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Review article

Treatment of specific phobia in adults

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Abstract

This is a comprehensive review of treatment studies in specific phobia. Acute and long-term efficacy studies of *in vivo* exposure, virtual reality, cognitive therapy and other treatments from 1960 to 2005 were retrieved from computer search engines. Although specific phobia is a chronic illness and animal extinction studies suggest that relapse is a common phenomenon, little is known about long-term outcome. Treatment gains are generally maintained for one year, but longer follow-up studies are needed to better understand and prevent relapse. Acutely, the treatments are not equally effective among the phobia subtypes. Most phobias respond robustly to *in vivo* exposure, but it is associated with high dropout rates and low treatment acceptance. Response to systematic desensitization is more moderate. A few studies suggest that virtual reality may be effective in flying and height phobia, but this needs to be substantiated by more controlled trials. Cognitive therapy is most helpful in claustrophobia, and blood-injury phobia is uniquely responsive to applied tension. The limited data on medication have not been promising with the exception of adjunctive D-cycloserine. Despite the acute benefits of *in vivo* exposure, greater attention should be paid to improve treatment acceptance and retention, and additional controlled studies of more acceptable treatments are needed.

Keywords: Specific phobia; Systematic desensitization; Cognitive behavior therapy; Exposure therapy; Virtual reality; Medication; Follow-up

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Specific phobia is characterized by an excessive, irrational fear of a specific object or situation, which is avoided at all cost or endured with great distress. Four subtypes are recognized in the fourth edition of the Diagnostic Statistical Manual (DSM-IV): animal (*e.g.*, spiders), natural environmental (*e.g.*, heights, water), situational (*e.g.*, flying, closed spaces), blood-injection-injury (*e.g.*, blood, dentist), and an "other" category for phobias that do not fit into the designated subtypes (APA, 1994). Specific phobia was formerly recognized as a distinct category called "simple phobia" in DSM-III (APA, 1980). Prior to this, it was classified under "phobic reaction" in DSM-I (APA, 1952) and "phobic neurosis" in DSM-II (APA, 1968).

Specific phobia is one of the most common psychiatric disorders in the U.S., with a lifetime prevalence of 12.5% (Kessler et al., 2005). It is about twice as common in women, with a childhood onset for most subtypes and a later age of onset in the twenties for the situational subtype (Craske et al., 1996).

Although specific phobia is a chronic illness, it is generally considered a benign disorder since anxiety is circumscribed and alleviated when the phobic situation is avoided. However, avoidance can interfere with work and leisure activities and impact quality of life (Magee, Eaton, Wittchen, McGonagle, & Kessler, 1996). Significant medical consequences can also result from avoidant behavior, as in dental phobia (Hallstrom & Halling, 1984; Peretz, Katz, Zilburg, & Shemer, 1996), blood-injection-injury phobia (Kleinknecht & Lenz, 1989; Lloyd & Deakin, 1975; Marks, 1988) and fear of vomiting (Manassis & Kalman, 1990). In cases where the phobic stimulus is unpredictable as in severe weather (Westefeld, 1996) or thunderstorm phobia (Liddell & Lyons, 1978) or where the stimulus is an internal sensation as in fear of vomiting (Lipsitz, Fyer, Paterniti, & Klein, 2001), the phobia can be very debilitating. In addition, specific phobia is highly co-morbid with other mental disorders, particularly anxiety disorders (Magee et al., 1996).

Since the advent of behavioral therapy, specific phobia has been considered one of the success stories in the field of psychiatric treatment and is often seen as a solved problem (Antony & Barlow, 2002). But how effective are the available treatments acutely, and how long does treatment last? Many studies addressing these questions were conducted in non-clinical settings and have methodological limitations such as small sample sizes or uncontrolled designs. Prior reviews emphasized treatment of agoraphobia and were based on studies that included subjects with agoraphobia, social and/or specific phobia (Linden, 1981; Marks & Gelder, 1969). The purpose of this review is to evaluate controlled trials that focus on the acute and long-term efficacy of treatments for specific phobia.

The review is organized around different treatment modalities: behavior therapy, cognitive therapy, and other less well-accepted treatments (*e.g.*, supportive therapy, hypnotherapy, and pharmacotherapy). The categories of behavioral

therapy evaluated include: systematic desensitization/imaginal exposure, *in vivo* exposure, interoceptive exposure, virtual reality exposure and applied tension. Within each section, the acute treatment studies are presented followed by long-term follow-up studies.

The results are presented in a narrative format with the "best evidence" approach (Slavin, 1995) as opposed to a meta-analysis. The best evidence method minimizes selection bias by using *a priori* inclusion criteria, and allows a comprehensive overview of the different treatment modalities. Given that specific phobia is a heterogeneous disorder, this method also highlights any phobic subtype's differential response to treatment.

1. Literature search method

A computer search of PsychInfo, Medline and Evidenced Based Medicine reviews (Cochrane DSR, ACP Journal Club, DARE and CCTR) from 1960 to December 23, 2005 was conducted using the search terms: specific phobia, simple phobia, phobic neurosis, phobic reaction, claustrophobia, and acrophobia. The terms "phobic disorders," "phobia" and "fear" were combined with the following terms: 1) snakes, insects, bats, birds, rats, mice, rodents, cockroaches, cats, dogs, spiders (animal phobias); 2) heights, water, pool, lake, thunder, lightening, wind, storms (environmental phobias); 3) blood, injection, sharp objects, knives, hatchets, dentists, doctors, physicians, medical procedures, needles (blood-injury phobias); 4) closed spaces, elevators, small rooms, driving, crowded places, dark places, airplanes, aircrafts, flying, plane crashes, cars, buses, subways, traffic, boats (situational phobias) 5) vomiting, choking, dead bodies, cemeteries, funerals (other phobias); 6) treatment, therapy, virtual reality, interoceptive exposure, cognitive therapy, exposure therapy, behavior therapy, cognitive behavior therapy, behavioral modification, systematic desensitization, flooding, hypnosis, hypnotherapy, eye movement desensitization therapy, supportive therapy, psychotherapy (psychological treatments); and 7) drug therapy, pharmacotherapy, medication, antidepressant agents, paroxetine, fluoxetine, sertraline, citalopram, escitalopram, fluvoxamine, adrenergic blocking drugs, venlafaxine, benzodiazapine (medication treatment). The list of phobias was partly derived from the list of irrational fears in the Fear Schedule Survey (Wolpe & Lang, 1969), common fears mentioned in Marks' text (Marks, 1969), and fears evaluated in the National Comorbidity Study (Curtis, Magee, Eaton, Wittchen, & Kessler, 1998). The titles and abstracts generated by the search engines were screened for inclusion criteria listed below. If an abstract was not available or did not contain adequate information, the full article was screened. Relevant journal articles cited in book chapters and article references were also screened.

Acute treatment studies were included if they met the following criteria. 1) published in English language, between 1960 to December 23, 2005, 2) adult sample age 18 and over, 3) initial sample size of at least 10 subjects per treatment group. 4) subjects with a specific irrational fear or specific phobia and 5) controlled study design comparing at least two treatment conditions in parallel, where at least one condition is the treatment of interest (described above). For cognitive therapy treatment, we included only the form of therapy that used cognitive restructuring as the main treatment component. Results of the studies were considered statistically significant if p-values were less than 0.05. Follow-up studies were included if they meet criteria 1–4, had a follow-up period of at least six months and reported that the treatment of interest was superior to baseline or control conditions during the acute treatment phase.

We excluded three types of studies 1) Dismantling studies that only control for variations of a treatment component (*e.g.*, importance of relaxation, therapist involvement, attention factors) but did not have a separate control group such as another active treatment, a placebo-control, or a no-treatment/wait-list control [*i.e.*, dismantling studies that included a separate control group were included in the review]. 2) Studies with cross-over designs because a treatment effect can be confounded by carry-over and learning effects depending on the order of treatment administration (Millar, 1983).[1] 3) Studies with analogue samples because these may not be representative of the clinical population.[2] Subjects in analogue studies were often not evaluated clinically, not as severely impaired as clinical patients and not as motivated for treatment (Bernstein & Paul, 1971). This is particularly problematic in student volunteers who received extra credit or participated as part of a course requirement.

