Behavioral Treatments of Panic Disorder with Agoraphobia: Treatment Process and Determinants of Change.

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Abstract

The present dissertation comprises four empirical studies within the area of behavioral treatment of panic disorder with agoraphobia. The focus is on studying issues pertaining to outcome, treatment process and determinants of change. The first study is a randomized controlled treatment study of 73 patients undergoing 16 sessions of either exposure in vivo (E), or cognitive behavior therapy (CBT). Both treatments showed clear improvements at post-treatment that were well maintained at 1-year follow up, and there were no significant differences between the treatments. The second study concerned prediction of outcome in the same sample. From a variety of pre-treatment characteristics severity of avoidance was the one most related to outcome. Most predictors were found unrelated. Two approaches of prediction were also compared: treating outcome as a categorical vs. continuous variable. The different approaches yielded a somewhat dissimilar picture of the impact of pre-treatment severity of avoidance. The third study examined different aspects of the therapeutic relationship, and their relation to outcome. Clients' perceptions of therapists and their ratings of the working alliance were generally not related to outcome at any point. On the other hand, therapists' perceptions of patients as showing goal-direction and active participation were related to outcome from early on in therapy. The fourth study examined different aspects of change. It was found that change in indices of the frequency of panic attacks was not closely related to change in agoraphobic avoidance at post-treatment. Change in avoidance was also more related to other aspects of outcome. At one-year follow-up, a more unitary picture, regarding the different aspects of change was observed.

Key words: Panic disorder with agoraphobia, cognitive-behavior therapy, exposure in vivo, outcome prediction, therapeutic relationship, working alliance

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To Karin, Beatrice and David

The present thesis is based on the following studies, which will be referred to by their Roman numerals:

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Study I and II was printed by permission from the publisher.

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Stockholm, February 2005

J.R.

List of abbreviations

AD	Anti-depressives
ADIS	Anxiety disorder interview schedule for DSM
APD	Avoidant personality disorder
AWOPD	Agoraphobia without history of panic disorder
BAT	Behavioral approach test
BDI	Beck depression inventory
BZD	Benzodiazepines
CBT	Cognitive behavioral therapy
CR	Conditioned response
CS	Conditioned stimulus
CSI	Clinically significant improvement
CT	Cognitive therapy
DSM	Diagnostic statistical manual of mental disorders
E	Exposure
EMDR	Eye-movement desensitization and reprocessing therapy
GAD	Generalized anxiety disorder
GM	Guided mastery therapy
OCD	Obsessive compulsive disorder
PAS	Panic attack scale
PD	Panic disorder
PDA	Panic disorder with agoraphobia
QOL	Quality of life
SSRI	Selective serotonin reuptake inhibitor
STAI-T	State-trait anxiety inventory - trait
TCRS	Therapist-client rating scale
UCR	Unconditioned response
UCS	Unconditioned stimulus
WAI	Working alliance inventory

1. Introduction

The success story

In his influential book, *Anxiety and its disorders* (1988), David H. Barlow labels the behavioral treatments of agoraphobia as one of the success stories of behavior therapy, or psychotherapy in general. These treatments, at the time mainly based on exposure, yielded very consistent results of 60-70 % clinically significant improvement among participants (Shapiro, Pollard & Carmin, 1993). This percentage showed a remarkable stability over various sites and different variants of the basic treatment.

Yet, this success story has more to it than just a reasonable success rate. Agoraphobia is a prevalent disorder afflicting approximately 1 person in 20 in the general population; it is a disorder commonly developed in early adulthood and with a high risk of a chronic course (Wittchen & Essau, 1991). It is associated with high degrees of comorbidity (Brown, Anthony & Barlow, 1995) and reduced quality of life comparable to severe mental disorders (Maisson, Meredith & Keller, 1993).

Exposure-based treatments are conceptually rather simple in their basic idea of systematic exposure to the subjectively feared event in order to extinguish the fear- and avoidance evoking functions of the event. These treatments have been shown to have a reasonable degree of generalization of symptoms, to be very tolerable to clients (Otto, Pollack & Maki, 2000), and can be executed with limited contact with a therapist (Ghosh & Marks, 1987).

“Success story” indeed seems a reasonable opinion. Still, even a success story has its drawbacks. The implications are that, in spite of the success rate, 30-40 % of the patients do not achieve satisfying results in therapy. The stability over different variants of the treatment has its drawbacks; namely, a failure to specify the necessary and crucial components. The demonstrated general applicability to subjects also contains a lack of ability to identify those who could be expected to have a poor prognosis in behavioral therapies. The variability of modes of administration that show equal efficacy has its drawbacks; namely, a failure to clarify the functional role of the contact with the therapist. This provides a gap in the understanding of the basic contingencies of learning in this kind of therapy. Above that, the understanding of what constitutes the most crucial targets of change in this multifaceted disorder is far from clear.

2. The Description of Agoraphobia

2.1. Diagnosis

Fear of the marketplace

Different fears and phobias began to receive greater attention from the medical profession during the late 19th century. In 1871, the German physician

Westphal described a condition, in which he perceived the most pre-eminent features as experiencing anxiety when walking in open places or crossing empty streets. From the conventional nomenclature he thus suggested the label “agoraphobia”, from the word-stems *agora* (Greek for marketplace) and *phobia* (from the Greek word *phobos* meaning flight or terror); hence, a fear of the marketplace (Mathews, Gelder & Johnston, 1981).

Westphal’s paper covered descriptions of three patients with similar features. They reported anxiety under certain predictable circumstances: when crossing open spaces or streets, in churches, or in places where plenty of people were gathered. Their anxiety presented such symptoms as palpitations, heat sensations, blushing and trembling. Furthermore, he described anticipatory anxiety, the presence of the fear of dying, and the concern over drawing unwanted attention to oneself, when experiencing this anxiety. He also noted that this anxiety could be alleviated in several ways: a companion, a distracting conversation, alcohol, or carrying a stick. Interestingly, Westphal’s description contained important clinical features that were to become ingrained in the contemporary understanding of this disorder. Phenomena such as “fear of fear” (Goldstein & Chambless, 1978), “anxious apprehension” (Barlow, 1988), “catastrophic cognitions” (Clark, 1988) and “safety signals” (Rachman, 1984), were to be described in the basic concepts of cognitive-behavioral therapists more than a century later. Yet, there is one peculiarity in Westphal’s description; all his patients were men! Actually, when Legrand du Saule in 1885 described a female case of agoraphobia, he commented that this condition was mostly observed in men (Mathews et al., 1981). This should serve as a reminder of the cultural context’s influence over the definition of what should be considered a psychiatric disorder.

While Westphal should be given credit for identifying and naming a clinical disorder, he did not offer any comprehensive explanation for it. Psychoanalysis was the first theory to offer a psychological explanation of phobic behavior. The essential feature of the classical psychoanalytical conception of a phobia is that the original unconscious source of fear has been replaced by an alternative, representational object (Fenichel, 1946). The phobic avoidance thus serves the primary function of a symptom; namely, to let the real, original motive of the fear remain unconscious through the defense mechanisms of repression and displacement. The theory explains the phobic behavior in relation to an assumed underlying fixation, rather than, as now more customary, in a functional relationship to the anxiety. It is of special historical interest that Freud himself, instead, asserted: “we often find the recollection of a state of panic; and what the patient actually fears is a repetition of such an attack under those special conditions in which he believes he cannot escape it” (Cited in Mathews et al., 1981, p. 42). Actually, Freud’s writing should be given credit for being the first to recognize the relationship between panic and avoidance in agoraphobia (Barlow, 1988); a position that has gained general acceptance today.

Through the following history, several different labels like “platzschwindel”, “platzangst”, “anxiety hysteria”, “locomotor anxiety”, “phobic-anxiety depersonalization syndrome”, “phobic anxious states”, or “non-specific insecurity fears” show up in the psychiatric nomenclature. These labels described clinical states that share two important common denominators (Shapiro et al., 1993). They all have

described a fear of situations, where the possibility of escape or the access to security are threatened, and the presence of disturbing bodily symptoms and an exaggerated concern over these. Of all these labels, agoraphobia has been the one term that has survived.

Later diagnostic definitions

The diagnostics of anxiety disorders, before the DSM-III (APA, 1980), were dominated by two broad categories. The first category referred to a variety of phobias, phobic disorders, or phobic neuroses. These were identified by a characterization of anxiety and avoidance triggered by external events. The other broad category was characterized by anxiety, largely defined by autonomic responses, which occur in the absence of an identifiable external trigger. These disorders were described in the psychiatric lingua at that time using terms as “cardiac neuroses”, “effort syndrome”, “neurasthenia”, or “neurocirculatory asthenia”. In the DSM-II these two broad categories translate into the diagnoses “phobic neuroses” and “anxiety neurosis” (DSM-II, APA 1968).

When the DSM-III was published in 1980 it made a conceptual departure from earlier nosological systems, with its attempt to use an atheoretical language, and dropping the historically influential concept “neurosis”, which earlier included the area of anxiety disorders. The label “phobic disorders” was the descendent of the “phobic neuroses”. Under this label, along with “social phobia” and “simple phobia”, the diagnosis “agoraphobia” was found. Agoraphobia also came with the specification, i.e., with or without panic attacks. The former term “anxiety neurosis” was abandoned in favor of the term “anxiety states”. This term covered “panic disorder” and “generalized anxiety disorder”. The general concept of neurosis in DSM-II was more extensive, and contained sub-categories such as “hysterical neurosis” and “depressive neurosis” whose descendants are found in other categories than anxiety disorders.

