorder. Wiborg and Dahl⁴¹ compared clomipramine alone with psychodynamic therapy (15 sessions) associated with clomipramine in 80 subjects with panic disorder. Psychodynamic therapy was focused on dependence behaviors and related emotional problems. The randomization process did not work in that study: baseline Hamilton Anxiety, Hamilton Depression, and Handicap scales were significantly higher in the clomipramine group. Nevertheless, the authors contended that the combined condition (20% relapses) was superior to clomipramine alone (75% relapses) at a 9-month follow-up. As there was no waiting-list control, Wiborg et al's⁴¹ study does prove a specific effect of psychodynamic therapy in panic disorder.

Generalized anxiety disorder

CBT in GAD

Methods

Since the first operational definition of generalized anxiety disorder (GAD) in the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM-III)*, ⁴² the pathogenesis has been clearly concentrated on the concept of excessive worry. ⁴³ This cognitive point of view

considers the somatic symptoms as secondary manifestations of cognitive processes. Later, the *DSM-IV*⁴⁴ paid allegiance to the cognitive model with another criterion: the difficulty in controlling the worry. This new trend was supported by numerous studies assessing normal and abnormal thoughts showing the intolerance to uncertainty of GAD subjects. Pathological worry is viewed as shaped by cognitive distortions, which result from maladaptive schemata of danger. Ruminations and attention disturbances impede normal problem solving in everyday situations and worry represents for the patient an inefficient way to control possible negative events in the future.⁴⁵

In CBT, the patient is advised to consider his or her catastrophic view up to its ultimate consequences. At this point, Socratic questioning will help him or her substitute more probabilistic views instead. The patient can also be exposed in imagination to the catastrophic scenes to reach habituation. Then, basic schemata of danger are elicited and questioned. The treatment format classically involves about 15 sessions. The different levels of intervention are cue-controlled relaxation, cognitive restructuring, problem solving, in vivo exposure to feared real-life situations, and exposure in imagination in order to obtain habituation to highly improbable situations. The aim is to replace the worry by effective coping strategies.

Outcomes

A meta-analysis by Gould et al^{46,47} found CBT and pharmacotherapy equally effective. This meta-analysis included 35 controlled studies, which had been published between 1974 and 1996: 13 studies dealt with CBT and 22 with medication. The size effect was 0.70 for CBT and 0.60 for the pharmacological treatment. However, the drug samples had higher dropout rates and showed a loss of efficacy at withdrawal, while the effects of CBT were maintained. Studies assessing the CBT plus drug combination were lacking.

Psychoanalytic therapy in GAD

Two studies reported negative outcomes for psychoanalytic therapies (*Table II*).⁴⁸⁻⁵³ In Durham et al's⁴⁸ study psychoanalytic therapy had within-group positive effects, but these effects were significantly inferior to those of CBT immediately after the test and at 1-year follow-up. One should also mention that the psychoanalytic method used by White⁴⁹ was less than optimal.

Rogerian nondirective therapy in GAD

Two studies reported equal effects of Rogerian therapy and CBT. Two reported a better effect of CBT. Further studies should be done to clarify this point. *Table II* also presents the outcomes of these four studies. ⁵⁰⁻⁵³

Posttraumatic stress disorder

CBT in PTSD

Methods

Treatment of PTSD is the center of a growing interest in the literature. Therapeutic programs involve relaxation, which is beneficial in case of high emotional arousal, exposure to avoided situations or images related to the trauma, and CT. Five methods have been proposed. All the methods insist on the necessity of respecting the pace of the patient to reach the peak of the horror that is at the center of the traumatic experience.

- Systematic desensitization presents the feared stimuli in imagination under relaxation in a graded way prior to in vivo exposure.
- Exposure in imagination and in vivo aims at habituating the patient to the aversive stimulus, by reducing abnormal reactivity and avoidance. In vivo exposure to the nondangerous situations being avoided is then suggested.
- Stress management emphasizes the development of coping strategies to deal with fears (relaxation, social skills training [SST], modification of anxious verbalization, or thought stopping).

- Cognitive therapy also suggests exposure in imagination and representation of coping strategies, but puts a greater emphasis on dealing with automatic thoughts and dysfunctional attitudes (personalization, guilt, illusion of a safe world, and necessity of revenge).
- Eye movement desensitization and reprocessing (EMDR) consists in inducing eye movements when concentrated on feared imagery, bodily sensations, and negative statements associated with the trauma, in order to reduce anxiety and hence modify cognition in a positive way. Sessions last 90 minutes and are limited to 4 or 5. This method was hypothesized to work on neuropsychological functions. In fact, there is no clear evidence that EMDR is no more than a variant of the usual CBT programs. A controlled study found that EMDR with or without ocular movements gave the same positive outcomes as a standard psychiatric procedure at posttest and a 6-month follow-up. Nonspecific factors might be implied in EMDR.

Outcomes: meta-analysis

Most of the studies showed positive results. There is no difference in outcomes between CT and BT.⁵⁶ About 60% of patients respond to the treatment. Follow-up studies seldom exceed 6 months or 1 year.

Van Etten and Taylor⁵⁷ conducted a meta-analysis of 61 treatment outcome trials for PTSD. Treatments included drug therapies (tricyclic antidepressants, carbamazepine, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors [SSRIs], and BDZs), psychological therapies (BT, EMDR, relaxation training, hypnotherapy, and psychodynamic therapy), and control conditions (pill placebo, waiting-list controls, supportive psychotherapies, and nonsaccade EMDR control). Psychological therapies demonstrated significantly lower dropout rates than

Outcome	Duration of follow-up	Reference
 CBT versus psychoanalytic therapy 		
CBT > psychoanalytic therapy	1 year	Durham et al,⁴8 1994
CBT > psychoanalytic therapy		White et al,49 1992
 CBT versus Rogerian nondirective therapy 		
CBT > ST	6 months and 1 year	Borkovec and Mathews,50 1987
CBT > ST	1 year	Borkovec and Costello,51 1993
CBT = ST	6 months	Blowers et al,52 1987
CBT = ST	6 months	Stanley et al,53 1996

Table II. Generalized anxiety disorder: cognitive behavior therapy (CBT) versus other therapies. ST, supportive therapy.

pharmacotherapies (14% versus 32%). The attrition rate was uniformly low. Follow-up results were only available for BT and EMDR: outcome was maintained at 15-week follow-up.

Psychodynamic therapy and hypnotherapy in PTSD

Brom et al's^{ss} randomized study compared systematic desensitization with psychodynamic therapy, hypnotherapy, and a waiting-list control in 112 patients. The results showed a reduction in symptoms in all three groups at posttest: improvement rate was 41% for systematic desensitization, 34% for hypnotherapy, and 29% for psychodynamic therapy. The between-group difference was nonsignificant. The study had no follow-up.

Debriefing for PTSD prevention

DSM-IV⁴⁴ considers that 1 month of stress reaction is required to make a diagnosis of acute PTSD, and 6 months for chronic PTSD. Many subjects present spontaneous remissions in the 1-month interval following the trauma. Debriefing was introduced by Mitchell⁵⁹ as a short-term early intervention, which takes place in the immediate aftermath of the trauma (within 48 h). The aim is to reduce immediate posttraumatic distress and to prevent PTSD occurring through discussing and reliving the traumatic event step by step. Debriefing consists of a single group or individual session that lasts 3 h. Typically, seven stages are implemented by a psychologist or in some cases by laypersons in a didactic format that progressively reaches the emotional core of the trauma: "introduction," "facts," "thoughts," "reactions," "symptoms," "teaching," and "relating."