[1] There were only a handful of cross-over studies that also met criteria 1–4.

[2] Bandura, Blahard and Ritter's (1969) study was included despite a few students in the sample because the majority were clinical subjects (n=48), and had significant functional impairment as a result of fear of snakes.

2. Outcome measures in treatment studies

The main measure in most studies is a behavioral approach test (BAT), which consists of a series of behavioral tasks in which the subject is observed approaching the feared object or situation. The strength of a BAT is that it is objective and visible. The investigator can actually "see" what happens when the patient encounters the phobic object. Three aspects of anxiety can be measured in a BAT: 1) Avoidance level corresponding to a BAT score of how close the subject was able to approach the phobic object, 2) Subjective anxiety indicated by a visual analog scale such as a fear thermometer scale (0–10) or a Subjective Units of Distress Scale (SUDS) (0 to 100) and 3) Physiological response such as heart rate or galvanic skin response (GSR). Studies commonly measure subjective anxiety and/or avoidance levels. In most cases, a positive treatment response was defined as a statistically significant difference in mean change or absolute BAT scores between the study conditions.

Self-report measures are also frequently used and can provide information on daily life functioning. These complement BATs because achievements in a BAT do not necessarily reflect "real life" gains. However, its accuracy depends on recollection of subjective and often highly emotionally charged events. Many studies use both self-report and BAT.

However, statistically significant change on a BAT or a self-report questionnaire does not necessarily reflect clinically significant improvement. Many definitions of clinical significance have been proposed and among these include: the ability to achieve a high end-state functioning (Mavissakalian, 1986); the concept of "social validation," which requires a degree of behavioral change that is recognized as important by his/her peers and significant others, and places the person within the normal range of behavior as that of his/her peers (Kazdin, 1977); a "normative comparison," which requires objective evidence that after treatment, the person is no longer distinguishable from a normal reference group based on behavior observations, standard self-report measures and ratings by significant others and blinded evaluators (Kendall & Grove, 1988). Jacobson, Follette and Revenstorf (1984) further proposed that a statistically reliable change should be demonstrated, such that a score in the range of a dysfunctional population at pretreatment should fall within the range of a normal population after treatment. Subsequent to this proposal, several alternative statistical methods to calculate a statistically reliable change have been advanced (Bauer, Lambert, & Nielsen, 2004). Despite the importance of assessing clinically significant changes, only a handful of the *in vivo* exposure studies have incorporated these assessments, which commonly adapt Jacobson et al.'s criteria.

3. Systematic desensitization and imaginal exposure

3.1. Acute treatment

This section includes studies of imaginal exposure and systematic desensitization. Imaginal exposure therapy involves exposure to the phobic stimulus through imagination, *i.e.* active visualization of the phobic stimulus. The goal of treatment is to achieve habituation and eventual extinction of the phobic reaction. Only one study met the inclusion criteria, which will be discussed in the *in vivo* exposure section (Rentz, Powers, Smits, Cougle, & Telch, 2003).

Systematic desensitization also includes exposure to the phobic stimulus through imagination, but the goal is to suppress anxiety with deep muscle relaxation (Wolpe, 1982). Most of the early studies of systematic desensitization included analogue samples, and reviewed elsewhere (McGlynn, Mealiea, & Landau, 1981; Paul, 1969). Eight studies met the inclusion criteria,[3] five of these compared desensitization to a placebo or wait-list control and three compared it to another active treatment. The placebo or wait-list control studies are discussed here and the comparison studies will be discussed in the section under the respective comparison treatments.

The five controlled studies of systematic desensitization consistently reported improved subjective anxiety, but effects on avoidance were mixed. These studies included two in animal phobia (Barrett, 1969; Rosen, Glasgow, & Barrera, 1976), one in height phobia (Baker, 1973), one in flying phobia (Howard, Murphy, & Clarke, 1983) and one in height and claustrophobia (Lazarus, 1961). In both studies of animal phobia, subjects treated with desensitization reported less anxiety than the control condition, with one of them additionally reporting a lower heart rate response (Rosen et al., 1976). However, results were quite different in post-treatment avoidance level. One study found no effect

[3] One study in dental phobia comparing imaginal exposure to relaxation controls was not included because 5 out of 10 controls dropped out of study and control data was not analyzed in the paper (Mathews & Rezin, 1977).

on avoidance (Rosen et al., 1976), whereas the other reported that 11 of 12 subjects in the desensitization group compared to 1 of 12 in the control group were able to touch or hold a live snake at post-treatment ($p < 0.01$) (Barrett, 1969). In height phobia, Baker (1973) also reported significant improvement in subjective anxiety in height phobia, but avoidance level was not measured. In the study of flying phobia, systematic desensitization also decreased self-report anxiety, but both treated and control subjects displayed highly anxious behavior and elevated heart rate during a post-study test flight (Howard et al., 1983). In addition, the test flight did not distinguish overt avoidance behavior between the two groups; 9 of 10 in desensitization *vs*. 7 of 10 in control group were able to complete a test flight. However, only subjects who had previously flown were included in the study. In the last study of height and claustrophobia, systematic desensitization was compared to a control treatment based on "insight therapy" (Lazarus, 1961). Outcome was based on "recovery" status one month after acute treatment. Subjects were considered to have recovered if they passed a BAT and provided self-report that the phobia no longer impaired their daily functioning. Systematic desensitization resulted in a greater proportion of subjects who recovered compared to the control treatment (8 of 14 *vs*. 2 of 14), but the difference was not statistically significant ($p = 0.0625$) in this sample size.

3.2. Long-term follow-up of imaginal exposure/systematic desensitization

There are no follow-up studies of imaginal exposure, but four follow-up studies of systematic desensitization, one in animal phobia (Barrett, 1969), one in height phobia (Baker, 1973) and two in flying phobia (Denholtz, Hall, & Mann, 1978; Solyom et al., 1973) (See Table 1). The animal phobia study assessed clinical status using a BAT whereas the others used self-report measures. The length of follow-up ranged from six months to 3.5 years, with the flying phobia study having the longest follow-up period. All of these reported that initial treatment gains were maintained at the time of follow-up. In the flying phobia study by Solyom et al. (1973), subjects were followed 8 to 24 months after systematic desensitization, and 70% of the 32 patients reported minimal or no anxiety during subsequent flights. However, subjects in the other treatment groups did similarly well. This may be because all the subjects participated in a test flight immediately following acute treatment, which might have acted as an unintended *in vivo* exposure treatment. In the second study of flying phobia, subjects treated with systematic desensitization were followed 3.5 years after treatment (Denholtz et al., 1978). Approximately 60% of initial responders (*i.e.*, patients who flew immediately after the study) reported that they continued to fly during the follow-up period, but actual avoidance level (*e.g.*, BAT) was not assessed.

4. *In vivo* exposure

4.1. Acute treatment

During *in vivo* exposure, the patient confronts the actual phobic stimulus, such as a live snake in the treatment of snake phobia or standing on a rooftop in the treatment of height phobia. This is usually conducted in a graduated fashion, starting from the least anxiety-provoking aspect to the most anxiety-provoking aspect of the stimulus. Exposure generally lasts several hours, in either one-long session (three hours) or, over five, one-hour sessions. There are 14 controlled studies that met the inclusion criteria- four compared *in vivo* exposure to a placebo or wait-list control, six compared it to another active treatment, four included both an active comparison and control condition, making a total of eight studies that included a control condition. As with the studies on systematic desensitization, the main outcome measure was a BAT. Half of the studies additionally reported the proportion of subjects who were able to achieve the terminal task in the BAT, and two in particular utilized Jacobson et al.'s criteria to assess proportion of subjects who achieved clinically significant improvement. In contrast to the studies of systematic desensitization, the results of the *in vivo* studies were consistently positive compared to control conditions.