The revision of DSM-III to DSM-III-R (APA, 1987) had a crucial impact on the conceptualization of agoraphobia. While keeping the distinction between phobic disorders and anxiety states, agoraphobia was now made an auxiliary feature of panic disorder, and thus came under the heading “anxiety states”. Two categories were defined as “panic disorder with agoraphobia” and “panic disorder without agoraphobia”. Under “phobic disorders”, the category “agoraphobia without a history of panic disorder” was found. Finally, in DSM-IV (APA, 1994), the same three diagnostic labels are found, but under the super-construct “anxiety disorders”.

Diagnosis according to DSM-IV

DSM-IV defines panic attacks and agoraphobia separately, where the former is defined as a:

...discrete period of intense fear or discomfort in the absence of real danger that is accompanied by at least 4 of 13 somatic or cognitive symptoms. Symptoms can be somatic or cognitive in nature and include palpitations, sweating, trembling or shaking, sensations of shortness of

breath or smothering, feelings of choking, chest pain or discomfort, nausea or abdominal distress, dizziness or lightheadedness, derealization or depersonalization, fear of losing control or “going crazy”, fear of dying, paresthesias, and chills or hot flushes. The attack has a sudden onset and builds up to a peak rapidly (usually 10 minutes or less) and is often accompanied by a sense of imminent danger or impending doom and an urge to escape (p. 430, DSM-IV TR, 2000).

Panic attacks can then be specified as *unexpected* or *uncued*, in that they are not associated with a clearly distinguishable precipitating event for the individual. The attacks are perceived as occurring “out of the blue” as opposed to *situationally bound* or *cued* attacks that are defined by occurring almost invariably immediately on exposure to, or in anticipation of a situational cue or trigger. *Situationally predisposed* panic attacks are similar but less invariably associated with a triggering event. The concept “*limited symptom attacks*” is used when fewer than 4 symptoms are present.

The criteria for agoraphobia are stated as:

- A. Anxiety about being in places or situations from which escape might be difficult (or embarrassing) or in which help may not be available in the event of having an unexpected or situationally predisposed panic attack or panic-like symptoms. Agoraphobic fears typically involve characteristic clusters of situations that include being outside the home alone; being in a crowd or standing in a line; being on a bridge; and traveling on a bus, train, or in an automobile.
- B. The situations are avoided (e.g., travel is restricted) or else endured with marked distress or with anxiety about having a panic attack or panic-like symptoms, or require the presence of a companion.
- C. The anxiety or phobic avoidance is not better accounted for by another mental disorder, such as social phobia (e.g., avoidance limited to social situations because of fear of embarrassment), specific phobia (e.g., avoidance limited to a single situation like elevators), obsessive-compulsive disorder (e.g., avoiding getting dirty by someone with an obsession about contamination), posttraumatic stress disorder (e.g., avoiding stimuli associated with a severe stressor), or separation anxiety disorder (e.g., avoiding leaving home or relatives).

The diagnostic definitions are then combinations of the above-specified concepts. *Panic disorder without agoraphobia* (300.01) is defined by the presence of recurrent unexpected panic attacks and that one of the attacks has been followed by one of the following: (a) persistent concerns about having additional attacks; (b) worry about the implications of the attack or its consequences; (c) a significant change in behavior related to the attacks. As the diagnostic label implies, the absence of agoraphobia is required. And a further differentiation is made, in that the anxiety attack is not due to physiological effects of a substance or a general medical condition, or better accounted for by another mental disorder.

Panic disorder with agoraphobia (300.21) contains the same diagnostic criteria, apart from the main distinction that (as the label implies) the presence of agoraphobia is required. The third category, *agoraphobia without history of panic disorder* (300.22), is defined by the presence of agoraphobia and is related to panic-like symptoms like dizziness or diarrhea, but panic disorder as defined above is

absent. It also states that, if a medical condition is present, the fear, taken as the basis for labeling the condition agoraphobic, clearly exceeds that which is usually associated with this medical condition.

2.2. Clinical features

Prevalence

While early estimates indicated that agoraphobia was a relatively rare disorder (Agras, Sylvester, & Oliveau, 1969), later studies have documented that a substantial proportion of the population has difficulties that correspond to these diagnostic concepts.

Wittchen and Essau (1991) summarized several epidemiological studies and concluded that over several studies a high consistency is found in prevalence rates. This was not only in studies using proper sampling and case-finding procedures, but also in studies covering culturally diverse samples. Panic disorder (PD) occurred in the adult population with a lifetime prevalence of approximately 2%, and a 6-month prevalence of 1.2%. Agoraphobia, which was more common, occurred with a lifetime-prevalence of about 5%, and a 6-month prevalence of 4%. The largest epidemiological study conducted in this area was the Epidemiological Catchment Area Study (ECA; Regier & Robins, 1991). It was conducted in five sites in the United States, and included adults from the age of 18 upwards. In all, 18,572 subjects were interviewed in a structured format for the DSM-III diagnoses. The adjusted overall results from the ECA study found a lifetime prevalence for any anxiety disorder of 15.1%, and for agoraphobia, 4.8%.

Recent epidemiological studies using the DSM-III-R criteria found similar lifetime prevalence figures for panic disorder with agoraphobia (PDA); 6.7% in the USA (National Comorbidity Survey; Magee, Eaton, Wittchen, McGonagle & Kessler, 1996), and 6.1% in Norway (Kringlen, Torgersen & Cramer, 2001). So far no epidemiological study using DSM-IV (APA, 1994) criteria and assessment by clinical interview has been published.

The category “agoraphobia without a history of panic disorder” (AWOPD) has been the topic of a great deal of controversy. Several epidemiological surveys usually have found a substantial proportion of subjects that present avoidance (even severe), but do not report a history of panic attacks. The National Comorbidity Survey reported a lifetime prevalence of 3.5% for PD or PDA, while the prevalence for AWOPD was 5.3% (Kessler et al., 1994). Clinicians, on the other hand, have in clinical material tended to report the phenomenon as a rare or virtually non-existent one (Barlow, 2002).

Age of onset

PDA is a disorder with a common onset in early adulthood. Both clinical and epidemiological evidence support the picture that panic disorder most frequently starts in the late 20s and the early 30s. In the Munich Follow-up Study (MFS), a community survey across West Germany using structured format for DSM-III defined disorders on 1366 subjects, an onset of panic disorder before the age of 10 was reported for 0%, while, in the same interval, the figure for agoraphobia was 16%

(Wittchen & Essau, 1991). The corresponding figures, for the age interval 11-20, were 14% for PD, and 21% for agoraphobia. Between the ages 21-30 the onset of agoraphobia peaked at 24%, while, at the interval 31-40, the onset of panic disorder peaked at 35%. From ECA, a bimodal distribution of onset age for panic disorder was found (Eaton, Kessler, Wittchen & Magee, 1994). In the age intervals of 15-24 and 45-54, peaks in the distribution were observed.

Clinical course

While being common disorders, the natural course of anxiety disorders in untreated subjects is basically unknown. A rare prospective study of untreated anxiety disorders was published in 1972 (Agras, Chapin & Oliveau). The authors reported no spontaneous remission at all in agoraphobia over a 5-year period. It should be noted though that this is based on the observation of 6 patients.

The MFS data indicated that the most common symptom pattern of anxiety disorders in general can be characterized as chronic and persistent, with an overall low rate of spontaneous and complete remission, when assessed in retrospect (Wittchen & Essau, 1991). One study of agoraphobic patients awaiting treatment found that the symptoms did not change over a 3-month period (Michelson & Mavissakalian, 1983). Another study that employed a psychological placebo treatment (group discussion without exposure instruction) reported that no change occurred in phobic symptoms (McDonald et al., 1979). Thus, it has been concluded that spontaneous remission and regression to the mean are unlikely confounds in the estimate of treatment effects in agoraphobia. (Mattick, Andrews, Hazdi-Pavlovic & Christensen, 1990). Placebo medication alone brought about only small changes in agoraphobia, while panic is a more variable measure that could be expected to be more affected by placebo treatment.

In a naturalistic one-year follow-up on 309 patients participating in the Harvard/Brown Anxiety Research Project (Keller et al., 1994), a 39% probability of full remission for uncomplicated PD was found. This is compared to a 17% probability of full remission for PDA. The difference between the two categories persisted even when the criteria for remission were less stringent. Full remission here allowed none or only slight symptoms ("Some slight anxiety in the situation (or in anticipation of the situation) but no avoidance"). There have been reports indicating that subjects with and without agoraphobia show similar degrees of improvement in both treated and untreated samples (Noyes, Garvey, Cook & Samuelson, 1989). However, the majority of studies seem to convey a picture consistent with the view that panic disorder has a more chronic course with higher rates of relapse after remission and longer episodes, when agoraphobia is part of the constellation of symptoms (Aronsson & Louge, 1987; Pollack et al., 1990).