Debriefing has been strongly advocated and widely used in many countries, but well-designed evaluative studies come out with negative outcomes. A meta-analysis of 11 high-quality RCTs was carried out⁶⁰ and found that single-session debriefing did not reduce distress, depression, or anxiety, and did not prevent PTSD from occurring. Moreover, the risk of developing PTSD was higher in those patients who received debriefing, compared with those who did not, in one important trial. In conclusion, the authors stated that compulsory debriefing should cease. It seems that debriefing sensitizes the patients, rather than enhancing habituation process. It may also represent a second trauma that "prints" the event in the autobiographical memory.

Patients with ruminations seem more likely to have negative reactions.

Obsessive-compulsive disorder

CBT in OCD

Methods

The main behavioral strategy is in vivo exposure with response prevention, which was initiated by Janet⁵ and developed by Meyer⁶¹ and Marks.⁸ Exposure with response prevention means that exposure is carried out while compulsions are not allowed to the patient. The aim is to reach habituation to obsession-triggering stimuli. Nonetheless, it is less time-consuming and very cost-effective to give homework assignments, which are agreed on with the patient. It is also helpful to involve the patient's partner as a cotherapist. For patients for whom the trigger is more internal, eg, fear of internal representation rather than environmental cues or having covert rituals, prolonged exposure in imagination is the recommended procedure.

A cognitive behavioral model for OCD was proposed by Salkovskis.⁶² First, the intrusive thought, which is unacceptable and egodystonic, is viewed as a "normal" process failing to habituate for biological and/or psychological reasons. Second, the obsessive thought (automatic thought) is an evaluation of the intrusive ideas through overresponsibility schemata deep-seated in the long-term memory. This leads to rituals (overt behavior) and neutralizing thoughts (covert behavior), which represents an attempt to control and suppress intrusive thoughts. Such neutralizations prevent habituation to intrusive thoughts from occurring. Hence, Salkovskis proposed a triple intervention: cognitive exposure to intrusive thoughts with neutralization prevention, Socratic questioning of the automatic thoughts and overresponsibility schemata, followed by behavioral experiments (in vivo exposure) to disconfirm the schemata. Treatment classically involves 20 to 25 sessions.

Results of BT

BT has been clearly demonstrated to be superior to placebo and relaxation. The outcome with BT is close to that of serotonergic antidepressants, which have detrimental side effects and a high relapse rate after withdrawal.⁸ The limitations of BT could be summed up as follows: dropout or refusals 25%; no or poor effect 25%; and relapse 20% (3 months to 3 years). The controlled studies combining BT with antidepressants show a better outcome on rituals and depression in the long term. In particular, Cottraux et al^{63,64} showed fluvoxamine plus

BT compared with placebo plus BT to give better results at 3 months on rituals and at 6 months on depression with equivalent results at 12 and 18 months. The outcomes of the combination studies are summarized in *Table III*. 63-70

Study	Patients (n)	Hamilton Depression Scale (17 items)	Outcome
Solyom and Sookmann,65 1977	27		 Short term (6 weeks) CMI = imaginal flooding (ruminations) CMI > thought stopping (ruminations) CMI < E (rituals)
Marks et al,66 1980	40	17	• Short term (7 weeks) CMI + E > CMI + R
	37		 Long term (2 years) CMI + E > PBO + E at weeks 7 to 18, waning at week 36
Marks et al, ⁶⁷ 1988	49	10	• Short term (17 weeks) CMI + E >> CMI + A
	39		 Long term (2 years) CMI + E > PBO + E at week 8, waning at week 17
Cottraux et al,63 1990	60	19	• Short term (8 weeks) FLV + E or FLV > PBO + E (rituals)
	44		 Mid term (24 weeks) FLV + E or FLV > PBO + E (depression)
	37		• <i>Long term</i> (1 year) FLV + E = PBO + E = FLV
Cottraux et al, ⁶⁴ 1993	33		 Long term (18 months) FLV + E = PBO + E = FLV Still under antidepressants PBO + E and FLV + E = 18% versus FLV = 60% (P<0.05)
Foa et al, ⁶⁸ 1992	19	20	 Short term (6 weeks) IMI > PBO (depression) Long term (2 years)
	19	11	IMI + E = PBO + E
	19	20	IMI + E = PBO + E
Baxter et al, ⁶⁹ 1992	18	9	 Short term (10 weeks) FLUOX = E on symptoms and reduction of right caudate hypermetabolism (PET)
Van Balkom, ⁷⁰ 1994	104		Short termFLV = CBT > WL (rituals)CBT > FLV > WL (anxiety)

Table III. Obsessive-compulsive disorder: exposure with response prevention and antidepressants. A, anti-exposure; CBT, cognitive behavior therapy; CMI, clomipramine; E, exposure; FLUOX, fluoxetine; FLV, fluvoxamine; IMI, imipramine; WL, waiting list; PET: positron emission tomography; PBO, placebo; R, relaxation.

Long-term follow-up of CBT

When addressing the long-term follow-up question, O'Sullivan and Marks¹⁶ reviewed 9 cohorts of patients over 1 to 6 years (mean of 3 years). They found 9% dropout and 78% improvement, with a 60% mean reduction in rituals. Nonetheless, residual symptoms were a rule and liability for depression remained unchanged.

Meta-analysis of CBT

Now that BT is firmly established, several meta-analyses have been carried out. The latest meta-analysis⁷¹ included 77 studies with 4651 patients and showed that BT was superior to SSRI antidepressants as a class. Nevertheless, this difference should be taken with caution as BT is limited by the problem of availability, accessibility, and third-party payment in many countries.

CT in OCD

The status of CT is still under investigation and there have recently been some new studies published (*Table IV*).⁷²⁻⁷⁹ To date, the usefulness of CT for OCD has been assessed in 8 controlled studies. Emmelkamp et al⁷² did not find a superior effect when adding cognitive modifications to in vivo exposure. Nevertheless, the design of the experiment aimed at teaching the patient to replace negative thoughts by positive ones. This could have been

used as neutralizing thoughts. Emmelkamp et al73 compared CT without exposure to self-managed exposure. Six months after the end of treatment, both groups showed equivalent reduction in rituals, generalized anxiety, and social anxiety. Only the cognitive group showed change on the measures of depression. In a study with a more impaired population, Emmelkamp and Beens⁷⁴ found similar results at a 6-month follow-up. Van Oppen et al75 randomized 71 patients in either Beckian CT or exposure. After 16 sessions, they found a superiority of cognitive interventions over exposure. Danger schemata were better modified by CT than with exposure. Unfortunately, this study had no long-term follow-up. A multicentered study (76) compared CT with intensive BT. Sixty-five ambulatory patients with *DSM-IV* OCD and without major depression were randomized into two groups for a 16-week psychological treatment: either CT, or exposure and response prevention, for a 4-week intensive treatment period followed by a maintenance phase of 12 weeks. No medication was prescribed. At week 16, the rates of responders were comparable in the two groups. Depression (bipolar type I) was significantly more improved in the group that received CT. At weeks 26 and 52, improvement was retained in both groups without a between-group difference. Cognitive measures of obsessions changed equally in the two groups. This study replicated on a larger scale the findings of Emmelkamp and coworkers. 73,74

Freeston et al⁷⁷ presented a study comparing a waiting list with a group treated with CBT. In a group of OCD