All eight studies that included a control condition reported significantly better outcome in the *in vivo vs*. the control condition. Compared to the controls, *in vivo* exposure resulted in greater decrease in both subjective anxiety and avoidance in animal phobia (Bandura et al., 1969; Gilroy, Kirkby, Daniels, Menzies, & Montgomery, 2000; Gotestam & Hokstad, 2002), water phobia (Egan, 1981), height phobia and driving phobia (Williams, Dooseman, & Kleinfield, 1984), flying phobia (Walder, McCracken, Herbert, James, & Brewitt, 1987) and claustrophobia (Booth & Rachman, 1992; Ost, Alm, Brandberg, & Breitholtz, 2001). Three of these studies also reported that approximately 80% to 90% of treatment completers were able to perform the terminal task in the BAT, which was assessed by raters blinded to the study condition (Bandura et al., 1969; Ost et al., 2001; Williams et al., 1984). In subjects with animal phobia, 92%

Table 1
Follow-up studies in specific phobia

Source	F/U period	Treatment conditions	Subjects		Main outcome measures	Results at follow-up
			Initial *n*	% F/U		
Animal phobia						
Barrett (1969)	6 months	1 Systematic desensitization	36	?	BAT: avoidance and anxiety	Gains maintained, 1=2
		2 Implosion therapy				1, 2>3
		3 Wait-list control				
Lang, Melamed, and Hart (1970)	8 months	1 Systematic desensitization: therapist-guided	29	83	BAT: avoidance and anxiety	Gains maintained, 1=2
		2 Systematic desensitization: self-directed				
Ost (1991)	12 months	1 *In vivo* exposure: therapist-guided	42	100	BAT: avoidance, anxiety, HR and BP	1: 71% CSI
		2 *In vivo* exposure: self-directed			Spider Q	2: 6% ″
Arntz and Lavy (1993)	12 months	*In vivo* exposure:				
		1 with elaboration (description of spider)	41	90	Spider Phobia Q	Gains maintained, 1=2
		2 without elaboration			Watson and Marks's phobia scales	
Hellstrom and Ost (1995)	12 months	*In vivo* exposure:				
		1 therapist directed in clinic	52	92	BAT: avoidance, anxiety, HR and BP	1: 80% CSI
		2 specific manual-based tx in clinic			Spider Q	2: 63% CSI
		3 specific manual-based tx at home				3: 10% CSI
		4 general manual-based tx in clinic				4: 9% CSI
		5 general manual-based tx at home (all in maintenance program)				5: 10% CSI
Ost (1996)	12 months	*In vivo* exposure: 3–4 per group	42	100	BAT: avoidance, anxiety, HR and BP	1: 95% CSI
		2 *In vivo* exposure: 7–8 per group			Spider Phobia Q Spider Q	2: 75% CSI
Ost et al. (1997)	12 months	1 *In vivo* exposure: direct	46	87	BAT: avoidance and anxiety	1: 75% CSI
		2 *In vivo* exposure: observed			Spider Phobia Q	2: 14% CSI
		3 Video exposure: indirect			Spider Q	3: 44% CSI
Gotestam and Hokstad (2002)	12 months	*In vivo* exposure	25	?	BAT: avoidance Fear Q	Gains maintained
Koch et al. (2004)	12 months	1 *In vivo* exposure	40	?	BAT: avoidance and anxiety	Gains maintained, 1=2
		2 *In vivo* exposure and cognitive therapy			Spider Phobia Q Cognitive Somatic Anxiety Q	
Height phobia						
Baker (1973)	8 months	1 Systematic desensitization: therapist-guided	22	91	Acrophobia Q	Gains maintained.
		2 Systematic desensitization: self-directed				2>1 in doing more self-exposure
Emmelkamp et al. (2002)	6 months	1 Virtual reality	33	85	Acrophobia Q	Gains maintained, 1=2
		2 *In vivo* exposure			Attitude Towards Height Q	
Krijn et al. (2004)	6 month	1 Virtual reality: head mounted display	28	79	Acrophobia Q	Gains maintained, 1=2
		2 Virtual reality: computer automatic virtual environment			Attitude Towards Height Q	

(continued on next page)

Table 1 (*continued*)

Source	F/U period	Treatment conditions	Subjects		Main outcome measures	Results at follow-up
			Initial *n*	% F/U		
Claustrophobia						
Ost et al. (1982)	14 months	1 *In vivo* exposure	34	82	BAT: avoidance, anxiety, and HR	Gains maintained, 1=2
		2 Applied relaxation			Claustrophobia Scale	71% passed BAT elevator
					Autonomic Perception Q	96% passed BAT small bathroom
Ost et al. (2001)	13.8 months	1 *In vivo* exposure: one session (3 hrs)	41	100	BAT: avoidance, anxiety, BP and HR	1: 100% CSI
		2 *In vivo* exposure: five sessions			Claustrophobia Scale	2: 81% CSI
		3 Cognitive therapy: five sessions				3: 93% CSI
Flying phobia						
Solyom et al. (1973)	8 – 24 months	1 Systematic desensitization	40	80	Self-report on subjective anxiety	1: 70% reported no anxiety
		2 Aversion relief				2: 80% reported no anxiety
		3 Habituation				3: 70% reported no anxiety
		4 Group psychotherapy				4: 50% reported no anxiety
Denholtz et al. (1978)	3.5 years	Systematic desensitization: 1 standard with graded exposure	51	84	Self-report flying activity	60% reported flying
		2 with continuous presentation of scenes				(not separated by tx)
		3 without training in relaxation				
		4 Relaxation with placebo scenes (if txs 2–4 failed, then assigned to tx 1)				
Walder et al. (1987)	3 years	*In vivo* exposure with coping strategies	38	87	Self-report flying activity	61% reported flying
						26% reported not flying
Ost et al. (1997)	12 months	1 *In vivo* exposure: one session (3 h)	28	100	Test-flight: avoidance and anxiety	Both 1, 2 did worse at f/u.
		2 *In vivo* exposure: five sessions			Fear of Flying Scale	64% completed test-flight.
					Fear of Flying Inventory	
Van Gerwen et al. (2002)	12 months	1 *In vivo* exposure	1026	62	Self-report flying activity	1: 100% reported flying
		2 *In vivo* exposure and cognitive therapy				2: 98.6% reported flying
Rothbaum et al. (2002)	12 months	1 Virtual reality	30	80	Self-report flying activity	Gains improved over time
		2 *In vivo* exposure			Q: Attitudes Towards Flying	1: 92% reported flying
					The Fear of Flying Inventory	2: 69% reported flying
Muhlberger et al. (2003)	6 months	1 Cognitive therapy	47	79	Self-report flying activity	1: 45% reported flying
		2 Cognitive therapy and virtual reality			General Fear of Flying Q	2: 62% reported flying
		3 Wait-list control				3: 27% reported flying
Wiederhold and Wiederhold (2003)	3 years	1 Virtual reality: physiological feedback	30	90	Self-report flying activity	1: 100% reported flying, no meds
		2 Virtual reality: no physiological feedback				2: 60% reported flying, no meds
		3 Systematic desensitization				3: 14% reported flying, no meds

Table 1 (*continued*)