Comorbidity

While the diagnostically distinguishing features of PDA are focusing exclusively on panic attacks and phobic avoidance, agoraphobic patients have been noted to show generally more severe impairment (Wittchen & Essau, 1991), and

usually a high comorbidity with other anxiety disorders and mood disorders (Brown, Anthony & Barlow, 1995). They are consistently found to suffer from a plethora of clinical problems (Chambless, 1985). Wittchen and Essau (1991) summarized several studies and concluded high comorbidity for panic disorder and agoraphobia with depression, somatization, and substance abuse. In the MFS data, panic disorder had a later onset and the highest comorbidity rates with other anxiety disorders. Cases with agoraphobia with and without panic attacks were generally more severely impaired and had a markedly higher comorbidity rate for depression than did other phobias.

When reviewing epidemiological studies, about a third to one half of the patients with PD were reported to also have agoraphobia (Slaap & den Boer, 2001). In clinical samples, this proportion was closer to 80%. A prevalence of comorbid depression has in different studies been reported in the range from 23% to 53%. The percentages of those fulfilling criteria for an additional anxiety diagnosis range between 44% and 83.3%, with generalized anxiety disorder (GAD), social phobia and specific phobia being the most frequent. Regarding comorbid axis-II diagnoses, percentages ranging from 27% to over 50% have been reported for this group. This is compared to the normal population, where the range was 5.9% to 18% (Slaap & den Boer, 2001).

Maisson et al. (1993) examined the impact of PD and GAD, quality of life (QOL) and the implications for other nosological categories for a total of 357 subjects diagnosed with either disorder. Significant impairment in QOL was noted for both disorders. Comorbidity of PD and GAD was associated with significantly lower levels of QOL, as well as greater impairment in emotional health and social relationships. But neither the severity of panic, nor the severity of agoraphobia differed significantly with the presence of GAD.

Data from the ECA study showed that a lifetime diagnosis of panic disorder was associated with pervasive social and health consequences, similar to or greater than those associated with major depression (Markowitz et al., 1989). These consequences included the subjective experience of poor physical and emotional health, alcohol and other drug abuse, impairment in social and marital functioning, financial dependency, increased use of psychoactive medications, health services and hospital emergency departments. It should be noted that social impairment was similar whether or not agoraphobia was present. The only difference was a more frequent use of sleeping pills among agoraphobics. In the Maisson et al. study it was noted that subjects with PD without agoraphobia were more likely to report a history of drug abuse.

The above-mentioned findings focus on what is presumed to be the consequences of panic disorder. It should be noted that 43%, in a cohort of DSM-III defined agoraphobics with panic attacks, reported chronic stressors of either marked or moderate severity that were not judged to be mere consequences of their anxiety disorder. The two most prevalent kinds of stress were marital difficulties and relationship problems with somebody else other than the spouse (Wade, Monroe & Michelson, 1993).

Gender factors

Agoraphobic patients have been referred to, in derogatory terms, as “housebound housewives” (Salkovskis & Hackman, 1997). This reflects the basic fact that a majority of the afflicted individuals are female. In an epidemiological sample the gender rate was 70% female vs. 30% male (Keller et al., 1994). In clinical samples an even larger proportion of female subjects has been identified. Oei, Wanstall and Evans (1990) investigated gender differences in 272 patients with a DSM-III diagnosis of agoraphobia with panic attacks, and found that 82% of the agoraphobic patients were female. It has also been reported that the proportion of female patients rises with increasing severity. Barlow (2002) reported that 89% of the patients at their clinic with the most severe level of avoidance were women.

It has been assumed from clinical experience that male agoraphobics are different, not only regarding their response to treatment, but also displaying a somewhat different symptomatology (Burke, Drummond & Johnston, 1997). Hafner (1981) found that the male patients did differ, but not significantly so, in that they were less phobic of social situations but more concerned about somatic symptoms and related fears. No differences were found regarding panic symptoms, situational fears and most measures used in the study by Oei et al. (1990). There were, however, differences in the clinicians’ rating of anxiety, depression and one measure of fear. Moreover, significantly more female than male agoraphobics were married. It was noted that the differences in clinician-rated anxiety, but not self-rated, might contain a bias that women are more likely to be rated as displaying more symptoms than males are in general. The verbal reports about anxiety symptoms from male agoraphobics to the clinicians might also portray these as being less severe. The authors conclude that this would be consistent with the suggestion that women are more willing than men to express their symptomatology.

3. The Explanation of Agoraphobia

3.1. The conditioning of fear

While the diagnosis of PDA has become generally accepted, explanatory accounts of agoraphobia have been more heavily debated. When behavior therapy established itself during the late fifties, it was based on methodological behaviorism and the respondent conditioning theories that Watson borrowed from Pavlov in the early days of behaviorism (Dougher & Hayes, 1999). Respondent conditioning offered an explanation of phobias that became successfully popularized. In the early conditioning theories (e.g., Eysenck & Rachman, 1965), no particular distinction was made between different types of phobias. They were uniformly considered as conditioned avoidance reactions.

Historically, these explanations are based on the two-factor theory of Mowrer (1960). The first factor, in this theory, is explained in terms of respondent, or Pavlovian conditioning and the second in terms of operant conditioning. The first factor is constituted when, for example, an aversive event occurs in the presence of a

hitherto neutral stimulus, which acquires the property of a conditioned aversive stimulus. It thereby becomes capable of eliciting a fear response. The classical conditioning of anxiety also makes it possible for new operant behaviors to be reinforced negatively, when they are instrumental in escaping or reducing the fear. This process constitutes the second factor.

Accordingly, the therapeutic agent in behavioral treatments, where the client is systematically exposed to these anxiety-evoking events, has been explained in terms of extinction of conditioned fear, which becomes possible when avoidance behavior is eliminated. The theory, in its rather simple form, contained all that was needed to explain the results of behavioral treatments (Matthews et al., 1981).

The classical conditioning position of agoraphobia has been criticized in that there is seldom a reasonable historical account of a conditioning event in a person's history (e.g., Rachman, 1977). Hallam (1978) even argued against viewing agoraphobia as a phobia, in the sense of a learned avoidance reaction, since it often contains a lack of predictability of the avoidance of places. The fluctuations in avoidance run counter to the stability that would be expected in a straightforward stimulus-response formulation. A further line of criticism came from a number of experiments that failed to show that escape strengthened the avoidance behavior (Rachman, Craske, Tallman & Solyom, 1986).

The conditioning of agoraphobia

Goldstein and Chambless (1978) introduced a distinction between "simple" agoraphobia and "complex" agoraphobia. The first concept includes patients who developed phobic anxiety and avoidance in response to a specific event. The treatment is directed at the specific situational fears and may consist of a singular treatment technique. On the other hand, the complex variant of agoraphobia referred to a syndrome that they asserted had four distinctive features: (i) the person has developed panic attacks, which have become an object of anticipatory anxiety and hence this leads to fear-of-fear cycle; (ii) the person shows signs of generally low self-sufficiency, independence, and assertiveness; (iii) the person has difficulties in appropriately attributing the source of the distressing feelings; (iv) the onset of symptoms is supposed to develop against a background of conflict, usually of an interpersonal nature, rather than as a result of a specific conditioning event. These four features were supposed to interact to produce agoraphobic fear and avoidance.

This theoretical point of view contains several aspects of interest. Apart from considering the broader social context, in which agoraphobia arises, they reintroduced the notion of interoceptive conditioning (Razran, 1961), in which low-level somatic sensations of anxiety or arousal effectively became CSs associated with higher levels of anxiety or arousal. It also contains two further aspects of special interest: the individual's perception of anxiety attacks as unconnected to external stressors in life and, what they call "semantic generalization" (e.g., being trapped in a bad marriage bears resemblance to those feelings that are evoked by being trapped in an elevator). Taking a more general stance in considering the function of agoraphobic behavior, they stated that it could, in a way, be seen as solving interpersonal issues. As the agoraphobic avoidance rules out the prospect of an independent life, it is no

longer an option to consider. The situation may also contain reinforcements (help and support) for an avoidant and dependent lifestyle. One of the logical consequences deduced from their conclusion regarding treatment was that exposure has to contain the key phobic stimuli, the experience of anxiety itself.

Their account has been criticized for being vague and speculative regarding the specific relationship between the stimuli and avoidance and lack of evidential support for dependency as a pre-requisite for agoraphobia (Mathews et al., 1981).

3.2. Panic as disorder – biological and epidemiological models

The position that agoraphobia may not exist as a distinct clinical entity, but that it develops as a complication of the presence of panic attacks was particularly stressed by Klein (1980). It was proposed that panic attacks were a distinct type of anxiety, amenable to treatment with anti-depressant medication, and that this type of anxiety was determined by a discrete biological mechanism. Avoiding places and also the more generalized aspects of the complaint were conceptualized as a secondary response to the threat of recurring panic attacks.

A staged model is posited (Klein, Ross & Cohen, 1987), where the occurrence of spontaneous panic attacks is the starting point. The mechanisms involved in the panic attacks were seen as uncontrolled discharges of activity in the bio-behavioral anxiety system producing semi-random bursts of panic. This is followed by the cognitive appraisal of these symptoms as harmful and a process of sensitization to symptoms, i.e., anticipatory anxiety. Thereafter, avoidance develops as a further complication. Agoraphobia will then be considered at a later stage and/or a more severe variant of the same disease entity, giving it the status of a secondary phenomenon.