Study	Outcome		
CT versus BT (ERP)			
Emmelkamp et al, ⁷² 1980	Self-instructional training + ERP = ERP (follow-up 6 months)		
Emmelkamp et al, ⁷³ 1988	CT = ERP on rituals		
	CT > ERP on depression (follow-up 6 months)		
Emmelkamp and Beens,74 1991	CT = ERP (follow-up 6 months)		
Van Oppen et al,75 1995	CT > ERP (posttest)		
Cottraux et al, 76 2001	CT = ERP on rituals		
	CT > ERP on depression (posttest)		
Comparison with a waiting list			
Freeston et al, ⁷⁷ 1997	In pure obsessions: CBT > waiting list (follow-up 6 months)		
Jones and Menzies,78 1998	CT > waiting list at posttest only. No difference at 3-month follow-up		
Comparison with SSRI (fluvoxamine antidepressant)			
Van Balkom et al, ⁷⁹ 1998	ERP, CT, or SSRI combined with ERP or CT: same positive outcomes at 16 weeks		
	Active treatments better than a waiting list at week 8		

Table IV. Cognitive therapy (CT) in obsessive-compulsive disorder: controlled studies. BT, behavior therapy; CBT: cognitive behavior therapy; ERP: exposure and response prevention; SSRI, selective serotonin reuptake inhibitor.

patients with exclusively covert rituals, that the superiority of CBT over the waiting list was maintained at 6 months' follow-up. Jones and Menzies⁷⁸ found that CT was superior to a waiting list at posttest only. Only one study dealt with the problem of combination of CBT with SSRI fluvoxamine⁷⁹ and found no difference between active conditions (*Table IV*).

In conclusion, although there is still is a clear need for more controlled studies, there is good evidence in favor of a positive effect for the cognitive approach in OCD.

Psychodynamic therapy for OCD

There is a dearth of controlled data in this field. An uncontrolled study by Kringlen⁸⁰ found that 20% of OCD patients improve during an interval ranging from 13 to 20 years versus 21% of the patients treated with psychoanalytic therapy during the same interval.

Psychosurgery

Since the introduction of prefrontal leukotomy by Moniz,81 several techniques have been developed: stereotactic leukotomy, stereotactic cingulotomy, 68,69 and the gamma-knife radiosurgery technique of capsulotomy. In general, the orbitofrontal and cingulate regions are the targets for intervention.82 However, the literature only reports series of uncontrolled case studies. About 25% of a panel of 33 patients who presented an intractable OCD responded in the long term.83 The side effects are severe—epilepsy, personality disorders, and depression—and there have been cases of suicide.84-86 Even the gamma-knife, which was supposed to be more precise and safer, presented detrimental effects in the form of extensive local brain necrosis after irradiation.87 There is obviously a lack of scientific evidence for a durable effect of these techniques in a sizeable number of severe patients. Ethical problems, low effectiveness, and side effects explain why psychosurgical decisions are under the control of ethical committees in most of the countries.

Transcranial stimulation

There is quite limited preliminary evidence that repetitive transcranial magnetic stimulation of prefrontal areas may improve compulsive urges, which were increased after midoccipital stimulations.88 There was no difference

between right and left brain prefrontal stimulations. These experiments were uncontrolled carried out in severe OCD. A positive transient response was found in only 25% of patients.

Social phobia

CBT in social phobia

Methods

Early behavioral interventions were based either on systematic desensitization or assertiveness training. Social skills deficit was hypothesized as being at the core of performance anxiety and social phobia. SST through role play with rehearsal, shaping, and modeling by the therapist was shown to be effective in treating social phobic patients in the early seventies.

A move towards a cognitive model was the next step. According to the cognitive model of social phobia, 90 cognitive factors may be particularly important in the development and maintenance of the negative emotions and avoidance behaviors in social phobic patients. The patients assume that other people are inherently critical, and attach particular importance to being negatively appraised by others. This could be related to a basic cognitive schema of inferiority.91 CT consists in identifying negative automatic thoughts and schemata, and then modifying them by more realistic interpretations. Current therapeutic models tend to mix cognitive and behavioral methods. The patient's evidence for his or her negative belief is cognitively questioned, but emphasis is also put on behavioral experiments to test the irrational assumptions. Treatment classically involves about 15 to 20 sessions in individual and/or group.

Outcomes

The effectiveness of BT on various types of social anxiety has been demonstrated in several controlled trials. Social phobia, as such, attracted the interest of clinical researchers after its inclusion in *DSM-III*, ⁴²⁻⁴⁴ and was studied in controlled trials of SST, systematic desensitization, and in vivo exposure. ^{92,93} CT, too, demonstrated its effectiveness in studies using waiting list or other therapies as control. ⁹⁴⁻⁹⁶ Two studies reported some advantages of CT combined with exposure over exposure alone, ^{97,98} while one did not. ⁹⁹ Another study ¹⁰⁰

found, in a mixed sample of socially inadequate and phobic patients, that role playing and exposure were superior to cognitive restructuring at a 6-month follow-up.

Some researchers noticed that the gains of exposure therapy were often limited by the negative influence of cognitive factors that impeded anxiety reduction. ¹⁰¹ To deal with this problem, a study ¹⁰² designed a Cognitive Behavioral Group Treatment (CBGT), which was compared with a credible placebo: lectures and ST. At a 6-month follow-up, CBGT demonstrated clearly higher effects: 75% of the patients in CBGT were improved versus 40% of those in ST. This was confirmed in follow-ups ranging between 4 and 6 years. ¹⁰³

A dismantling study¹⁰⁴ comparing CBGT with exposure found that each of the two methods was superior to a waiting list, with a slight advantage of exposure over CT on some measures. The rate of responders was not statistically different in the two active conditions. Surprisingly, there was no greater improvement on cognitive measures in the CBGT group. At a 6-month follow-up there was no longer any between-group difference.

Another trial¹⁰⁵ showed, in limited social phobias, that CT followed by exposure, exposure followed by CT, or the combination of both had the same positive effects without significant difference at a 3-month follow-up. The same authors¹⁰⁶ demonstrated that CT followed by exposure was better than their combination or exposure followed by CT in generalized social phobia, at a 3-month follow-up.

A meta-analysis¹⁰⁷ of 12 CBT and 9 exposure studies concluded that CBT did not yield better outcomes than exposure therapy, on self-report measures of social anxiety, cognitive symptoms, and depressed/anxious mood, at posttest and follow-up.

Another meta-analysis¹⁰⁸ included 42 treatment outcome trials and tested 6 conditions: waiting list, placebo, exposure, CT, CT plus exposure, and SST. All the interventions, including placebo, produced larger effect sizes than a waiting list and did not differ in dropout proportions (12% to 18%). However, only CT associated with exposure yielded an effect size that was larger than placebo (1.06 versus 0.48, respectively). Exposure alone had an effect size of 0.81, nonsignificantly different from placebo. Effect sizes tended to improve at follow-ups.

CBT effectiveness was confirmed by Gould's metaanalysis in which pharmacotherapy (11 studies) had an effect size of 0.62 versus placebo, while CBT (16 studies) reached 0.74 compared with control conditions.

In summary, meta-analytic approaches of the research suggest that CBT is effective and exposure is a crucial component of CBT, while the effect of CT remains in discussion.