Source	F/U period	Treatment conditions	Subjects		Main outcome measures	Results at follow-up
			Initial *n*	% F/U		
Blood-injury phobia						
Ost, Salkovskis et al. (1991)	12 month	1 Applied tension	30	100	BAT: avoidance, anxiety, BP and HR	1: 100% CSI
		2 Tension only			Mutilation Q	2: 90% CSI
		3 *In vivo* exposure			Fear Q	3: 50% CSI
Hellstrom et al. (1996)	12 month	1 Applied tension: five sessions	30	100	BAT: avoidance, anxiety, BP and HR	1: 60% CSI
		2 Applied tension: one session (3 hrs)			Mutilation Q	2: 70% CSI
		3 Tension only: one session (3 h) (all in maintenance program)			Injection Phobia Scale	3: 60% CSI
Dental phobia						
Hakeberg et al. (1993)	10 yearrs	1 Systematic desensitization and biofeedback	39	74	Dental attendance	1: 92% continued dental care
		2 Diazepam			Corah Dental Anxiety Scale (DAS)	2: 63% continued dental care
		3 General anesthesia (all received dental treatment)				3: 34% continued dental care 1 is less anxious than 3
Moore et al. (1996)	12 months	1 Hypnotherapy	106	75	Dental attendance	1: 54% continued dental care
		2 Relaxation with video exposure: group			Corah Dental Anxiety Scale (DAS)	2: 63% continued dental care
		3 Relaxation with video exposure or clinical rehearsal: individual (all received dental treatment)				3: 88% continued dental care
Johren et al. (2000)	12 months	1 Psychological tx	50	?	Dental attendance	1: 70% continued dental care
		2 Midazolam			Corah Dental Anxiety Scale (DAS)	2: 15% continued dental care
		3 Wait-list control (all received dental treatment)				3: 10% continued dental care Only 1 reported lower anxiety
Willumsen and Vassend (2003)	5 years	1 Cognitive therapy	62	65	Corah Dental Anxiety Scale (DAS)	Gains maintained
		2 Applied relaxation				
		3 Nitrous oxide				
de Jongh et al. (1995)	12 months	Cognitive therapy	29	72	Dental attendance	41% continued dental care.
					Corah Dental Anxiety Scale (DAS)	Anxiety improved over time
Studies with several types of phobias						
Biran and Wilson (1981)	6 months	1 *In vivo* exposure	22	81	BAT: avoidance and anxiety	Gains maintained.
		2 Cognitive therapy, then *in vivo* exposure				
Lipsitz et al. (1999)	10–16 years	1 Behavioral therapy and pill placebo	81	34	Clinician interview	Relapse rate of 45%.
		2 Behavioral therapy and imipramine				63% of subjects symptomatic
		3 Supportive therapy and imipramine				

Note: ? = not reported; Q = questionnaire; CSI = clinically significant improvement based on Jacobson et al.'s criteria.

treated with *in vivo* exposure compared to 0% of controls were able to handle the animal without fear after treatment ($p<0.001$) (Bandura et al., 1969). In a group of subjects with either height or driving phobia, 87% of treated subjects were able to achieve maximal performance in the BAT (*e.g.* ability to stand at the railing of a 12-story building in height phobia, and driving 6 miles of congested urban freeway in driving phobia) (Williams et al., 1984). In a study of claustrophobia, 79% of patients in the *in vivo* condition compared to only 18% in the control condition achieved clinically significant improvement ($p<0.0002$) (Ost et al., 2001).

In the studies that compared *in vivo* exposure to another active treatment, two compared it to systematic desensitization (Bandura et al., 1969; Egan, 1981), one to imaginal exposure (Rentz et al., 2003), one to vicarious *in vivo* exposure (*e.g.*, observing someone else receiving treatment) (Ost, Ferebee, & Furmark, 1997), two to virtual reality exposure (Emmelkamp et al., 2002; Rothbaum, Hodges, Smith, Lee, & Price, 2000), three to cognitive therapy (Biran & Wilson, 1981; Booth & Rachman, 1992; Ost et al., 2001), and one to applied tension (Ost, Fellenius, & Sterner, 1991). The studies of virtual reality, cognitive therapy and applied tension will be discussed in detail in those respective sections.

In vivo exposure was significantly more effective than systematic desensitization (Bandura et al., 1969; Egan, 1981), but not in comparison to imaginal exposure (Rentz et al., 2003). Compared to snake phobics treated with systematic desensitization, Bandura et al. (1969) reported that a greater proportion of subjects treated with *in vivo* exposure was able to touch a snake with bare hands (25% *vs*. 92%, respectively, $p<0.001$). In Egan's (1981) study, subjects with aquaphobia treated with *in vivo* exposure had lower avoidance level (*e.g.* higher BAT score in swimming test) compared to those treated with desensitization ($p<0.05$), but the proportion achieving the final goal in the BAT was not reported.

In contrast, Rentz et al.'s (2003) study of 82 dog phobics found *in vivo* exposure to be no better than imaginal exposure. In this study, response rates based on ability to perform a BAT were not significantly different among the study conditions: 73.1%, 62.1% and 51.9% for the *in vivo*, active-imaginal and imaginal exposure, respectively. It is possible that the amount of time in the exposure in the *in vivo* treatment (30 min) was not sufficient to produce a maximum therapeutic effect. One study found that the optimal amount of exposure, long enough to result in no anxiety for at least 1 min, is more effective than exposures that terminate at the highest point of anxiety (Marshall, 1985). Exposure times in the positive studies generally lasted between 2 to 4 h (Bandura et al., 1969; Gotestam & Hokstad, 2002; Ost et al., 2001).

In the study comparing *in vivo* exposure to vicarious exposure, Ost et al. (1997) assigned 46 spider phobics to one of three treatments: *in vivo* exposure (termed "direct treatment"), direct observation (observing someone else getting treatment) or indirect observation with video exposure (Ost et al., 1997). The percentage of responders as defined by Jacobson et al.'s criteria was significantly greater in the *in vivo* group (75%) compared to the other two groups (7% in direct observation and 31% in indirect observation) [$p<0.0005$].

These studies overall suggest that *in vivo* exposure results in good treatment outcome for most types of specific phobias, provided a sufficient length of exposure time.

4.2. Long-term follow-up of in vivo exposure

There are 16 follow-up studies that included subjects treated with *in vivo* exposure, seven in animal phobia, one in height phobia, two in claustrophobia, one in subjects with fear of heights, elevator or darkness, one in blood phobia, and four in flying phobia (see Table 1). Eleven of the 16 studies included a BAT as an outcome measure, and five had only self-report measures. The follow-up period ranged from 6 to 14 months. All of the studies in animal phobia (Arntz & Lavy, 1993; Gotestam & Hokstad, 2002; Hellstrom & Ost, 1995; Ost, 1996; Ost et al., 1997; Ost, Salkovskis, & Hellstrom, 1991), height phobia (P. Emmelkamp et al., 2002), claustrophobia (Ost et al., 2001; Ost, Johansson, & Jerremalm, 1982) and the one study of fear of heights, elevators or darkness (Biran & Wilson, 1981) reported that acute treatment gains of *in vivo* exposure were either maintained or improved further over time. There was no difference in overall outcome in studies using BAT or only self-report measures. In contrast, the follow-up studies in flying phobia reported different results dependent on the outcome measures used. Three of the four studies that used only self-report measures reported improved subjective anxiety or flying activity over time (Rothbaum, Hodges, Anderson, Price, & Smith, 2002; Van Gerwen, Spinhoven, Diekstra, & Van Dyck, 2002; Walder et al., 1987). Although informative, self-report of flying activity does not take into account other factors that can affect flying activity, such as differences in opportunity to fly, financial issues, accompanying person or use of medication during the flight. One of the four studies

that used a test flight found a less favorable outcome; the number of participants able to complete a test-flight decreased from 93% immediately post-study to 64% at follow-up (Ost, Brandberg, & Alm, 1997).

Lastly, the follow-up study of blood phobia suggested that *in vivo* exposure may not have much long-term efficacy for this type of phobia. Only 50% of subjects treated with *in vivo* exposure were considered clinically significant improved after one year (Ost, Fellenius et al., 1991).

5. Interoceptive exposure

5.1. Acute treatment

Interoceptive exposure is a form of behavioral therapy in which internal physical sensations (such as feelings of choking, dizziness) are reproduced and the patient is exposed to them in a controlled setting. This is in contrast to exposure to an external stimulus as in *in vivo* exposure. Interoceptive exposure therapy is used in panic disorder, but has also been studied in claustrophobia. Booth and Rachman (1992) assigned 48 claustrophobics to a control condition or one of three treatments: *in vivo* exposure, interoceptive exposure, or cognitive therapy (Booth & Rachman, 1992). The subjects' heart rate, subjective anxiety, physical symptoms, and cognitions were noted during a BAT both pre- and post-treatment. Compared to the control group, the interoceptive group had fewer negative cognitions ($p<0.05$) and less unpleasant physical sensations ($p<0.05$). It was equal to the other two treatments in decreasing cognitive distortions, anxiety and physical sensations. All three treatments led to increased ability of the subjects to stay in closed situations. While further work is obviously needed, interoceptive exposure appears to be a promising treatment for claustrophobia.