This symptom-progression model has been part of the same debate as the AWOPD-category mentioned above. In epidemiological studies it is generally found that the majority of individuals that fulfill the criteria for agoraphobia do not fulfill the criteria for a history of panic disorder (Wittchen & Essau, 1991), thereby invalidating the crucial role of panic attacks for agoraphobia to develop. However, there seems to be a general consensus that in clinical samples it is uncommon to find agoraphobic avoidance not preceded by panic attacks or limited symptom attacks (Thyer & Himle, 1985; Craske & Barlow, 1988).

In spite of the generally alleged importance of initial panic attacks for the development of agoraphobia, the staged model and the hypothesis that the duration of panic disorder is a critical variable for agoraphobia development has been criticized for not being empirically very well supported (Salkovskis & Hackman, 1994).

3.3. Cognitive model of agoraphobia

The cognitive model regards the proximal cause of anxiety to be a threat appraisal, and anxiety-related behaviors that are directly related to such appraisals. More specifically, anxiety in a given situation may be inappropriately raised if the person overestimates the probability of danger and the awfulness of that danger, or if

they underestimate their ability to cope, if the threat were to happen (Clark, 1988; Salkovskis & Hackman, 1994). This process of estimation will be determined by pre-existing negative beliefs that may contribute to the experience of anxiety.

Stated simply, anxiety disorders can be said to arise when situations are perceived as more dangerous than they really are. In the case of panic disorder, this is assumed to arise from an underlying tendency to misinterpret certain bodily sensations as a sign of imminent disaster (Clark, 1988). The catastrophes most commonly feared during a panic attack include passing out, having a heart attack, going crazy, and losing control over one's behavior. From this misperception of threat follows three mechanisms: selective attention to threat-relevant stimuli, physiological arousal and safety seeking behaviors, which include avoidance and escape. These behaviors not only involve physically avoiding the place, but also doing different kinds of maneuvers to reduce or avoid unpleasant sensations while in the situation. The reactions that occur as a response to threat and anxiety may serve to amplify, or maintain the important "threat belief". Safety seeking behaviors are considered particularly important in this sense. Avoidance behavior prevents disconfirmation of threat appraisals, but the patient is unaware of the anxiety-maintaining effects of these behaviors. As panic and avoidance become more chronic, the behaviors involved become habitual and the awareness of the specific cognitive component of avoidance diminishes, except when directly challenged by deliberate or accidental exposure.

In this model, agoraphobia is not necessarily related to panic, but may be (Salkovskis & Hackman, 1994). Agoraphobic patients are generally described as believing that entering situations such as crowded shops are likely to result in some catastrophic bodily or mental harm. However, their negative appraisals of agoraphobic situations are not justified, in the sense that they (objectively) do not pass out, have a heart attack, go insane and so on. This is, of course, less clear when appraisals concern difficulties with coping, trembling, showing anxiety etc.

The cognitive analysis of phobic avoidance involves an analysis of the avoidance responses as behaviors, which are intended to avoid possible future disaster, rather than explaining them in terms of prior experiences of arousal/relief associated with the specific situation. Given that the cognitive theory suggests that anxiety is a direct consequence of threat appraisal, a belief change is assumed to be the key to improvement.

The cognitive model of anxiety has been criticized for being vague about the operationalization of key concepts and rendering theories that are empirically untestable. This vagueness concerns, among other things, the concept "catastrophic misinterpretations"; how they are acquired, who acquires them, and how they can be measured independently of panic itself (Bouton, Mineka & Barlow, 2001).

3.4. Panic conditioning theory – learned alarms

Bouton et al. (2001) outline an extensive theoretical account of the etiology of panic disorder where they elaborate on the role of classical conditioning, especially of interoceptive stimuli. Central to their account is making a distinction between two aversive motivational states: anxiety and panic. The experience of unexpected panic

attacks seems to be relatively common in the population at large, presumably as a non-specific response to stress (Barlow, 1988). This most often benign phenomenon is referred to as “false alarm”, to be distinguished from fear occurring in situations that pose a tangible threat to the organism, i.e., “true alarms”. Individuals with panic disorder are clearly discriminable from non-clinical individuals that experience panic attacks, in that the former develop anxiety focused on the next potential attack (Craske & Barlow, 1988).

It is thus the fundamental emotion of unconditioned fear, occurring at the wrong time, which is labeled “false alarm”. However, that the alarm is “false” makes less difference to the process of classical conditioning. The cues that will become conditioned stimuli can include exteroceptive stimuli, such as specific social situations or entering general shopping malls or public transportation etc., and interoceptive stimuli. The latter are also more directly involved in the panic response, such as the bodily sensations arising from hyperventilation. Most likely, both types of cues are thought to be involved. A feature of interoceptive conditioning noted in the early experimental literature was that it was especially resistant to extinction (Razran, 1961).

The conditioned responses are considered adaptive and preparative responses, and are thought to engage whole behavior systems, or sets of behaviors that are functionally organized to deal with different UCSs. Just as appetitive conditioning can be designed to help the animal get ready for food, fear conditioning is designed to prepare the organism to deal with an upcoming dangerous event.

The panic attack (the UCS) is understood as an immediate response to an insult to the organism. It may involve topographic features such as cognitions about impending doom, but it has temporal and other properties that help the organism deal with an aversive event that is already in progress. Anxiety (the CR), in contrast, is described as a more “forward looking” response, functionally organized to prepare for a possible upcoming insult. While acknowledging the topographical part of cognitive processes, this theory downgrades the causal role of cognitive processes, as opposed to the prior model.

The theory posits that the occurrence of a panic attack constitutes a conditioning trial that, often in the absence of tangible threatening stimuli, establishes the internal bodily sensations that accompany the early onset of the attack as a CS. These sensations become historically associated with the availability of the rest of the attack; hence, a conditioning account of the “fear of fear”.

As in the earlier conditioning theories, it is stressed that CSs that elicit anxiety can also modulate or influence the strength of ongoing operant or instrumental behaviors. The establishment of a learned alarm makes way for a broad array of behaviors functioning as escape or avoidance of the aversive stimuli. This would include the lifestyle we would label agoraphobia, but their theory posits the possibility of a multitude of more or less obviously detectable behaviors (safety behaviors) to be reinforced. As with all avoidance responses they may serve to prevent the CR’s extinction. Agoraphobic avoidance is simply viewed as one of the possible learned consequential behaviors from having severe unexpected panic attacks. There is some support for the notion that a panic attack occurring in a difficult-to-escape situation will increase the likelihood of conditioning the anxiety

(Craske & Barlow, 1988). Further, factors like occupational status and the social acceptance and reinforcement of avoidance can be assumed to play a part in this development (Barlow, 1988; de Jong & Bouman, 1995).

What makes people agoraphobic?

While theorizing in later years has been largely focused on the development and maintenance of panic attacks (Bouton et al., 2000; Clark, 1986), these attacks are not a unique feature of panic disorder. Rather they are prevalent in most anxiety disorders and major depression (Barlow et al., 1985).

When it comes to distinguishing patients with PDA from those with PD, several studies have found that neither frequency nor severity of panic symptoms were significantly associated with avoidance (Telch, Brouillard, Telch, Agras & Taylor, 1989; Cox, Endler & Swinson, 1994). Studies have failed to find a substantial relationship between the reoccurrence of spontaneous panic and avoidance behavior (Street, Craske & Barlow, 1989; Telch et al., 1989). Neither was the anticipation of spontaneous attacks found to be predictive of levels of agoraphobia (Cox et al., 1995). Rather than spontaneous panics per se, it seems as if the expectation of having panic attacks, while in a particular situation, is linked to the development of agoraphobia (Craske, Rapee & Barlow, 1988; Telch et al., 1989). Cox et al. (1994) found that the patients generally tended to avoid situations, where they expected panic to occur, regardless of the levels of agoraphobia.

In the attempt to differentiate PDA from PD, several studies have compared symptom profiles and other anxiety-related measures. Agoraphobic subjects not only described a significantly greater number of panic symptoms than panic patients without agoraphobia, but also significantly more adverse consequences of panic attacks (Starcevic, Kellner, Uhlenhuth & Pathak, 1993). Depersonalization and derealization as prominent features of panic attacks have been found to be associated with more extensive avoidance (Cassano et al., 1989). Others have found that hypersensitivity to the opinions of others and heightened social-evaluative anxiety, or excessive fear of the loss of control, predispose for a stronger tendency towards phobic avoidance in response to panic attacks (Pollard & Cox, 1988). A greater concern over embarrassing social consequences of anxiety have been proposed as a possible predisposition of agoraphobic avoidance in panic disorder (Telch et al., 1989). Patients with panic disorders with agoraphobia reported generally more negatively perceived consequences of panicking and lower self-efficacy in coping with panic compared to those patients that had panic disorder without agoraphobia (Telch et al., 1989). Agoraphobic patients have also been found to report significantly greater fear of bodily sensations (Chambless & Gracely, 1989).

A problem that arises with this line of research is that it may not identify genuinely qualitatively unique features of agoraphobia, but rather what happens with increasing severity within a diagnostic area. Sturt (1981) has shown that the hierarchical pattern in the distribution of psychiatric symptoms generally is as follows: the more severe the symptom, the greater the likelihood of showing features of other syndromes. The rarer the symptoms reported, the greater the likelihood of

having other symptoms. A positive association between severity and psychosocial dysfunction can also be expected.