Medication and CBT in social phobia

Main outcome studies

Buspirone was less effective than CBT at 6 weeks in reducing performance anxiety in musicians. 110 Gelernter et al111 compared four groups: CBT, phenelzine, alprazolam, and placebo. All four groups received instruction of self-exposure. All groups improved significantly at 2 months with few differences between them. However, this equal improvement could have resulted from the exposure instructions. BT was superior to atendol at 3 and 6 months.¹¹² A positive combination of exposure with sertraline was found at 24 weeks. Combination was superior to placebo, but equal to sertraline alone. 113 Few differences, but in favor of clonazepam, were found in a comparison of this BDZ with behavioral group therapy¹¹⁴; patients were only rated at 4, 8, and 12 weeks. CBGT was found to be superior to pill-placebo and educational group therapy, but slightly inferior to phenelzine on some measures at the 12 weeks' evaluation in a randomized trial.¹¹⁵ Follow-up data found that, after withdrawal of the medication, CBGT was better, especially in generalized social phobia.116

Meta-analysis of CBT and medication

A meta-analysis¹¹⁷ of psychological and pharmacological treatments for social phobia was conducted: 108 treatment-outcome trials were entered in this meta-analysis. Eleven treatment conditions were compared: waiting-list control, pill placebo, BDZ, SSRIs, monoamine oxidase inhibitors, attention placebo, exposure, cognitive restructuring, and applied relaxation. The most consistently effective treatments for social phobias were pharmacotherapies. BDZs and SSRIs were equally more effective than control conditions. Dropout rates were similar among all the active treatment conditions. The durability of treatment gains for pharmacotherapies was not assessed because of an insufficient number of drug studies with follow-up data. The treatment gains of

CBT, although moderate, continued during the follow-up period. BDZs and SSRIs seem to be effective treatments for social phobia, at least in the short term. The authors recommended assessment of the long-term outcome and evaluation of the inclusion of a CBT during the drug-tapering period.

Psychoanalytic therapies in performance anxiety

A randomized study by Paul¹¹⁸ in 1966 in students with lack of social skills and a fear of speaking in public showed the superiority of systematic desensitization over a control (attention-placebo) and psychodynamic therapy at a 2-year follow-up. Psychodynamic therapy demonstrated no better outcomes than the waiting list. Although the study recruited a sample of students and the *DSM* criteria for social phobia were not used in those days, Paul's¹¹⁸ study suggests a significant positive effect of systematic desensitization, and a lack of effectiveness of psychodynamic therapy, in performance anxiety.

Supportive therapy

One trial¹¹⁹ dealt with a comparison of ST with CBT. The aim of the trial was to study the effectiveness of CBT versus ST carried out "as usual." Sixty-seven DSM-IV social phobic patients were randomly allocated into two groups. Group 1 (CBT) received eight 1-hour sessions of individual CT for 6 weeks, followed by six 2-hour sessions of SST in group weekly. Group 2 received ST for 12 weeks (six 30-minute sessions), and then the patients were switched to CBT. No medication was prescribed. At week 6, after CT, group 1 was better than group 2 on the main social phobia measure. At week 12, after SST, group 1 was better than group 2 on most of the measures and demonstrated a significantly higher rate of responders. This finding was replicated after switching group 2 to CBT. Sustained improvement was observed in both groups at follow-up. In summary, CBT was more effective than ST and had long-lasting effects.

Sympathectomy for ereuthophobia

Endothoracic sympathectomy has been carried out for the fear of blushing¹²⁰ with a questionable rationale assuming that emotional response is mainly a peripheral problem.¹²¹ Despite early claims of high rate of success, follow-up studies were less optimistic: 67% of the patients had compensatory sweating, 50% gustatory sweating, and Horner's syndrome in 2.5%. Moreover, the number of initially satisfied patients declined over time from 98% to 66%. 122 The survey was made through a simple questionnaire. There was no control group. It is obvious that this is not a treatment of choice for an anxiety problem related to a fear of blushing, more than to real blushing.

Specific phobias

CBT methods for specific phobias

Simple phobia is often considered as a normal fear, like the fear of animals or of blood. Nevertheless, it affects 7% of the general population. In some cases, anxiety and avoidance behaviors become a handicap severe enough to lead to consultation. Treatment classically involves about 10 to 15 sessions of exposure and imagination and/or in vivo and cognitive restructuring.

Outcomes

There is a lack of controlled studies. In many controlled trials, simple phobias are often part of mixed samples of phobic patients. Follow-up studies showed a 54% improvement from baseline, which is maintained at follow-up ranging from 1 to 5 years with BT.16 Early controlled studies of CT showed negative results. 123,124 A study by Getka and Glass¹²⁵ compared four groups for dentist phobia: systematic desensitization, CT and stress management, interview with a warm practitioner prior to intervention, and waiting list. At 1-year follow-up, BT and CT produced equivalent results and were superior to the two other conditions, but this needs more investigation. Virtual reality was introduced as a tool to expose height and flying phobias with positive results in a controlled study of low statistical power. 126 To summarize, despite a scarce literature, in vivo exposure seems the treatment of choice for simple phobia, 127 while pharmacology has not been demonstrated to have positive effects. 128

Conclusion

This review shows that CBT has been proven to be effective in all the *DSM-IV* categories of anxiety disorders, in numerous RCT and several meta-analyses. Other forms of psychotherapy either have not been tested, or

generally have lesser effects than CBT in RCTs. Surgical approaches proposed for OCD and ereuthophobia are of limited value and may have detrimental side effects, without mentioning their lack of scientific evidence. However, some words of caution may temperate this positive picture of CBT for anxiety disorders.

The cost-containment issues led the procedures to become increasingly simplified. Some attempts have been made to turn many techniques into self-help procedures, or computer-assisted therapy, or therapy administered by nurses, social workers, counselors, priests, or lay people, using treatment manuals. However, manualized therapies have limitations, especially when the therapists are facing patients with multiple *DSM* Axis I and Axis II problems. Those patients represent at least 50% of the referrals in anxiety disorder units. There is obviously a limit to simplification: computer-administered treatment appeared less effective than therapist-administered treatment in OCD.¹²⁹

There are no conflicting issues between biological and psychological theoretical explanations. In practice, the combination of CBT with antidepressants has been shown to be effective in panic disorder and OCD. However, theories and practice may be in competition. CBT, due to the limited number of practitioners, even in developed countries, can be difficult to find. One of the reasons for this limited accessibility rests on the reduced

CBT training opportunities in the faculties of medicine and psychology in many countries. Medication is easier to administer, hence it tends to be the first line of intervention, despite the demonstrated efficacy and long-term effectiveness of CBT, and the fact that after stopping medication most of the patients relapse while the outcomes of CBT are stable. In the long-term, CBT costs less than medication, as it prevents relapses from occurring, as shown by cost-effectiveness surveys. ¹³⁰

Another stumbling block is the gap between basic research and practice. CBT practice is far ahead of theoretical explanations. Since the adoption of empiricism in the study of normal and abnormal psychology, we should note that the interest in fundamental psychology has tended to fade away. The first behaviorists relied heavily on basic research works, but the gap between practice and basic sciences has grown larger.