5.2. Long-term follow-up of interoceptive exposure

There are no follow-up studies of interoceptive exposure.

6. Virtual reality therapy

6.1. Acute treatment

In the last few years, virtual reality exposure has gained a great deal of attention in the treatment of height and flying phobia (North, North, & Coble, 1998; Rothbaum, Hodges, & Kooper, 1997; Rothbaum & Hodges, 1999). In virtual reality exposure, a computer program generates a virtual environment that simulates the phobic situation by integrating real-time computer graphics, visual displays, body tracking devices and other sensory input devises (Rothbaum et al., 1997). There are seven controlled studies in virtual reality treatment of specific phobia, six of which looked at virtual reality as the sole treatment and one as an adjunctive treatment to cognitive therapy (Muhlberger, Wiedemann, & Pauli, 2003). Of the six studies, two compared virtual reality to *in vivo* exposure (Emmelkamp et al., 2002; Rothbaum et al., 2000), one to systematic desensitization (Wiederhold et al., 2002), and three to a control group — two with wait-list controls (Garcia-Palacios, Hoffman, Carlin, Furness, & Botella, 2002; Krijn et al., 2004) and one with a relaxation control (Muhlberger, Herrmann, Wiedemann, Ellgring, & Pauli, 2001).

The two studies that compared virtual reality to *in vivo* exposure found virtual reality to be equally effective. The first was a study of flying phobia in which subjects were assigned to virtual reality exposure, *in vivo* exposure or a wait-list control condition (Rothbaum et al., 2000). The number of subjects who completed a graduation flight in the virtual reality condition was similar to that in the *in vivo* exposure [8 of 15 (53%) *vs*. 10 of 15 (67%), respectively] but higher than that of the wait-list control [1 of 15 (7%), $p<0.01$]. Self-report questionnaires also indicated that both treatments resulted in lower anxiety during the flight than the control ($p<0.01$). The second study with similar findings was of height phobia (Emmelkamp et al., 2002). Both the virtual reality and *in vivo* exposure group improved significantly on all dependent measures, including the BAT score for avoidance and self-report questionnaires of anxiety ($p<0.001$), and there was no difference between the two treatments. However, the proportion of subjects who were able to complete the BAT terminal approach task was not reported.

Virtual reality was compared to systematic desensitization in one study of flying phobia (Wiederhold et al., 2002). Virtual reality was equal to desensitization in alleviating subjective anxiety, but more effective in increasing flying

activity. The number of subjects who flew post-study was 18 out of 20 in the virtual reality group and 1 of 10 in the desensitization group ($p<0.001$).

In the adjunctive treatment study, virtual reality enhanced the effects of cognitive therapy in flying phobia based on self-report measures (Muhlberger et al., 2003). In this study, subjects were treated with cognitive therapy alone or cognitive therapy and virtual reality. A wait-list control group was later added. The cognitive/virtual reality condition resulted in less anxiety than the other two conditions.

In contrast to the active comparison studies, three studies that compared virtual reality to control conditions reported less consistent results. Two found virtual reality to be superior to wait-list controls (Garcia-Palacios et al., 2002; Krijn et al., 2004) whereas one reported that it was effective (*e.g.* improvement from pre to post study), but the amount of change over time was not significantly different from a relaxation control group (Muhlberger et al., 2001). In the two positive studies, virtual reality exposure resulted in less subjective anxiety and avoidance than wait-list conditions in spider phobia (Garcia-Palacios et al., 2002) and height phobia (Krijn et al., 2004) based on self-report questionnaires and a BAT. In the study by Muhlberger et al. (2001), virtual reality treatment was compared to 1 h of deep muscle relaxation exercise conducted in the virtual reality chair but without the head-mount display of virtual images. Both groups had significant pre- to post-study reduction in physiological responses and self-report anxiety during a virtual test-flight. Although virtual reality resulted in a larger treatment effect (*e.g.*, SUDS ratings during the pre- to post-virtual test-flight went from 35.8 to 10.1 in the virtual group, and 30.2 to 19.6 in the relaxation group, $p=0.15$), this difference did not reach statistical significance in this sample size ($n=28$). It is also not known if results would have been similar during an actual test-flight. In addition, the subjects in this study might not have met the phobia criteria since screening of subjects was based on self-report questionnaires and not on clinical assessments.

In summary, these studies suggest that virtual reality treatment may be as effective as *in vivo* exposure for flying and height phobia, and more effective than systematic desensitization. As an adjunctive treatment, virtual reality also enhanced the effects of cognitive therapy for flying phobia in one recent study. The overall results are promising, but larger controlled studies would be needed to further support the efficacy of virtual reality for the treatment of height and flying phobia. Virtual reality provides a much needed alternative and convenient treatment option for specific phobia, in particular for fear of flying. In contrast to flying phobia, the cost-effectiveness of virtual reality treatment for spider phobia is questionable given the ease of obtaining a spider for *in vivo* exposure.

6.2. Long-term follow-up of virtual reality

There are five follow-up studies of virtual reality exposure, two in height phobia and three in flying phobia (see Table 1). Outcome was based on self-report measures, and the follow-up periods ranged from six months to three years. In the two height phobia studies, treatment gains were maintained, with virtual reality doing as well as *in vivo* exposure in one of the studies (Emmelkamp et al., 2002). Of the three flying phobia studies, two followed virtual reality as a solo treatment (Rothbaum et al., 2002; Wiederhold & Wiederhold, 2003) and one as adjunct to cognitive therapy (Muhlberger et al., 2003). As a solo treatment, both studies reported that gains were maintained at follow-up based on self-report flying activity. Virtual reality did as well as *in vivo* exposure in one of the studies (Rothbaum et al., 2002) and better than systematic desensitization in the other (Wiederhold & Wiederhold, 2003). However, the addition of virtual reality to cognitive therapy did not affect long-term outcome (Muhlberger et al., 2003). In this study, 62% of subjects in the adjunctive therapy, 45% in the cognitive therapy and 50% in the wait-list condition reported taking an actual flight during the six months follow-up period, and there was no significant difference among the groups ($p=0.62$). One reason for the high rate of flying in the control group was that the subjects were not severely impaired at baseline since the diagnosis of specific phobia was based on self-report questionnaires and not on a clinical evaluation.

7. Applied muscle tension

7.1. Acute treatment

Most cases of blood injury phobia have a unique characteristic of a biphasic physiological response to blood, wound and injury stimuli (Marks, 1988). There is an initial sympathetic response with increased blood pressure and heart rate followed shortly by a parasympathetic response with a drop in blood pressure and heart rate. Taking advantage of this phenomenon, Ost devised an applied muscle tension method for the treatment of blood-injury phobia (Ost & Sterner,

1987). Applied tension is a combination of muscle tension and *in vivo* exposure. Subjects first learn to recognize the early signs of decrease blood pressure, and then practice muscle tension alone-tensing and releasing the tension in the body. Then muscle tension is used in combination with *in vivo* exposure in order to reverse the drop in blood pressure and prevent fainting.