Since those patients with agoraphobic avoidance generally are more disabled, they would be expected to present more symptoms, and also rarer ones. It is, therefore, uncertain whether this line of research captures anything more than a general severity dimension. Chambless (1985) investigated the relationship between avoidance behavior and panic frequency with other measures of psychopathology in patients with a DSM-III diagnosis of agoraphobia. Generally, avoidance was more correlated with other aspects of psychopathology, especially depression, neuroticism and social phobia, than panic frequency was. What should be noted is that psychoticism, on the other hand, was uncorrelated with avoidance. This gives an indication that the correlations are not mere indicators of a general correlation between severity and an overall tendency to present the symptoms on the checklists. It restricts the hypothesis raised by Sturt's research in this area, but it may still be valid within a more circumscribed area of symptoms traditionally labeled "neurotic".

The level of avoidance of agoraphobic situations has been found to be more accurately predicted by the anticipatory anxiety surrounding panic attacks (Craske et al., 1988), than the attacks themselves. However, Cox et al. (1995) found that it was only in agoraphobic situations that the anticipation of panic was predictive of agoraphobia. But what was also notable was that general anxiety regarding ambiguous or novel situations was predictive of agoraphobic avoidance. Panic expectancy was found in a longitudinal study to be predominantly influenced by a trait-like expectancy component and uninfluenced by the anxiety experienced on a daily basis (Rodebaugh, Curran & Chambless, 2002).

Summing up these studies, the picture implies a rather loose connection between agoraphobic avoidance and the re-occurrence of spontaneous panic attacks. On the other hand, avoidance shows a strong connection with the likelihood of showing further symptoms and seems to be associated with a higher level of anticipatory anxiety, which might be rather general.

Language and stimulus generalization

Apart from elaborating the complexities of the respondent's conditioning processes presumably involved in panic disorder, the account of Bouton et al. (2001) has two additional features: i) it explicitly de-emphasizes the role of verbal symbolic processes; ii) it also makes all avoidance behaviors, of any kind, a secondary phenomenon. The learning processes involved in these behaviors are not especially elaborated. In line with the claims of Forsyth and Eifert (1996), the etiologies of specific avoidance behaviors must be accounted for in any model of anxiety. For agoraphobia, in particular, an account must be made for avoidance of situations previously unencountered or not previously directly associated with aversive experiences.

In the classical use of the concept "stimulus generalization", a response conditioned to a stimulus transfers to another stimulus. The degree of transfer varies directly along a gradient of stimulus similarity. A rather common clinical scene is the patient, who after initial panic attacks in their home, reporting fear of and starting to

avoid previously pleasant situations (like traveling, shopping etc.), where they have no actual experience of panic. On the other hand, the patient may report an increased sense of security at home and start spending almost all of their time in this place that has close proximity to the actual experience of panic attacks. This poses a challenge for explaining the principles of stimulus generalization.

To account for the generalization over a multitude of different situations, the concept of higher-order conditioning avoids the lack of accounting for every stimulus that has acquired aversive functions by making reference to the experience of a direct pairing of the UCS/UCR and the to-be-conditioned stimuli. However, a generally understood principle of higher order conditioning states that with the addition of each new neutral stimulus, a decrement in the established eliciting functions of the additional CSs can be expected (Forsyth & Eifert, 1996). This principle poses a central obstacle for explaining important aspects of stimulus generalization and the establishment of avoidance behavior in anxiety disorders.

Chambless and Goldstein (1978) proposed a mechanism of semantic generalization to account for a process that did not follow the obvious route. As mentioned, this theoretical position was criticized for being vague and speculative (Mathews et al., 1981). But raising the issue of verbal learning processes would perhaps not seem as far-fetched today. While biologically derived CNS responses can be considered to be at the core of anxiety problems, these responses require some negative verbal or symbolic evaluation in order to be called an emotion (Forsyth & Eifert, 1996). The concept “emotion” is by definition related to meaning and function. There are no special requirements about the form of a special system response to represent a particular emotional description or experience as fear (Forsyth, 1999).

One important function of language is that it can provide humans with emotional experiences without actual contact with the physical stimuli or events that ordinarily elicit those responses (Staats & Eifert, 1990). The directly established stimulus functions of words have shown the propensity to transfer to other words, symbols, and other events via higher order conditioning (Forsyth & Eifert, 1996). Another process of generalization inherent in language is described in the concept “stimulus equivalence”. It appears that once humans learn that certain members of a class of verbal and nonverbal events belong together (i.e., they are functionally equivalent), learning a new psychological function to one member of the class can result in that function transferring to all members of the class without direct pairings. This has been shown for several functional relationships, among them, respondent learning (Dougher, Augustsson, Markham, Greenway & Wulfert, 1994) as well as conditioned reinforcement and punishment (Greenway, Dougher & Wulfert, 1996). Augustsson and Dougher (1997) have experimentally demonstrated that the transfer of avoidance evoking functions can be established within stimulus equivalence classes by pairing an aversive experience with one event in that class.

Apart from serving as a means for generalizing stimulus functions, language also provides a distinction between feeling and behaving (Forsyth, 1999). This referential quality in the language of emotion also renders panic and anxiety as being perceived as reasonable causes of avoidance.

The centrality of avoidance

The tradition of the two-factor theory (Mowrer, 1947) that has been so influential on behavioral therapies does not only view anxiety disorders as involving learned aversive reactions. It also highlights behavioral predispositions for escape or avoidance as a key factor in the maintenance of anxiety disorders. In fact, as Forsyth (1999) asserts, it would be hard to imagine any of the anxiety disorders in the absence of humans reacting to their own responses or environmental events in an effort to control, reduce, eliminate, escape, or avoid them.

While there has been a failure to demonstrate in agoraphobic subjects that avoidance trials strengthen the avoidance behavior (Rachman et al., 1986), an intriguing line of research indicates that avoidance deserves far more attention than the status of a secondary phenomenon or complication. Craske, Miller, Rotunda and Barlow (1990) found that clients rated as “extensive avoiders” actually tended to develop more anxiety disorders over time than did “minimal avoiders”. No such differences were evident before the clients’ first panic episode. In addition, the more severely agoraphobic have been found to show generally more clinical distress (Brown et al., 1995). A pervasive tendency to avoid thus seems to be associated with more, rather than less distress.

This is indeed in line with the experimental research that has shown that attempts to avoid and control unwanted private events not only were largely ineffective, but have also been found to result in the occurrence of more, rather than less unwanted private events (Purdon, 1999; Cioffi & Holloway, 1993). Attempts to control anxiety in the face of ongoing stress have been shown to exacerbate physiological arousal (Wegner, 1994). Gross and Levenson (1997) found that instructions aimed at emotional suppression did result in the subjects showing less visible signs of displaying emotions during the task, but it was also associated with increased sympathetic activation.

With special interest for the field of panic disorder, Karekla, Forsyth and Kelly (2004) compared individuals, who were judged to have a high tendency to avoid emotions and thoughts, with those low in avoidance on a symptom provocation task by CO₂-inhalation. The more avoidant individuals endorsed more panic symptoms, more severe cognitive symptoms, more fear and perceived loss of control than those less avoidant. The magnitude of autonomic response did not, however, distinguish the two groups. They also found that avoidance co-varies, but was not synonymous with trait-anxiety.

When comparing the emotional responses to hyperventilation between normal controls, PD and PDA patients (the clinical groups) did not differ significantly regarding the levels of reported symptom intensity or fear during the task (Telch, Jaquin, Smits & Powers, 2003). The clinical and non-clinical subjects did differ in the expected direction. However, the duration with which the subjects persisted with the task did differ between the two clinical groups. The PDA patients persisted for a significantly shorter period. Thus, it was not the individual sensitivity per se that differentiated the two clinical groups, but rather their behavioral tolerance to these symptoms.

In an attempt to experimentally manipulate avoidance, Feldner, Zvolensky, Eifert and Spira (2003) compared subjects, who were instructed to inhibit the aversive emotional state induced by the inhalation of 20% CO₂-enriched air with those that were instructed simply to watch and try not to interfere with the reactions. They found that persons who were classified as high on “emotional avoidance”, compared to those classified as low, responded with greater anxiety and affective distress. Individuals high in emotional avoidance perceived less efficacy, in terms of their ability to regulate emotions, despite a similar capacity to follow experimental instructions. They also reported higher anxiety in the response-suppression condition, whereas those low in emotional avoidance reported that the efforts to suppress emotional responding resulted in a decrease in self-reported anxiety. One trial compared the effects of training individuals in accepting vs. controlling symptoms, when applying a CO₂-inhalation task (Eifert & Hefner, 2003). Compared to the control condition and no-instruction, the subjects trained to accept reported less intense fear and cognitive symptoms and fewer catastrophic thoughts during the task. These subjects also showed less avoidance regarding the task. Similar results were found in a study of patients with panic disorder (Levitt, Brown, Orsillo & Barlow, 2004). While symptom intensity during CO₂-inhalation did not differ between the two conditions, those instructed to suppress panic were more anxious and avoidant of the task.