Marks¹³¹ recently pointed out that, as far as clinical effectiveness and efficiency are concerned, CBT is coming of age, but it is a toddler in terms of the scientific explanations of its effects. Historically, CBT was the first evidence-based treatment for anxiety disorders, long before evidence-based medicine was a bandwagon, ¹³² but now needs to be more empirically grounded. Filling this gap will be the endeavor of the 21st century researchers dedicated to the psychological approaches to anxiety disorders. □

REFERENCES

- 1. Ost LG, Westling B, Hellström K. Applied relaxation, exposure in vivo and cognitive methods in the treatment of panic disorder with agoraphobia. *Behav Res Ther.* 1993;31:383-394.
- **2.** Ost LG, Westling B. Applied relaxation vs cognitive behavior therapy in the treatment of panic disorder. *Behav Res Ther.* 1995;33:145-158.
- **3.** Ost LG, Westling B. Applied relaxation vs cognitive behaviour therapy in the treatment of panic disorder. *Behav Res Ther.* 1995;33:145-158.
- 4. Perroud M. Note sur l'agoraphobie. Lyon Médical. 1873;11:80-90.
- 5. Janet P. Les obsessions et la psychasthénie. Paris, France: Alcan; 1903.
- **6.** Freud S. Lines of Advance in Psychoanalytical Psychotherapy. 1919. Standard edition, vol 17. London, UK: Hogarth Press; 1955:157-158.
- 7. Wolpe J. *The Practice of Behavior Therapy*. 2nd ed. New York, NY: Pergamon Press; 1973.
- 8. Marks I. Fears, Phobias, and Rituals: Panic, Anxiety, and their Disorders. New York, NY: Oxford University Press; 1987.
- 9. Barlow D, Craske MG. Mastery of your Anxiety and Panic. Albany, NY: Graywind Publication; 1989.
- **10.** Mattick R, Andrews G, Hadzi-Pavlovic D, et al. Treatment of panic and agoraphobia: an integrative view. *J Nerv Ment Dis.* 1990;178:567-576.
- **11.** Cox BJ, Endler NS, Lee PS, Swinson RP. A meta-analysis of treatments for panic disorder with agoraphobia: imipramine, alprazolam and in vivo exposure. *J Behav Ther Exp Psychiatry*. **1992**;23:175-182.
- **12.** Clum GA, Clum G, Surls RA. Meta-analysis of treatments for panic disorder. *J Consult Clin Psychol.* **1993**;61:317-326.

- **13.** Van Balkom AJLM, Bakker A, Spinhoven P, Blaauw B, Seemk S, Ruesink B. A meta-analysis of the treatment of panic disorder with or without agoraphobia: a comparison of psychopharmacological, cognitive-behavioral and combination treatments. *J Nerv Ment Dis.* 1997;185:510-516.
- **14.** Bakker A, Van Balkom A, Spinhoven P, Blaauw B, Van Dyck R. Follow-up on the treatment of panic disorder with or without agoraphobia. A quantitative review. *J Nery Ment Dis.* **1998**:186:414-419.
- **15.** Gould RA, Otto MW, Pollack MH. A meta-analysis of treatment outcome for panic disorder. *Clin Psychol Rev.* **1995;8:819-844**.
- **16.** O'Sullivan G, Marks I. Long-term outcome of phobic, and obsessive-compulsive disorders after treatment. In: Noyes R, Roth M, Burrows GD, eds. *Handbook of Anxiety. Vol 4. The Treatment of Anxiety.* Amsterdam, The Netherlands: Elsevier: 1990.
- 17. Zitrin C, Klein D, Woerner M. Treatment of agoraphobia with group in vivo exposure and imipramine. *Arch Gen Psychiatry*. 1980;37:63-72.
- **18.** Telch M, Agras S, Barr-Taylor C, et al. Combined pharmacological and behavioral treatment for agoraphobia. *Behav Res Ther.* **1985;22:325-335**.
- **19.** Agras S. Behaviour therapy and psychopharmacology. Combined pharmacological and psychological treatment of panic disorder: current status and future direction. In: Wolf BE, Maser JD. *Treatment of Panic Disorder*. Washington DC: American Psychiatric Press; **1994**.
- **20.** de Beurs E, van Balkom A, Lange J, Koele P van Dyck R. Treatment of panic disorder with agoraphobia: comparison of fluvoxamine, placebo, and psychological panic management combined with exposure and of exposure in vivo alone. *Am J Psychiatry*. 1995;152:683-691.

Tratamientos no farmacológicos para los trastornos de ansiedad

Se presenta una revisión basada en la evidencia de los tratamientos no farmacológicos para los trastornos de ansiedad. Gran parte de la investigación controlada está dedicada a la terapia cognitivo conductual (TCC) y muestra su eficiencia y eficacia en los meta-análisis para todos los trastornos de ansiedad de la IV Edición del Manual Diagnóstico y Estadístico de los Trastornos Mentales (DSM-IV). En unos pocos estudios controlados se ha examinado la relajación, las terapias psicoanalíticas, la terapia Rogeriana no directiva, la hipnoterapia y la terapia de apoyo, lo que impide cualquier conclusión definitiva acerca de su eficacia en fobias específicas, agorafobia, trastorno de pánico, trastorno obsesivo compulsivo (TOC) o trastorno por estrés postraumático (TEPT). La TCC fue claramente mejor que la terapia psicoanalítica para el trastorno de ansiedad generalizado (TAG) y para la angustia de rendimiento. El debriefing psicológico para el TEPT resultó perjudicial para los pacientes en un metaanálisis de alta calidad. Estudios no controlados de técnicas de psico-cirugía para el TOC intratable demostraron un éxito limitado y efectos laterales indeseables. Se obtuvieron resultados similares para la simpatectomía en la ereutofobia. La neuroestimulación transcraneal para el TOC está en una fase preliminar de estudio. Se discuten los problemas teóricos y prácticos de la propagación de la TCC.

Traitements non pharmacologiques des troubles anxieux

Il est présenté ici une revue basée sur les preuves des traitements non pharmacologiques des troubles anxieux. La grande majorité de la recherche contrôlée est consacrée à la thérapie cognitivocomportementale (TCC) et des métaanalyses on montré la pertinence et l'efficacité de cette thérapie dans tous les troubles anxieux du Manuel diagnostique et statistique des troubles mentaux (DSM-IV). La relaxation, les thérapies psychoanalytiques, la thérapie non directive dite de « Rogers », l'hypnothérapie, et les thérapies de soutien ont été examinés dans quelques études contrôlées, qui écartent toute conclusion définitive sur leur efficacité dans les diverses formes de phobie, l'agoraphobie, le trouble panique, le trouble obsessionnel compulsif (TOC), et l'état de stress posttraumatique (ESPT). La TCC était manifestement plus efficace que le traitement psychanalytique dans les troubles anxieux généralisés (TAG) et l'anxiété de performance. Le « debriefing » psychologique pour l'ESPT est apparu dommageable aux patients dans une métaanalyse de haute qualité. Des études non contrôlées des techniques de psychochirurgie pour les TOC rebelles ont démontré un succès limité et des effets secondaires fâcheux. Idem pour la sympathectomie dans l'éreuthophobie. La neurostimulation transcrânienne pour les TOC a fait l'objet d'études préliminaires. Les problèmes théoriques et pratiques pour la diffusion de la TCC sont discutées.