There are two controlled studies evaluating the efficacy of applied muscle tension in blood phobia (Ost, Salkovskis et al., 1991; Ost, Sterner, & Fellenius, 1989). The response rate was defined as the proportion of patients with clinically significant improvement based on Jacobson et al.'s criteria. The first study demonstrated that applied muscle tension was as effective as applied muscle relaxation (combination of muscle relaxation and *in vivo* exposure) and required fewer sessions for treatment response (Ost et al., 1989). The second study found muscle tension alone to be as effective as applied muscle tension, both of which were more effective than *in vivo* exposure alone (Ost, Salkovskis et al., 1991). Subjects treated with applied muscle tension, muscle tension or *in vivo* exposure had a response rate of 90%, 80% and 40%, respectively. Compared to the *in vivo* group, the group that received muscle tension was able to watch a film with bloody scenes for a longer period of time and had less fainting behavior. These two studies support the use of muscle tension or applied muscle tension in blood-injury phobia.

7.2. Long-term follow-up of applied tension

There are two follow-up studies of blood phobia (Hellstrom, Fellenius, & Ost, 1996; Ost, Salkovskis et al., 1991) (see Table 1). Outcome measure was based on a BAT (watching a film with bloody scenes) and the follow-up period was 12 months in both cases. One study found subjects treated with muscle tension only or applied muscle tension remained well over time (90% to 100% clinically significant improvement) (Ost, Salkovskis et al., 1991), but the other found a lower percentage of subjects with clinically significant improvement (60% to 70%) despite a maintenance program (Hellstrom et al., 1996). The authors attributed the difference in response rates to the expertise of the therapist, with the former study using therapist with more experienced compared to that of the latter study.

8. Cognitive therapy

8.1. Acute treatment

Cognitive factors are considered an important component of anxiety, and cognitive therapy has gained wide popularity in the treatment of anxiety disorders in general. Phobic beliefs, such as an irrational fear of the potential danger of the stimulus, also play a role in specific phobia (Thorpe & Salkovskis, 1995), but cognitive therapy has only recently been recognized as a possible treatment modality. The focus of cognitive therapy is cognitive restructuring in which distorted or irrational thoughts that are associated with the feared stimulus or situation are modified, with a resulting decrease in anxiety and avoidance. For example, cognitive therapy would attempt to help a flying phobic reevaluate the possibility of a plane crash given actual data, or an animal phobic to reassess the realistic danger of the animal causing harm.

Cognitive therapy has been studied both as a solo treatment and as an adjunctive therapy. There are six studies examining it as a solo treatment (Biran & Wilson, 1981; Booth & Rachman, 1992; Capafons, Sosa, & Vina, 1999; de Jongh et al., 1995; Ost et al., 2001; Willumsen, Vassend, & Hoffart, 2001), three as an adjunctive to *in vivo* exposure (Craske, Mohlman, Yi, Glover, & Valeri, 1995; Koch, Spates, & Himle, 2004; Van Gerwen et al., 2002), and one in combination with virtual reality as previously discussed (Muhlberger et al., 2003). With the exception of one negative study (Biran & Wilson, 1981), the five other studies found cognitive therapy to be an effective solo treatment. As an adjunctive treatment, the findings have been mixed but overall promising in the use of cognitive therapy.

As a solo treatment, cognitive therapy was as effective as *in vivo* exposure in two studies of claustrophobia (Booth & Rachman, 1992; Ost et al., 2001). In Booth and Rachman's study, cognitive therapy resulted in less subjective anxiety, physical symptoms and negative cognitions. The reduction of fear was associated with removal of dysfunctional thoughts relating to fear of being "trapped," "suffocation," and "lose control" (Shafran, Booth, & Rachman, 1993). In Ost et al.'s (2001) study, a greater number of subjects treated with cognitive therapy or *in vivo* exposure (combined) achieved clinically significant improvement as defined by Jacobson et al.'s criteria, compared to the control condition (79% *vs*. 18%, respectively $p<0.0002$). There was no group difference between *in vivo* exposure and cognitive therapy.

In contrast, Biran and Wilson (1981) reported that cognitive therapy was ineffective in decreasing avoidance in subjects with a fear of heights, elevators or darkness. Compared to *in vivo* exposure, fewer subjects in cognitive therapy completed all the tasks in a post-study BAT (9 of 11 *vs*. 1 of 11, $p<0.01$). One reason for the poor response may be that the method of cognitive restructuring in this study emphasized "self-instructional training" in the use of positive self-statements (replacing nonproductive self-statements with more positive and productive ones), as opposed to guided discovery or Socratic questioning based on Beck's theory. It is unclear how effective self-instructional training is in restructuring phobic beliefs.[4] Cognitive therapy in the other positive studies followed Beck's theory using guided discovery.

For flying phobia, cognitive therapy produced a better outcome than no-treatment controls in one study (Capafons et al., 1999) but not another (Muhlberger et al., 2003). In the study by Capafons et al. (1999), subjects treated with cognitive therapy did better than controls on all of the self-report measures of anxiety ($p<0.001$) and in some physiological variables (heart rate, muscle tension) ($p<0.05$) during viewing of a videotape of a flight. In Muhlberger et al.'s (2003) study (previously mentioned in virtual reality section) cognitive therapy was no better than the wait-list control condition based on self-report measures.

Cognitive therapy was also used to treat dental phobia with some effectiveness in two studies (de Jongh et al., 1995; Willumsen et al., 2001). In the first study, cognitive therapy resulted in less self-report anxiety and decreased frequency and believability of negative thoughts associated with dental treatment compared to no treatment (de Jongh et al., 1995). In the second study, cognitive therapy was as effective as two other treatments, nitrous oxide sedation and applied muscle tension, in lowering self-report dental anxiety (no behavioral measures) (Willumsen et al., 2001). However, all the subjects also received actual dental treatment during the study, which could have confounded the study conditions.

As an adjunctive treatment, cognitive therapy enhanced the effects of *in vivo* exposure therapy of claustrophobia in one study (Craske et al., 1995). However, it did not improve outcome of *in vivo* exposure treatment of spider (Koch et al., 2004) or flying phobia (Van Gerwen et al., 2002). It is not clear if a ceiling effect was present because *in vivo* exposure by itself was very effective in these studies. In the spider phobia study, the response rate in each treatment group was not reported, but 33 of 40 subjects in the groups combined were able to complete a post-study BAT with minimal anxiety. In the flying phobia study, *in vivo* exposure resulted in less subjective anxiety after treatment (pre-study mean of 7.6 and post-study mean of 2.18 in a 0–10 visual analog scale). Eighty-five percent of the subjects treated with exposure therapy also reported flying at three months post-study.

Overall, there is strong evidence supporting the efficacy of cognitive therapy for the treatment of claustrophobia, either alone or as an adjunct to *in vivo* exposure. Thus, cognitive therapy may be a good alternative to *in vivo* exposure for claustrophobia. As a solo treatment, there is also some evidence that cognitive therapy may benefit dental and flying phobia, but it does not seem to add much to *in vivo* treatment of animal or flying phobia.

8.2. Long-term follow-up of cognitive therapy

There are four follow-up studies of cognitive therapy as a solo treatment [one in claustrophobia, one in flying phobia, and two in dental phobia], and one follow-up of cognitive therapy as an adjunct to *in vivo* exposure in animal phobia (see Table 1). The outcome measure included a BAT in the claustrophobia and animal study, but self-report measures only in the flying and dental phobia studies. The follow-up periods ranged from 6 to 14 months, with one dental phobia study at five years. As an adjunctive treatment to *in vivo* exposure, gains were maintained in the animal phobia study (Koch et al., 2004).

As a solo treatment, cognitive therapy appears to be long-lasting in claustrophobia, but less so in flying or dental phobia. In claustrophobia, 93% percent of subjects treated with cognitive therapy maintained acute treatment gains at 13.8 months follow-up (Ost et al., 2001). In contrast, only 45% of patients with flying phobia reported flying at six months follow-up, which was not significantly different from those in the wait-list control (27%) (Muhlberger et al., 2003). In dental phobia, subjects maintained improved subjective anxiety in both studies, but avoidance was still prominent. The five-year follow-up study by Willumsen and Vassend (2003) did not measure avoidance, but de Jongh

[4] Indeed, the use of positive self-statements alone produced more anticipatory anxiety than placebo treatment before a test flight in a small study of flying phobia (Girodo & Roehl, 1978).

et al. (1995) reported that only 41% of subjects attended dental appointments on a regular basis at one-year follow-up. However, the rate of dental attendance in non-phobic patients was not included in these studies.