3.5. Concluding remarks on learning theory

From a learning perspective, the core of panic disorder with agoraphobia is biologically derived CNS-responses. However, it is not the responses per se, but rather the subjective reaction to these responses that is the pathological feature (Bouton et al., 2001; Clark, 1988). This is an assertion that is well in line with the research reviewed above. But both experimental and clinical studies indicate that avoidance should not be treated as merely a consequence of anxiety-related pathology, but rather as a toxic strategy for emotion regulation that explains the shift from normal and adaptive experiences of anxiety and fear to ones that are disordered and maladaptive. Conditioned emotional responses may become problematic largely by the individual's effort not to have them. Thereby chronic and inflexible patterns of avoidance, which are insensitive to environmental circumstances, could be considered an important diathesis and risk factor for anxiety disorders. Moreover, these strategies can result in a limited ability to engage in effective and meaningful action, decreased contact with reinforcing consequences, and significant social and interpersonal suffering (Forsyth, 1999).

The essential role of avoidance in agoraphobia is also spelled out in the cognitive model (Salkovskis & Hackman, 1997), where agoraphobia is given the status of “motivated avoidance”. But, by explaining this motivation in terms of “threat beliefs”, it introduces mediational elements that are not subject to direct observation and manipulation, and thereby “...are at best inferences and at worst hypothetical constructs” (Forsyth & Eifert, 1996, p. 612).

As shown above, avoidance can be measured independently and manipulated for experimental purposes. It could be argued that this, in essence, is what is done in behavioral therapies.

4. Treatment of Agoraphobia

4.1. Background

The early days of behavior therapy

Meyer and Gelder (1963) asserted that “phobic symptoms appear to be particularly suitable for behavior therapy; they are seen commonly in the clinic, and they are difficult to treat by other means” (p. 19). This served as a rationale for their early approach to the treatment of agoraphobia. It was labeled “graded retraining”. The patients were taught to relax and then, accompanied by the therapist, exposed to increasingly fearful real life situations, while trying to maintain a relaxed state.

The idea that patients with phobic disorders should be encouraged to seek out the situations they feared and perform some sort of retraining was neither new nor unique to the emerging behavior therapy movement. Freud suggested that psychoanalysis should be modified for patients with phobic symptoms, and that they should be encouraged to return to the feared situations during the analysis (Mathews et al., 1981). After him several writers have recommended some form of retraining procedure as an adjunct to insight-oriented therapy. Terhune (1949) described an analytically oriented therapy, where patients, as a part of the therapeutic task, were encouraged to place themselves in the situations they feared, since the standard analytic techniques were considered insufficient. In this context, it is important to note the difference for the emerging behavior therapy movement; namely, there was a central conviction to use experimentally verified principles in clinically applied settings (Dougher & Hayes, 1999). Thus, regarding the retraining Meyer and Gelder stated: “Learning theorists hold that retraining, guided by modern learning theory, has far wider application than the earlier writers supposed” (1963, p. 27).

However, their treatment was extraordinarily time-consuming and the results disappointing, so their verdict on behavior therapy for agoraphobia was not optimistic. This conclusion was criticized by Eysenck (1965), partly because of the study design. His main criticism though was their favoring of the retraining method, and not systematic desensitization (Wolpe, 1958), which he considered a superior therapeutic technique. This comment has been regarded representative of the zeitgeist of that time; namely, the downgrading of the role of practicing real life situations and the favoring of less direct, imaginative methods (Mathews et al., 1981).

Wolpe himself made no assertions for his method to be particularly designed for treating agoraphobia. His classical book described therapeutic procedures derived from conditioning theory and experimental work on neurosis over a range of disorders. The two agoraphobic cases described in his book were actually examples of inclusions of other treatment techniques other than systematic desensitization. One case, treated by Wolpe himself, was a 23-year-old university graduate, presented as “Case 11: A Case of Social Inadequacy and Extreme Agoraphobia”. At their initial

contact the patient entirely refused to leave her home, and was reported to be "...practically bedridden, apart from very tense wall-hugging journeys between her bed and a couch in the drawing room" (p. 174). The case was presented under the headline of "reciprocal inhibition of anxiety by a dominating motor response" as an illustration of the therapeutic use of an experimental procedure to aid her in what is described as an extreme fear of the images of herself falling. Interestingly, Wolpe described his work as incorporating a rather wide clinical scope. Apart from a reciprocal inhibition technique for the image described, his treatment included working with her social anxieties, increasing her control of interpersonal situations and liberating herself from her parents, where especially the mother is described as unduly overprotective. Less than 4 years later few remaining, minor difficulties were reported and it was said, "...that she had never before been so happy. Therapy had then progressed with 185 sessions." (p. 179).

The first controlled prospective study of behavior therapy for agoraphobia was published by Gelder and Marks (1966). Twenty patients were randomly allocated to either behavior therapy or a control group. Therapy comprised of graded retraining together with systematic desensitization in imagination and training assertive responses (as also recommended by Wolpe). The overall results were disappointing and the conclusion was that behavior therapy was not recommended for agoraphobia as anything but in adjunct to general psychiatric management.

Eventually, when tried on an outpatient basis (Gelder, Marks, & Wolff, 1967; Marks, Gelder & Edwards, 1968) with different phobic disorders (among them agoraphobia), it was found that systematic desensitization carried out imaginatively with instructions to practice in reality between sessions was more effective than a variety of psychotherapeutic procedures. Hence, faith in the method was established. It should be noted that a cardinal feature of the method was that anxiety should be avoided whenever possible.

Flooding

Stampfl and Lewis (1967) launched a treatment that was supposed to be a learning-based, psychodynamic approach called "implosion therapy". This was radically different from the above-mentioned approach in that the patient was exposed to highly aversive, imagined scenes. These included not only phobic stimuli, but also material that was considered relevant from a psychodynamic point of view. When used without this dynamic overlay the method became known as "flooding". This treatment came to involve prolonged imaginal or in vivo exposure to highly aversive or anxiety-producing stimuli (Gelder et al., 1973). The mode of action was supposed to be that the anxiety responses to conditioned stimuli extinguished as a consequence of prolonged exposure to these stimuli in the absence of aversive consequences other than the anxiety itself. Secondly, avoidance or escape responses negatively reinforced in the past were prevented. Being within the realms of learning theory, it is a radical departure from Wolpe's desensitization hypothesis.

Flooding received preliminary support for agoraphobia in one study (Marks, Boulougouris & Marset, 1971), and seemed promising not only regarding the outcome, but also as being a far quicker approach than systematic desensitization. In

a later trial this difference only emerged in behavioral measures, but not for other outcome measures (Gelder, Bancroft, Gath, Johnston, Mathews & Shaw, 1973). However, later research seriously questioned any benefit of the imaginal component in comparison to the more direct in vivo approach (Mathews et al., 1976; Emmelkamp & Wessels, 1975).

Exposure in vivo

Another way of modifying agoraphobic behavior was ventured by Agras, Leitenberg and Barlow (1968). They experimented with using encouragement and verbal praise as social reinforcement. Agoraphobics were instructed to walk a course that led from the clinic to an increasingly busy downtown area, about a mile away. This was studied using an ABAB-design, where the intervention consisted of a discussion of the value of this exercise, along with verbal praise, that was administered contingent on the patients' success in walking further and further along this road. In this small study they noted that the patients, even in a short time of treatment, made remarkable efforts to pursue this task. The authors were convinced by the hypothesis that the therapeutic agent was praise and encouragement from a therapist. But, in fact, many of the patients started to improve at baseline, before the encouragement even was introduced and the slope of improvement was not substantially affected by the intervention. Later research experimentally disentangled the processes and indicated quite clearly that it was the opportunity to practice exposure tasks in a systematic way that was the critical ingredient (Leitenberg, Agras, Edwards, Thompson & Wincze, 1970). These findings coincided with a number of studies that emerged and showed the superiority of using real life situations in treating imagined situations (e.g., Mathews et al., 1976; Emmelkamp & Wessels, 1975).

By the early 1980s the efficacy for treatments based on exposure in vivo for agoraphobia could be considered fairly well established (Jansson & Öst, 1982; Mathews et al., 1981). A typical exposure in vivo treatment strongly encouraged the patient to approach feared situations in a graduated manner, and to remain in them until the experienced anxiety subsided. Unlike flooding and desensitization it was directed at real-life situations, and, unlike desensitization and graded retraining, there was no intention of keeping anxiety at a low level.

4.2. Treatment efficacy

The dominating treatment approaches for PDA have been pharmacological and exposure-based therapy, and several variations of them. Among psychological treatments various components have been added to the basic exposure principle during the later years, usually under the more general CBT label. Regarding the efficacy of various treatments for PDA, there are several meta-analyses available. However, the conclusions reached are not in unison.

Mattick et al. (1990) conducted a meta-analysis, where they calculated the pre-to post-effect sizes from 51 studies published between 1973 and 1988. Regarding pharmacological treatment they found support for high-potency benzodiazepines

and anti-depressives. Similar effect sizes between the two agents were found in phobia, panic and generalized anxiety, but a much larger effect in depression for anti-depressives. High-potency benzodiazepines were considered useful in the first line of intervention, but problems with dependency and withdrawal syndrome were noted.

Behavior therapies that did not include exposure (assertiveness training, cognitive therapy, or imaginal exposure) yielded effect sizes comparable to those of medication alone for phobia measures, but negligible effect sizes for panic measures. In contrast, the studies, which employed behavior therapies based on in vivo exposure, showed substantial effects on phobia measures, but more moderate effects on panic, depression and generalized anxiety. Those studies that used cognitive therapy in conjunction with exposure had smaller effects on phobia, but slightly better on the other variables. However, in these treatments, fewer hours were devoted to exposure. The authors noted that, while there was consensus on the fact that exposure is beneficial for phobic avoidance, it was disputed whether exposure therapy without drug therapy can reduce panic. The studies that included a combination of anti-depressives and exposure yielded better improvement in the phobia measures than drug treatment alone, but not superior to exposure alone. Only two out of twelve of the studies yielded superior results for the combination treatment. The authors argued that their data provided quite strong evidence that the effects on panic were by way of psychological treatments verified.