- **21.** Oehrberg S, Christiansen PE, Behnke K, et al. Paroxetine in the treatment for panic disorder. A randomised, double-blind, placebo-controlled trial. *Br J Psychiatry*. 1995;167:374-379.
- **22.** Sharp DM, Power KG, Simpson RJ, et al. Fluvoxamine, placebo and cognitive behaviour therapy used alone and in combination in the treatment of panic disorder and agoraphobia. *J Anxiety Disord*. 1996;4:219-242.
- **23.** Barlow HD, Gorman JM, Shear MK, Woods SW. Cognitive-behavioral therapy, imipramine, or their combination for panic disorder: a randomized controlled trial. *JAMA*. 2000;283:2529-2536.
- **24.** Solyom C, Solyom I, LaPierre Y, et al. Phenelzine and exposure in the treatment of phobias. *Biol Psychiatry*. 1981;16:239-247.
- **25.** Marks I, Gray S, Cohen D, Hill R, Mawson D, Ramm L, Stern R. Imipramine and brief therapist aided exposure in agoraphobics having self-exposure homeworks. *Arch Gen Psychiatry*. **1983**;40:153-161.
- **26.** Mavissakalian M, Michelson L. Agoraphobia: relative and combined effectiveness of therapist-assisted in vivo exposure and imipramine. *J Clin Psychiatry*. **1986**:47:117-122.
- **27.** Fahy TJ, O'Rourke D, Brophy J, et al. The Galway study of panic disorder: clomipramine and lofepramine in *DSM-3-R* panic disorder. A placebocontrolled trial. *J Affect Disord*. **1992**;25:63-76.

- 28. Loerch B, Graf-Morgenstern M, Hautzinger M, et al. Randomised placebocontrolled trial of moclobemide, cognitive-behavioural therapy and their combination in panic disorder with agoraphobia. *Br J Psychiatry*. 1999;174:205-212. 29. Marks I, Swinson R, Basoglu M, et al. Alprazolam and exposure alone or combined in panic disorder with agoraphobia: a controlled study in London and Toronto. *Br J Psychiatry*. 1993;162:776-787.
- **30.** Wardle J, Hayward P, Higgit A, et al. Effects of concurrent diazepam treatment on the outcome of exposure therapy in agoraphobia. *Behav Res Ther.* 1994:32:203-215.
- **31.** Cottraux J, Note ID, Cungi C, et al. A controlled study of cognitive-behavior therapy with buspirone or placebo in panic disorder with agoraphobia. A one-year follow-up. *Br J Psychiatry*. 1995;167:635-641.
- **32.** Otto M, Pollack MH, Sachs G, et al. Discontinuation of benzodiazepine treatment: efficacy of cognitive-behavioral therapy for patients with panic disorder. *Am J Psychiatry*. 1993;150:1485-1490.
- **33.** Spiegel D, Bruce T, Gregg B, et al. Does cognitive behavior therapy assist slow-taper alprazolam discontinuation in panic disorder? *Am J Psychiatry*. 1994;151:876-881.
- **34.** Barlow D, Craske M, Cerny J, et al. Behavioral treatment of panic disorder. *Behav Ther.* 1989;20:261-282.

- **35.** Craske M, Brown T, Barlow D. Behavioral treatment of panic disorder: a two-year follow-up. *Behav Ther.* 1991;22:289-304.
- **36.** Clark D, Salkovskis P, Hackmann A, Middleton H, Anastasiades P, Gelder M. A comparison of cognitive therapy, applied relaxation and imipramine in the treatment of panic disorder. *Br J Psychiatry*. 1994;164:759-769.
- **37.** Ost LG. Applied relaxation versus progressive relaxation in the treatment of panic disorder. *Behav Res Ther.* 1988;26:13-22.
- **38.** Arntz A, Van den Hout M. Psychological treatment of panic disorder without agoraphobia: cognitive therapy versus applied relaxation. *Behav Res Ther.* **1996**;34:113-121.
- **39.** Beck AT, Sokol L, Clark DA, et al. A cross-over of focused cognitive therapy for panic disorder. *Am J Psychiatry*. 1992;149:778-783.
- **40.** Shear K, Pilkonis P, Cloitre M, et al. Cognitive-behavioral treatment compared with nonprescriptive treatment of panic disorder. *Arch Gen Psychiatry*. 1994;51:395-401.
- **41.** Wiborg IM, Dahl AA. Does brief dynamic therapy reduce the relapse rate of panic disorder. *Arch Gen Psychiatry*. **1996**;53:689-694.
- **42.** American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 3rd ed. Washington, DC: American Psychiatric Association; 1980.
- **43.** American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. **3rd ed, revised. Washington, DC: American Psychiatric Association; 1987**.
- **44.** American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: American Psychiatric Association; 1994.
- **45.** Wells A. Cognitive Therapy for Anxiety Disorders. A Practice Manual and Conceptual Guide. Chichester, UK: John Wiley and Sons; 1997.
- **46.** Gould RA, Buckminster S, Pollack MH, Otto MW, Yap L. Cognitive-behavioral and pharmacological treatment for social phobia: a meta-analysis. *Clin Psychol Sci Pract.* **1997**;4:291-306.
- **47.** Gould RA, Otto MW, Pollack MH, Yay L. Cognitive behavioural and pharmacological treatment of generalized anxiety disorder: a preliminary meta-analysis. *Behav Ther.* **1997**;28:285-305.
- **48**. Durham R, Murphy T, Allan T, Richard K, Treliving L Fenton G. Cognitive therapy, analytic psychotherapy and anxiety management for anxiety management training for anxiety disorder. *Br J Psychiatry*. **1994**;165:315-323.
- **49.** White J, Keenan M, Brooks N. Stress control: a controlled comparative investigation of large group therapy for generalized anxiety disorder. *Behav Psychother*. **1992**;20:97-114.
- **50.** Borkovec TD, Mathews AM, Chambers A, Ebrahami S, Lytle R, Nelson R. The effects of relaxation training with cognitive or nondirective therapy and the role of relaxation-induced anxiety in the treatment of generalized anxiety. *J Consult Clin Psychol.* **1987**;**55**:883-888.
- **51.** Borkovec TD, Costello E. Efficacy of applied relaxation and cognitive-behavioral therapy in the treatment of generalized anxiety disorder. *J Consult Clin Psychol.* 1993;61:611-619.
- **52.** Blowers C, Cobb J, Mathews A. Generalised anxiety: a controlled treatment study. *Behav Res Ther.* 1987;25:493-502.
- **53.** Stanley MA, Beck JG, Glassco JD. Treatment of generalized anxiety in older adults: a preliminary comparison of cognitive-behavioral and supportive approaches. *Behav Ther.* 1996;27:565-581.
- **54.** Wilson SA, Becker LA, Tinker RH. Eye movement desensitization and reprocessing (EMDR) treatment for psychologically traumatized individuals. *J Consult Clin Psychol.* 1995;63:928-937.
- **55.** Devilly GJ, Spence SH, Rapee R. Statistical and reliable change with eye movement desensitization and reprocessing: treating trauma within a veteran population. *Behav Ther.* 1998:435-455.
- **56.** Marks IM, Lovell K, Noshirvani H, Livanou M, Trasher S. Treatment of posttraumatic stress disorder by exposure and/or cognitive restructuring. *Arch Gen Psychiatry*. **1998**;5:317-325.
- **57.** Van Etten ML, Taylor S. Comparative efficacy of treatments for post-traumatic stress disorder: a meta-analysis. *Clin Psychol Psychother*. 1998;5:126-144. **58.** Brom D, Kleber RJ, Defares PB. Brief psychotherapy for post-traumatic stress disorders. *J Consult Clin Psychol*. 1989;57:607-612.
- **59.** Mitchell JT. When disaster strikes ... the critical incidents stress debriefing process. *J Emerg Med Serv.* **1983**;8:36-39.
- **60.** Rose S, Bisson J, Wessely S. Psychological debriefing for preventing post-traumatic stress disorder (PTSD). The Cochrane Library, Issue 3. Oxford, UK: Update Software. http://www.update-software.com/abstracts/ab000560.htm. Accessed 24 July 2002.