9. Other psychological treatments for specific phobia

Other psychological therapies that have been used for specific phobia included psychoanalysis, psychodynamic psychotherapy, Eye Movement Desensitization Reprocessing (EMDR), hypnotherapy and supportive therapy. With the exception of supportive therapy and hypnotherapy, there are no controlled studies of these other therapies that met the inclusion criteria.

10. Supportive psychotherapy

10.1. Acute treatment

There has been one study of supportive psychotherapy for specific phobia (Klein, Zitrin, Woerner, & Ross, 1983). This study included subjects with "simple phobia" ($n=81$), "mixed phobia" ($n=60$) [had spontaneous panic attacks and limited agoraphobia] and "agoraphobia" ($n=77$) [spontaneous panic attacks with severe agoraphobia] with results of each group analyzed separately. Supportive psychotherapy (dynamically oriented and non-directive approach) was compared to "behavioral therapy," which included supportive therapy with additional behavioral techniques: in-session systematic desensitization, *in vivo* self-exposure homework and assertiveness training. Supportive therapy was as effective as adjunctive behavioral therapy; approximately 82% of those treated with adjunctive behavioral therapy and 76% of those with supportive therapy were judged to be responders based on clinician, self and blind independent evaluator assessment of global improvement. It was surprising that both treatments were equally effective. However, the treatments had similar supportive elements and were conducted by the same therapists. In addition, subjects in the supportive group were also not instructed to refrain from self-exposure, if they initiated it on their own.

10.2. Long-term follow-up of supportive therapy

Lipsitz, Mannuzza, Klein, Ross, and Fyer (1999) conducted a follow-up of 35% (28 of 81) of patients who participated in the above mentioned study at 10–16 years after acute treatment. All subjects who could be located and consented to participate were evaluated. The assessment included history of the longitudinal course of the symptoms since the acute treatment period. The relapse rate was fairly high; 45% of those who had completely recovered eventually relapsed during the follow-up period. In addition, 63% of the subjects followed were symptomatic at follow-up. However, the sample size was too small to differentiate outcome for the different treatment groups and only a subset of subjects was followed. Nevertheless, this small study raises questions about the long-term effects of successful phobia therapy, and suggests that relapse may be much more frequent than previously thought.

11. Hypnotherapy

11.1. Acute treatment

Hypnotherapy is the application of hypnotic techniques to induce a "trance" or an altered state of consciousness or attention which increases the person's susceptibility to suggestions to experience various changes in sensation, perception, cognition or control over motor behavior (Crawford & Barabasz, 1993). Two studies of hypnotherapy in dental phobia reported mixed findings. Hypnotherapy had questionable efficacy in one study (Moore, Abrahamsen, & Brodsgaard, 1996) and no efficacy in the other (Hammarstrand, Berggren, & Hakeberg, 1995).

In the study by Moore et al. (1996), subjects were non-randomly assigned to wait-list condition, hypnotherapy or one of three types of video exposures. The hypnotherapy and two of the video exposure conditions included "clinical rehearsal," described as a simulated exposure to threatening dental situations combined with muscle relaxation. Hypnotherapy was concluded to be better than wait-list controls, and as effective as the other treatments in lowering self-report dental anxiety, but this was questionable given the overlap of clinical rehearsal in the treatments. In the study by Hammarstrand et al. (1995), subjects were assigned to one of three treatments: hypnotherapy, behavioral therapy

(applied relaxation to imagined scenes + EMG feedback) or general anesthesia. Hypnotherapy did not produce any change from pre- to post-study dental anxiety or the dentists' rating of behavior during a dental exam.

11.2. Long-term follow-up of hypnotherapy

One follow-up study of hypnotherapy in dental phobia suggested that hypnotherapy does not have a long-lasting effect (Moore et al., 1996). At one-year follow-up, only 54% of subjects in the hypnotherapy group continued regular treatment in the community, and dental anxiety was significantly higher at follow-up compared to immediately post-study based on self-report measures.

12. Medication treatment

12.1. Acute treatment

The general view is that medication has little benefit in specific phobia (Antony & Barlow, 2002; Harvey & Rapee, 2002; McGlynn & Vopat, 1994; Roy-Byrne & Cowley, 2002; Stanley & Beidel, 1993), but there is actually relatively little data addressing this issue. Seven medication studies met the inclusion criteria — five with medication as the sole treatment and two in combination with psychotherapy.

Of the five medication studies as a solo treatment, two evaluated benzodiazepine in the treatment of flying or dental phobia, and three compared the use of sedatives (general anesthesia or nitrous oxide) to psychotherapy in dental phobia. In the two benzodiazepine studies, results indicated that benzodiazepine has limited acute use for either flying phobia (Wilhelm & Roth, 1997) or dental phobia (Johren, Jackowski, Gangler, Sartory, & Thom, 2000). Wilhelm and Roth (1997) reported that one dose of alprazolam prior to a flight resulted in less subjective anxiety compared to a pill placebo, but one week later on a repeat flight without medication, the alprazolam group faired worse than the placebo group, with greater subjective anxiety, a higher rate of panic attacks and an even greater physiological response during the flight. In Johren et al.'s (2000) study, subjects received one dose of midazolam, one session of behavioral therapy (applied relaxation) or no intervention prior to dental treatment. Midazolam was helpful in lowering dental anxiety immediately, but three months later, anxiety returned to baseline in the midazolam group, whereas the behavioral therapy group continued to benefit.

The remaining three comparison studies with general anesthesia or nitrous oxide found that both can facilitate dental treatment, but in comparison to behavioral therapy, general anesthesia was less effective whereas nitrous oxide was as effective as behavioral therapy. Berggren and Linde (1984) reported that general anesthesia can lower anxiety, but compared to behavioral therapy, a smaller proportion of subjects were able to complete dental treatment (92% *vs*. 69%) and fewer were willing to follow-up in community dental clinics after the study (78% *vs*. 53%). In another study comparing general anesthesia to hypnotherapy or behavioral therapy, general anesthesia decreased anxiety from pre- to post-study, but comparison to other treatments were difficult to interpret since 41% of subjects dropped out of the study (Hammarstrand et al., 1995). In contrast, Willumsen et al. (2001) found that nitrous oxide sedation during dental treatment lowered dental anxiety as much as either 10 weekly sessions of cognitive or behavioral therapy (Willumsen et al., 2001).

Two studies evaluated the effects of medication in combination with psychotherapy. The first by Klein et al. (1983) was previously mentioned in the supportive therapy section. Imipramine did not enhance the effects of either behavioral or supportive therapy. However, a ceiling effect could not be ruled out since both psychotherapies alone resulted in approximately 80% of the subjects with either moderately or markedly improvement. BATs were not done in this study.

The second study looked at D-cycloserine, which is a partial agonist at the *N*-methyl-*d*-aspartate (NMDA) receptor site (Davis, 2002). The NMDA receptors may play an important role in extinction of conditioned fear. In animal studies, Davis and colleagues have shown that infusion of an NMDA receptor agonist into the amygdala of rats facilitated the extinction of conditioned fear whereas an NMDA antagonist blocked fear extinction (Davis, 2002; Davis, Walker, & Myers, 2003). These results have been replicated by other groups (Ledgerwood, Richardson, & Cranney, 2003; Ledgerwood, Richardson, & Cranney, 2004). In light of these findings, Davis and his colleagues hypothesized that D-cycloserine might also accelerate fear extinction in phobic patients undergoing exposure treatment. In a recent study, 28 subjects with height phobia were pre-medicated with either D-cycloserine or a pill placebo prior to

virtual reality exposure (Ressler et al., 2004). Consistent with predictions from animal data, the addition of D-cycloserine accelerated the effects of virtual reality exposure in lowering anxiety and increasing attempts at self-exposure to real height situations at one week and three months after the study.