Cox, Endler, Lee and Swinson (1992) conducted a meta-analysis of treatment studies published during the eighties. Studies were included if they focused on panic disorder with/without agoraphobia (or agoraphobia with panic attacks, if DSM-III nomenclature was used), and treatment with alprazolam, imipramine, in vivo exposure, or placebo. The most consistent strong effects on the variety of dependent variables considered were found for exposure treatment. Alprazolam showed significant effects on most of the dependent variables, but not depression. Imipramine showed the least number of significant effects, and was also associated with the highest mean dropout rate.

A meta-analysis of 43 controlled studies of panic disorder, which included 76 treatment interventions, was published by Gould, Otto and Pollack (1995). They were concerned with long-term, as well as short-term change. Effect sizes for overall improvement and change in panic frequency were calculated. The percentage of subjects reaching a panic-free end-state was also used as an outcome variable. Only studies with a control condition were included and the effect sizes were calculated between control- and active treatments. A serious limitation for the present purpose is that their material did not allow for a more thorough analysis of the impact of agoraphobia due to the lack of a more precise estimate of the degree of agoraphobic avoidance. The authors noted that a majority of the studies had a proportion of subjects (+ 75%) that were reported to be agoraphobic.

Support was found for the efficacy of high-potency benzodiazepines and anti-depressives in comparison with the placebo. A non-significant advantage for the latter over the former was detected. However, when eliminating studies that included auxiliary components (e.g., psychotherapy), and considering that treatment with anti-depressives tended to have higher dropout rates (25.4%) than

benzodiazepine-treatment (13.1%), the picture of equivalent results was strengthened.

The mean overall treatment effect for cognitive-behavioral interventions was significantly different from zero. Likewise, a significant, but slightly lower effect size was achieved, when panic frequency was considered as a separate outcome. A panic-free rate of 74.3% was observed, which was compared to the control group, where 27.1% were panic-free. The mean dropout rates were modest (5.6%). Among the CBT-studies, those involving a combination of interoceptive exposure and cognitive restructuring were associated with the largest effect sizes. The few studies explicitly addressing the effectiveness of cognitive re-structuring showed quite mixed effect sizes, and thereby not inviting any substantive interpretation. When comparing the mean effect sizes between the CBT-studies to those of pharmacological treatment, there was a non-significant advantage for CBT regarding panic frequency. Considering the percentage of panic-free subjects, this difference was significant. The combination of medication and exposure did not yield effect sizes that were significantly different from those achieved by medication alone. Furthermore, dropout rates, in the combined treatment, were at the same level as in the pure pharmacological conditions. In the long-term outcome, the greatest deteriorations were noted in the pharmacological studies, while the results of CBT and combined treatment were well maintained.

Now, when interpreting the results of Gould et al. (1995), it is crucial to take into consideration that the pill-placebo, customarily used in pharmacological studies, is a potentially stronger control group than the waiting-list control commonly used in psychotherapy studies. As acknowledged by the authors, this may contribute to larger effect sizes in the latter.

The largest meta-analysis identified was conducted by Van Balkom et al. (1997). They surveyed 106 studies, published between 1964 and 1995, pertaining to 222 treatment conditions for panic disorder with or without agoraphobia. The studies surveyed contained treatment with high-potency benzodiazepines, anti-depressives, psychological panic management, exposure in vivo and different combinations of those treatments. The outcome was considered for panic, agoraphobia, depression and anxiety. Since most studies did not have control conditions, the effect sizes were calculated from pre- to post-treatment. The authors also limited their analysis to completers only, since intent-to-treat data was not provided in the vast majority of the studies. Mean effect sizes were also calculated for control conditions.

They found support for a treatment effect in all of the compared treatments of panic disorder. Anti-depressives, panic management, exposure in vivo in combination with antidepressants were superior to the control over all four clinical outcome variables. High-potency benzodiazepines were not found to be effective against depression and pure exposure in vivo was not effective in treating panic attacks. For ameliorating agoraphobia, high-potency benzodiazepines and panic management were equally effective as exposure, but the combination of exposure and anti-depressives yielded superior results. The combination of panic management and exposure was not superior to exposure alone.

Their general conclusion was that, in the short-term, the combination of anti-depressives with exposure in vivo should be the treatment of choice for PDA. The

authors did not consider attrition rates. Dropout in these combined treatments was at the same level as in treatment with anti-depressives only. This attrition rate was considerably higher than for the benzodiazepines or psychological treatments.

An analysis of the long-term outcome of treatment, reviewing 68 studies, was published the year after (Bakker, van Balkom, Spinhoven, Blaauw & van Dyck, 1998). The mean duration of follow-up was 89 weeks, ranging from four weeks to eight years. Generally, the results were found to be well maintained at follow-up, but the authors noted the lack of information regarding whether or not the medication was continued during follow-up. They concluded that the superiority of the combination of anti-depressives and exposure found in the earlier study was confirmed at follow-up. Regarding pharmacological treatment for panic disorder, several authors have highlighted the problem with relapse and attrition (Mavissakalian & Perel, 1992; Noyes, Garvey, Cook & Suelzer, 1991). Relapse rates ranged from 54% to over 70% after the discontinuation of either anti-depressives or benzodiazepines.

Regarding attrition, psychological treatment has not been found to be less tolerable, though personally demanding for patients (Otto, Pollack & Maki, 2000). They found that, in general, CBT for panic disorder was widely acceptable and usually yielded small dropout rates (on average 5.6%), while pharmacotherapy received a substantially greater rate (19.8%).

A cautious attempt to summarize the studies above indicates that strong support has been found for exposure in vivo and treatments that occur under the more general CBT-label. Pharmacological treatment has proven effective, but problems arise regarding dropout and relapse. Regarding the alleged superiority of the combination of exposure in vivo and pharmacological treatment, the results are conflicting; especially considering that attrition rates in the combined treatment have been found to be at the same level as pharmacological treatment only. Combined treatments appear equally well maintained as pure psychological treatment, while considerable relapse rates have been reported after the discontinuation of pure pharmacological treatment conditions.

4.3. Methodological variation

While the efficacy of cognitive behavioral treatments for panic disorder is well supported and exposure in vivo can be considered the psychological treatment-of-choice for agoraphobic avoidance, the optimal mode of delivery is still an open question. There are three basic routes taken when trying to elaborate this question: using different variations regarding therapist contact; involving significant others and social support, and using additional therapeutic strategies to enhance the treatment outcome. This makes it possible for several variations of the common theme of exposure in vivo.

Mode of delivery

When considering the mode of delivery, it is not only a question of efficacy, but also the possibility of economizing treatments by minimizing the amount of therapist contact. Self-directed exposure has been used extensively for agoraphobia

and shown to be equally effective, regardless whether a therapist gave the instructions from a book or a computer (Ghosh & Marks, 1987). Exposure administered by telephone instructions was reported to produce gains comparable to those of more traditional modes of delivery (Swinson, Fergus, Cox & Wickwire, 1995). However, when Gould and Clum (1995) found support for the effectiveness of a self-help program combined with minimal therapist contact, as compared to a waiting-list, the pre- to post-effect sizes for agoraphobic avoidance were far below those expected for conventional behavioral treatments (e.g., Mattick et al., 1990). Likewise, while Lidren et al. (1994) found bibliotherapy equally efficacious as group therapy on a number of self-rated measures, the treatments were not equally effective regarding agoraphobic avoidance, where group therapy was superior. In the treatment of more severely agoraphobic patients, the utility of self-help manuals has been questioned after having been found ineffective when tried in a series of case-studies (Holden, O'Brien, Barlow, Stetson & Infantino, 1983). Standard CBT for panic disorder with or without agoraphobia has been found superior to a minimal therapist-contact condition and bibliotherapy, with bibliotherapy yielding the poorest results (Power, Sharp, Swanson & Simpson, 2000). On the other hand, in a comparison between 10 sessions of standard CBT to 5 sessions, supported by a self-help program (Botella & Garcia-Palacios, 1999), the standard treatment did show some advantage at post-treatment, but the two conditions proved equally effective at follow-up. Lately, Internet-based treatment has shown promise in treating panic disorder (Carlbring, Ekselius & Andersson, 2003; Carlbring et al., in press). Thus, while the support is not unequivocal, it generally favors the usefulness of self-help programs, especially if they have an interactive component.

Regarding the spacing and intensity of treatment, convention has generally favored spaced and graded exposure due to the findings that intense exposure was associated with higher attrition (Emmelkamp & Wessels, 1975) and greater relapse (Jansson & Öst, 1982). Later studies have not confirmed this picture of the detrimental effects (Chambless, 1990; Hahlweg, Fiegenbaum, Frank, Schroeder & von Witzleben, 2001). In fact, intense treatment of panic disorder with moderate to severe agoraphobia was regarded by Barlow (2002) to hold special promise for the future. But, in general, the question of the optimal mode of delivery must be considered far from settled.