- **61.** Meyer V. Modifications of expectations in cases with obsessional rituals. *Behav Res Ther.* **1966**:4:273-280.
- **62.** Salkovskis PM. Obsessional-compulsive problems. A cognitive behavioral analysis. *Behav Res Ther.* 1985;23:571-583.
- **63.** Cottraux J, Mollard E, Bouvard M, et al. A controlled study of fluvoxamine and exposure in obsessive-compulsive disorder. *Int Clin Psychopharmacol.* 1990;5:17-30.
- **64.** Cottraux J, Mollard E, Bouvard M, Marks I. Exposure therapy, fluvoxamine or combination treatment in obsessive-compulsive disorder: 1-year follow-up. *Psychiatry Res.* **1993**;49:63-75.
- **65.** Solyom L, Sookman D. A comparison of clomipramine hydrochloride (Anafranil) and behaviour therapy in the treatment of obsessive neurosis. *J Int Med Res.* 1977;5(suppl 5):49-61.
- **66.** Marks I, Stern RS, Mawson D, Cobb J, McDonald R. Clomipramine and exposure for obsessive-compulsive rituals. *Br J Psychiatry*. **1980**;136:1-25.
- **67.** Marks I, Lelliott P, Basoglu M, Noshirvani H, Monteiro W, Kasvikis Y. Clomipramine, self-exposure and therapist-aided exposure in obsessive-compulsive ritualisers. *Br J Psychiatry*. **1988**;**152**:522-534.
- **68.** Foa E, Kozak M, Steketee G, McCarthy PR. Treatment of depressive and obsessive-compulsive symptoms in obsessive-compulsive disorder by imipramine and behaviour therapy. *Br J Clin Psychol.* 1992;31:279-292.
- **69**. Baxter L, Schwartz J, Bergman K, et al. Caudate glucose metabolic rate changes with both drug and behavior therapy for obsessive-compulsive disorder. *Arch Gen Psychiatry*. **1992**;**49**:681-689.
- **70.** Van Balkom A. Comparative Treatment Studies in Panic Disorder with Agoraphobia and Obsessive-Compulsive Disorder. Thesis. Amsterdam, The Netherlands: Vrije Universiteit Amsterdam; 1994.
- 71. Kobak KA, Greist JH, Jefferson JW, Katzlenick DJ, Henk HJ. Behavioral versus pharmacological treatments of obsessive-compulsive disorder. *Psychopharmacology*. 1998;3:205-216.
- **72.** Emmelkamp P, Van der Helm M, Van Zanten B, Plochg I. Contribution of self-instructional training to the effectiveness of exposure in vivo: a comparison with obsessive-compulsive patients. *Behav Res Ther.* 1980;18:61-66.
- 73. Emmelkamp P, Visser S, Hoekstra RJ. Cognitive therapy versus in vivo exposure in the treatment of obsessive-compulsive patients. *Cogn Ther Res.* 1988:12:103-114
- **74.** Emmelkamp P, Beens H. Cognitive therapy with obsessive-compulsive disorder: a comparative evaluation. *Behav Res Ther.* 1991;29:293-300.
- **75.** Van Oppen P, de Haan E, Van Balkom AJ, Spinhoven P, Hogduin K, Van Dyck R. Cognitive therapy and exposure in vivo in the treatment of obsessive-compulsive disorder. *Behav Res Ther.* 1995;33:379-390.
- **76.** Cottraux J, Ivan Note I, Yao SN, et al. A randomized controlled trial of cognitive therapy versus intensive behaviour therapy in obsessive-compulsive disorder subjects. *Psychother Psychosomatics*. **2001**;**70**:288-297.
- 77. Freeston MH, Ladouceur R, Gagnon F, et al. Cognitive-behavioral treatment of obsessive thoughts: a controlled study. *J Consult Clin Psychol*. 1997:65:405-413.
- **78.** Jones MK, Menzies RG. Danger ideation reduction therapy (DIRT) for obsessive-compulsive washers, controlled trial. *Behav Res Ther.* 1998;36:959-970.
- **79.** Van Balkom AJLM, De Haan E, Van Oppen P, Spinhoven P, Hogduin KAL, Van Dyck R. Cognitive and behavioral therapies alone or in combination with fluvoxamine in the treatment of obsessive-compulsive disorder. *J Nerv Ment Dis.* 1998;186:492-498.`
- **80.** Kringlen E. Obsessional neurotics: a long-term follow-up. *Br J Psychiatry*. 1965:111:709-722.
- **81.** Moniz E. Prefrontal leucotomy in the treatment of mental disorder (May, 1937). *Am J Psychiatry*. 1994;151:237-239.
- **82.** Ballantine H, Bouckoms A, Thomas E, Giriunas I. Treatment of psychiatric illness by stereotaxic cingulotomy. *Biol Psychiatry*. 1987;22:807-819.
- **83**. Baer L, Rauch S, Ballantine T, et al. Cingulotomy for intractable obsessive-compulsive disorder. Prospective long-term follow-up of 18 patients. *Arch Gen Psychiatry*. 1995;52:384-392.
- **84.** Mindus P, Rasmussen SA, Lindquist C. Neurosurgical treatment for refractory obsessive-compulsive disorder: implications for understanding frontal lobe function. *J Neuropsychiatry Clin Neurosci.* **1994**;6:467-477.
- **85.** Hay P, Sachdev P, Cumming S, Smith JS, Kitchener P, Matheson J. Treatment of obsessive-compulsive disorder by psychosurgery. *Acta Psychiatr Scand.* 1993;87:197-207.