In summary, there are limited data suggesting that benzodiazepine may be helpful in acute situations, such as enabling a flying phobic to complete a flight or a dental phobic to undergo a procedure, but the anxiety returns without medication. In dental phobia, sedation with general anesthesia or nitrous oxide might also enable acute dental treatment, but general anesthesia is less effective than behavioral therapy whereas nitrous oxide may be as effective as behavioral therapy. Lastly, D-cycloserine may have promise as an adjunct to behavioral therapy, but this is only in its early stage of development.

12.2. Long-term follow-up of medication treatment

There are two follow-up studies of at least 10 years duration, one of a mixed group of specific phobia mentioned earlier (Lipsitz et al., 1999) and the other of dental phobia (Hakeberg, Berggren, Carlsson, & Grondahl, 1993) (see Table 1). In both studies, the number of subjects was too small to make any meaningful comparisons between treatment groups. Nonetheless, the study by Lipsitz et al. (1999) suggested that relapse is common after successful treatment with combination imipramine and therapy.

There are two other follow-up studies of dental phobia, a one-year (Johren et al. 2000) and a five-year follow-up (Willumsen & Vassend, 2003). Outcome measures were based on reports of dental attendance or self-report anxiety. Results were mixed. In the one-year follow-up study, acute benzodiazepine treatment did not continue to lower anxiety or help subjects continue with dental treatment over time (Johren et al., 2000). In the five-year follow-up study, nitrous oxide treatment maintained gains in dental anxiety, but dental attendance was not assessed (Willumsen & Vassend, 2003).

13. Efficacy *vs*. effectiveness in acute treatment

The results reported in the acute treatment studies were based on that of study completers. In this context, *in vivo* exposure demonstrated good efficacy for most types of specific phobia. However, the overall effectiveness of the treatments must also take into account treatment motivation and adherence. It is well known that patients with specific phobia tend not to seek treatment (Essau, Conradt, & Petermann, 2000; Magee et al., 1996). In addition, a survey of students with fear of spiders reported a similarly high refusal rate (Garcia-Palacios, Hoffman, See, & Botella, 2001). With the exception of one study reporting a refusal rate of 13.6% (Emmelkamp et al., 2002), treatment refusal rates were not mentioned in the other acute trials.

A high rate of dropout in the studies may also affect the interpretation of the results. The drop-out rates of the studies reviewed here (29 of 38 studies reported rates) ranged widely from 0% to 45%, with the highest rates in studies of dental phobia. These high rates were not surprising, particularly in dental phobia since these studies generally included severely impaired subjects treated in a specialized dental phobic clinic. Reasons for the high dropout have not been systematically studied in specific phobia, but studies in agoraphobia suggest that intolerance of anxiety during exposure is an important factor (Emmelkamp & Van Der Hout, 1983). Klein et al. (1983) reported that a major reason for dropouts (23.5%) in their study was that patients did not want to take medication. Given these results, it is likely that the treatments mentioned thus far may be less effective in the real world setting when treatment refusal and adherence are taken into account.

14. A final note on long-term outcome studies

There are several important issues that can affect outcome data. The first is whether or not subjects received additional treatment during the follow-up period. Only two studies discussed thus far explicitly reported that subjects were encouraged to continue self-exposure (Hellstrom et al., 1996; Hellstrom & Ost, 1995). Both of these studies reported good outcome, suggesting that self-exposure is important in maintaining acute treatment gains. The second important issue is whether the study was a snapshot view of the subject's clinical status (cross-sectional) or an assessment of functioning during the whole follow-up period (longitudinal). Since specific phobia is a chronic disorder, but phobic symptoms are episodic and usually only apparent during anticipation or exposure to the phobic stimulus, a

cross-sectional study may miss relapses during the follow-up period. With the exception of the study by Lipsitz et al. (1999), the other studies listed in Table 1 were assessments of the subject's status at the time of follow-up, and did not include relapse of symptoms during the follow-up period.

Another important issue is the length of follow-up period. The majority of studies have follow-up periods ranging from six months to one year. While the trend in these studies suggest that acute treatment gains are either maintained or improved over time, relapse rates beyond one year are less clear because studies with a longer follow-up period are scarce. The three available studies have contradictory results. Two studies of dental phobia reported that gains of behavioral intervention were generally maintained at five years (Willumsen & Vassend, 2003) and 10 years of follow-up (Hakeberg et al., 1993), but Lipsitz et al.'s (1999) study with different phobia subtypes suggested that relapse rates were fairly high at 10–16 years.

To our knowledge, there are no other long-term follow-up studies of specific phobia. Nevertheless, animal data in extinction of conditioned fear responses suggest that relapse over time is expected (Bouton, 2002, 2004). Extinction is the process by which a previously conditioned response is weakened after repeated presentation of the conditioned stimulus without the aversive stimulus. In rats, Bouton and his colleagues showed that extinction occurs through the development of a new association that competes with the conditioned fear response in a context-dependent manner (Bouton 2002, 2004). When presented with the conditioned stimulus over time, fear is more likely to return in rats in a new setting compared to that of the original environment where extinction first took place.

Three studies in humans partially support the important role of context in relapse of fear in humans as well. In these studies, students with fear of spiders were treated with *in vivo* exposure therapy, and then one to two weeks later, underwent a BAT in the original or a novel treatment context (different therapist/environmental cues). The first study did not find any significant difference in response between the groups tested in the original or novel context (Rodriguez, Craske, Mineka, & Hladek, 1999), but two later studies did, after modifying the novel context to be more distinct from the treatment context (Mineka, Mystkowski, Hladek, & Rodriguez, 1999; Mystkowski, Craske, & Echiverri, 2002). It would be interesting to see if similar results would hold over a longer follow-up period. Such data would help us to better understand the rates and sources of relapse in specific phobia, and how to improve retention of treatment effects.

15. Conclusion

The goal of this review was to comprehensively examine outcomes of evidence-based treatments for specific phobia in adults. Based on the acute clinical trials, the most robust treatment for most of the specific phobia types appears to be *in vivo* exposure therapy, with most studies finding it more effective than placebo or wait-list control, and a few studies supporting a response rate of 80 to 90%. However, these results should be interpreted with some caution given the high rate of dropout in some of studies. Future studies should explore reasons for treatment refusal and dropouts in order to improve the overall effectiveness of behavioral therapy.

Long-term follow-up studies in behavioral therapy suggest that treatment gains are generally maintained from six months to one year, and often improved if self-exposure is continued during the follow-up period. The three studies looking at longer follow-up periods had mixed results, with two studies in dental phobia reporting maintenance of gains and one in other phobia subtypes having high relapse rates. Since most of the follow-up studies relay on self-report measures and do not include evaluation of functional impairment, it is possible that even those considered to have sustained improvement may not be free of phobic symptoms. More research is needed to better understand and prevent relapse in patients with specific phobia.

The other acute treatments reviewed are not equally effective compared to each other, and have differential efficacy in the phobia subtypes. Virtual reality exposure may be comparable to *in vivo* exposure therapy for the treatment of height phobia and flying phobia. Since virtual reality is a relatively new treatment, larger controlled studies would be needed to demonstrate its efficacy in other phobia subtypes. The treatments of claustrophobia and blood-injury phobia are unique in that claustrophobia responds to interoceptive exposure and blood phobia to applied muscle tension. A limited number of studies suggest that cognitive therapy may be effective in the treatment of dental phobia and claustrophobia. It also appears to be a helpful adjunctive treatment for claustrophobia, but does not add much to exposure therapy of other phobia types. Systematic desensitization appears to be helpful in lowering subjective anxiety, but results in less consistent improvement of avoidance behavior. Finally, controlled studies in imaginal exposure, supportive psychotherapy, hypnotherapy and medication are scarce. The limited data suggest a possible role of

supportive psychotherapy for specific phobia, but the effectiveness of hypnotherapy in the treatment of dental phobia is questionable. Medication has limited use in the acute setting but is overall not that helpful, with the exception of D-cycloserine which shows promise as an adjunctive treatment.

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