- **86.** Jenike MA, Baer L, Ballantine T, et al. Cingulotomy for refractory obsessive-compulsive disorder. A long-term follow-up of 33 patients. *Arch Gen Psychiatry*. **1991**;48:548-555.
- **87**. Kihkström L, Guo WY, Lindquist C, Mindus P. Radiobiology of radiosurgery for refractory anxiety disorders. *Neurosurgery*. 1995;36:294-302.
- **88.** Greenberg BD, George MS, Martin JD, et al. Effect of prefrontal repetitive transcranial magnetic stimulation in obsessive-compulsive disorder: a preliminary study. *Am J Psychiatry*. **1997**;154:867-869.
- 89. Sachdev PS, McBride R, Loo CK, Mitchell PB, Malhi GS, Croker VM. Right versus left prefrontal transcranial magnetic stimulation for obsessive-compulsive disorder: a preliminary investigation. *J Clin Psychiatry*. 2001;62:981-984. 90. Beck AT, Emery G, Greenberg R. *Anxiety Disorders and Phobias*. A Cognitive Perspective. New York, NY: Basic Books; 1985.
- **91.** Yao SN, Cottraux J, Martin R, et al. Inferiority in social phobics, obsessive-compulsive and non-clinical controls. A controlled study with the inferiority scale. In: Sanavio E, ed. *Behaviour and Cognitive Therapy Today: Essays in Honour of Hans J. Eysenck*. London, UK: Elsevier; 1998.
- **92.** Marzillier J, Lambert C, Kellett J. A controlled evaluation of systematic desensitization and social skills training for socially inadequate psychiatric patients. *Behav Ther Res.* **1976**;14:225-238.
- **93.** Butler G, Cullington A, Monby M. Exposure and anxiety management in the treatment of social phobias. *J Clin Psychol.* 1984;52:642-650.
- **94.** Shaw P. A comparison of three behaviour therapies in the treatment of social phobia. *Br J Psychiatry*. **1979**;134:620-623.
- **95.** Kanter NJ, Golfried MR. Relative effectiveness of rational restructuring and self-control desensitization in the reduction of interpersonal anxiety. *Behav Ther.* **1979**;10:472-490.
- **96.** Emmelkamp PMG, Mersch PP, Vissia E, Van der Helm M. Social phobia: a comparative evaluation of cognitive and behavioural interventions. *Behav Res Ther.* **1985**:23:365-369.
- **97.** Jerremalm A, Jansson L, Ost LG. Cognitive and physiological reactivity and the effects of different behavioural methods in the treatment of social phobias. *Behav Res Ther.* **1986**;24:171-180.
- 98. Biran M, Wilson GT. Treatment of phobic disorders using cognitive and exposure methods: a self-efficacy analysis. *J Consult Clin Psychol.* 1981;49:886-899.
- 99. Mattick R, Peters L, Clarke C. Exposure and cognitive restructuring for social phobia: a controlled study. *Behav Ther.* 1989;20:3-23.
- 100. Stravinsky A, Marks I, Yule W. Social skills problems in neurotic outpatients. *Arch Gen Psychiatry*. 1982;39:1378-1385.
- **101.** Butler G. Exposure as a treatment for social phobia: some instructive difficulties. *Behav Res Ther.* **1985**;23:651-657.
- **102.** Heimberg R, Dodge C, Hope D, Kennedy C, Zollo L. Cognitive behavioural group treatment for social phobia: comparison with a credible placebo control. *Cogn Ther Res.* **1990**;14:1-23.
- 103. Heimberg R, Salzman D, Holt C, Blendell K. Cognitive behavioral group treatment for social phobia: effectiveness a five-year follow-up. *Cogn Ther Res.* 1993:17:325-339.
- **104.** Hope DA, Heimberg RG, Bruch MA. Dismantling cognitive-behavioral group therapy for social phobia. *Behav Res Ther.* **1995**;33:637-650.
- **105.** Emmelkamp PMG, Scholing A. Cognitive and behavioural treatments of fear of blushing, sweating or trembling. *Behav Res Ther.* 1993;31:155-170. **106.** Scholing A, Emmelkamp PMG. Exposure with and without cognitive therapy for generalized social phobia: effects of individual and group treatment. *Behav Res Ther.* 1993;31:667-681.
- **107.** Feske U, Chambless DL. Cognitive behavioural versus exposure only treatment for social phobia. *Behav Ther.* 1995;26:695-720.
- **108.** Taylor S. Meta-analysis of cognitive-behavioral treatments for social phobia. *J Behav Ther Exp Psychiatry*. **1996**;27:1-9.
- **109.** Gould RA, Buckminster S, Pollack MH, Otto MW, Yap L. Cognitive-behavioral and pharmacological treatment for social phobia: a meta-analysis. *Clin Psychol Sci Pract.* **1997**;4:291-306.

- **110.** Clark DB, Agras WS. The assessment and treatment of performance anxiety in musicians. *Am J Psychiatry*. **1991**;148:598-605.
- **111.** Gerlernter C, Uhde T, Cimbolic P, et al. Cognitive-behavioural and pharmacological treatments of social phobia. A controlled study. *Arch Gen Psychiatry*. 1991;48:938-945.
- **112.** Turner SM, Beidel DC, Jacob RG. Social phobia: a comparison of behavior therapy and atenolol. *J Consult Clin Psychol.* **1994**;62:350-358.
- **113.** Blomhoff S, Haug TT, Hellström K, et al. Randomised controlled general practice trial of sertraline, exposure therapy and combined treatment in generalised social phobia. *Br J Psychiatry*. **2001**;179:23-30.
- **114.** Otto MW, Pollack MH, Gould RA, Worthington JJ, McArdle ET, Rosenbaum JF. A comparison of the efficacy of clonazepam and cognitive-behavioral group therapy for the treatment of social phobia. *J Anxiety Disord*. 2000:14:345-358.
- 115. Heimberg R, Liebowitz M, Hope D, et al. Cognitive behavioral group therapy vs phenelzine therapy for social phobia. *Arch Gen Psychiatry*. 1998:55:1133-1141.
- **116.** Liebowitz RM, Heimberg R, Schneier FR, et al. Cognitive behavioral group therapy versus phenelzine in social phobia: long-term outcome. *Depression Anxiety.* **1999**;10:89-98.
- 117. Fedoroff IC, Taylor S. Psychological and pharmacological treatments of social phobia: a meta-analysis. *J Clin Psychopharmacol.* 2001;21:311-324.
- 118. Paul G. Insight Versus Desensitization in Psychotherapy. Stanford, Calif: Stanford University Press; 1966.
- **119.** Cottraux J, Note I, Albuisson E, et al. Cognitive behaviour therapy versus supportive therapy in social phobia: a randomised controlled trial. *Psychother Psychosomatics*. **2000**;**69**:137-146.
- **120.** Yilmaz EN, Dur AHM, Cuesta MA, Rauwerda JA. Endoscopic versus transaxillary thoracic sympathectomy for primary axillary and palmar hyperhidrosis and/or facial blushing: 5-year experience. *Eur J Cardiothorac Surg.* 1996:10:168-172.
- **121.** Drummond PD, Lance JW. Facial flushing and sweating mediated by the sympathetic nervous system. *Brain.* 1987;110:793-803.
- **122.** Herbst F, Plas EG, Függer R, Fritsch A. Endoscopic thoracic sympathectomy for primary hyperhidrosis of the upper limbs: a critical analysis and long-term results of 480 operations. *Ann Surg.* 1994;220:86-90.
- **123**. Ladouceur R. Participant modeling with or without cognitive treatment for phobias. *J Consult Clin Psychol*. 1983;51:942-944.
- **124.** Biran M, Wilson GT. Treatment of phobic disorders using cognitive and exposure methods: a self-efficacy analysis. *J Consult Clin Psychol.* 1981;49:886-899
- **125.** Getka EJ, Glass CR. Behavioural and cognitive-behavioural approaches to the reduction of dental anxiety. *Behav Ther.* **1992**;23:433-448.
- **126.** Rothbaum BO, Hodges LF, Kooper R, Opdyke D, Williford JS, North M. Effectiveness of computer-generated (virtual reality) graded exposure in the treatment of acrophobia. *Am J Psychiatry*. 1995;152:626-628.
- **127.** Rachman SJ. In: Salkovskis PM, ed. *Trends in Cognitive and Behavioural Therapy*. Chichester, UK: John Wiley and Sons Ltd; 1996.
- **128.** Zitrin C, Klein D, Woerner M. Behaviour therapy, supportive psychotherapy, imipramine and phobias. *Arch Gen Psychiatry*. **1978**;35:307-316.
- **129.** Greist JH, Marks IM, Baer L, et al. Behavior therapy for obsessive-compulsive disorder guided by a computer or by a clinician compared with relaxation as a control. *J Clin Psychiatry*. **2002**;63:138-145.
- **130.** Miller NE, Magruder KM. Cost-effectiveness of psychotherapy. Oxford, UK: Oxford University Press; 1999:224-234.
- **131.** Marks IM. The maturing of therapy: some brief psychotherapies help anxiety/depressive disorders but mechanisms of action are unclear. *Br J Psychiatry*. **2002**;180:200-204.
- **132.** Salkovskis PM. Empirically grounded clinical interventions: cognitive-behavioural therapy progresses through a multi-dimensional approach to clinical science. *Behav Coan Psychother*, **2002**:30:3-9.