Involving social support and significant others

Another line of research has been mainly interested in the beneficial effects of additional interventions in the social environment. Fostering social cohesion in group-based exposure in vivo has been found to be associated with further improvement and less relapse at follow-up (Hand, Lamontagne & Marks, 1974). Support for the beneficial effects of social cohesion was also provided, when studying the formation of neighborhood self-help groups in the treatment of agoraphobia (Sinnott, Jones, Scott-Fordham & Woodward, 1981). The patients treated in neighborhood groups reported less anxiety when approaching phobic situations and more frequent homework completion, as compared to patients treated in groups, where the participants came from geographically diverse areas.

The marriages of agoraphobics have been put forth as a possible obstacle for improvement (Hafner, 1977). Assumptions like this have provided a rationale for directing specific interventions in a couple's relationship. Involving the spouses in group treatment has been found advantageous, compared to not involving them (Jones, Sinnott & Fordham, 1980; Barlow, O'Brien & Last, 1984). In the Barlow et al. study, the group that included spouses did not only perform better on measures of agoraphobia, but also on social-, work-, and family ratings. Likewise, communication training of couples has been found to add beneficial effects to several outcome variables, both at post-test and follow up, when added to exposure (Arnow, Taylor, Agras & Telch, 1985). However, other studies have failed to find beneficial effects of involving the spouse as a co-therapist (Cobb, Mathews, Childs-Clarke & Blowers, 1984; Emmelkamp et al., 1992). Cobb et al. also noted that the marriages of those with some marital difficulties tended to improve whether or not the spouse was involved in therapy. In general though, independent support is provided for the beneficial effects of the involvement of social support and significant others.

Additional treatment strategies

The addition of components, auxiliary to in vivo exposure, has almost been the rule, rather than the exception. The rationale has often been in addressing a broader symptom profile than mere avoidance behavior or that specific strategies should target specific symptoms in this syndrome. The results achieved are somewhat conflicting.

Assertiveness training

Apart from the clinical notion of more prevalent marital difficulties among agoraphobics, these patients are often described as displaying dependency and low assertiveness (Goldstein & Chambless, 1978). This has provided a rationale for augmenting exposure treatment with assertiveness training. Emmelkamp, van der Hout and de Vries (1983) found that, while exposure in vivo was superior regarding phobic measures, assertiveness training produced greater gains in assertiveness than exposure. In a small study (Thorpe, Freedman & Lazar, 1985) exposure produced changes in several outcome variables, whereas assertiveness training only produced transient change in an inventory for assertiveness. These studies indicated that the result of assertiveness training was specific, rather than having an impact on the broader field of agoraphobia.

Relaxation

Michelson (1986) compared the addition of therapist-assisted graded exposure, paradoxical intention and deep muscle relaxation to instructions for self-directed exposure in vivo. While this study did not provide explicit support for adding relaxation per se, it provided some support for the hypothesis that a treatment that was consonant with the patients' dominant pre-treatment symptoms (behavioral, cognitive or physiological) yielded better results. This interaction was not replicated in a study by Öst, Jerremalm and Jansson (1984), and equal efficacy was found for 12 sessions of the physiologically focused method, applied relaxation

and exposure in vivo. A later study (Öst, Westling & Hellström, 1993) compared exposure in vivo, applied relaxation and cognitive therapy for PDA. All treatments contained instructions for self-exposure and yielded significant improvement, which was well maintained at follow-up.

Cognitive therapy

Cognitive therapeutic strategies have become commonplace in the psychological treatment of PDA. Initially, the rationale for including these techniques was often an alleged general beneficial effect. This has, however, more and more been replaced by the specific assertion that the efficacy of cognitive therapy for panic attacks (Clark 1988) could be expected to have a bolstering effect on the treatment of PDA. The rationale for this was obvious in models, where agoraphobic avoidance is considered to be a secondary phenomenon to these attacks.

The early studies failed to provide any support for self-instructional training, rational emotive therapy or cognitive coping techniques, when added to the basic exposure in vivo (Emmelkamp, Brilman, Kuiper & Mersch, 1986; Williams & Rappaport, 1983). In one study, cognitive therapy yielded better results for measuring assertiveness, but was otherwise not superior to plain exposure (Emmelkamp & Mersch, 1983). These earlier studies, however, are, by today's standards, considered to have used rather crude variants of cognitive therapeutic strategies. In the following studies, the cognitive therapeutic strategies used were more closely allied to treatment directly focused on panic attacks (Clark, 1988). These studies will be reviewed somewhat more in detail, since they have special relevance to study I.

The idea of differential effects of cognitive therapy and exposure received some support in a study by van den Hout, Arntz and Hoekstra (1994). They compared two groups of subjects. One group received 4 sessions of cognitive therapy for panic disorder followed by 8 sessions, where this was combined with exposure. The other group received 4 sessions of a non-specific associative therapy followed by 8 sessions of exposure in vivo. They found that the cognitive therapy reduced panic attacks significantly, but did not reduce agoraphobia. Exposure, on the other hand, reduced agoraphobia, but not panic. When comparing cognitive therapy with guided mastery therapy (a variant of exposure in vivo) in an intensive in-patient format for patients with agoraphobic avoidance at the more severe end of the spectrum, some advantages were found for the cognitive variety (Hoffart, 1995). However, as other ward activities were included in the treatment as well, the generality of this study is somewhat hampered.

Williams and Falbo (1996) compared 8 sessions of cognitive therapy, guided mastery therapy, or the combination of both. The results showed that all treatments led to significant improvements, but on 3 out of 9 measures guided mastery therapy evidenced larger change scores than cognitive therapy. The combination showed no advantages to guided mastery alone. This study has a weakness in that it does not contain any comprehensive assessment of agoraphobic avoidance, but it contradicts the conclusion drawn by Van den Hout et al. (1994) concerning the alleged inefficacy

of exposure in vivo regarding panic attacks. Clear improvement in this outcome variable was noted in both conditions.

Bouchard et al. (1995) compared cognitive therapy to exposure in vivo plus interoceptive exposure. Treatment was provided in small groups for 15 sessions, and had an interesting feature in that the cognitive variety contained explicit recommendations as opposed to the repetition or prolongation of any exposure exercises. Instead, the recall of logical disputation was encouraged. The authors' conclusion was that the two conditions did equally well on the individual measures and operated at the same pace. However, high end-state functioning, at post-test, was achieved by 86% of the exposure patients, as opposed to 64% of the CT-patients. High end-state functioning was defined as the presence of 3 out of 6 criteria, which included 0 panic attacks in 6 weeks; a score of panic apprehension less than 20%; or scoring in the normal range on any of the 4 different self-rating scales. These criteria included no measurement of agoraphobic avoidance, where exposure in vivo condition was significantly superior. Further, at follow-up, panic-free status was observed in 71% of the exposure in vivo condition, as compared to 43% of the cognitive therapy condition. The conclusion of treatment equality made in this study deserves further attention. This will be addressed further in the general discussion.

Michelson, Marchione, Greenwald, Testa & Marchione (1996) compared graded exposure alone and in combination with cognitive therapy or relaxation training delivered in small groups during 16 sessions that lasted for 3 hours. For most measures, there were no differences between the three conditions. However, at post-treatment, the cognitive condition outperformed the other conditions in 5 out of 19 measures. Likewise, regarding the proportion of patients that were classified as high end-state functioning at post-treatment and at follow-up, the cognitive condition was superior. High end-state functioning was defined as scoring a pre-determined non-clinical range on, at least, 4 out of 5 areas (panic, global assessment of severity, self-rated severity, phobic avoidance, or behavioral avoidance).

In a study of female agoraphobics, Burke et al. (1997) compared individually administered exposure in vivo (10 two-hour sessions) or CBT (10 three-hour sessions), where the amount of in vivo exposure between the two conditions was kept constant. The effects were equal for the two groups, except for the behavioral approach test, where the CBT-group completed more stages. Overall though, no clear advantage was demonstrated by adding cognitive techniques to exposure.

Breathing retraining and interoceptive exposure

The role of hyperventilation responses have been discussed both in terms of a possible etiological role and as a basis for viable treatment interventions in panic disorder (Barlow, 2002). In treatment, breathing exercises have been put forth both as a means of attempting to control anxiety and as way of exposure.

In an early study, Bonn, Readhead and Timmons (1984) noted a better long-term response in agoraphobic patients pre-treated with breathing retraining before exposure. Training in slow diaphragmatic breathing, as a coping technique, has become rather a standard feature of different psychological treatment packages. The empirical basis for this seems questionable, since repeated studies have failed to show any support for the beneficial effects of adding breathing retraining to

exposure in vivo (de Ruiter, Rijken, Garssen & Kraaimat, 1989; de Beurs, van Balkom, Lange, Koele & van Dyck, 1995). When breathing retraining was added to a standard package of CBT for panic disorder with or without agoraphobia, it did not add any clear benefits in comparison to the standard package (Schmidt et al., 2000). The results from this study even gave some suggestion that breathing retraining might have led to a less complete recovery and a greater risk of relapse. However, the major impression was generally more in line with the treatment equivalence between the conditions. Craske, Rowe, Lewin and Noriega-Dimitri (1997) compared breathing retraining to interoceptive exposure, which might be considered a theoretically opposite position, as additional components to standard CBT for panic disorder with agoraphobia. Treatments were equal for many measures, but exposure was better for panic frequency and general severity. The advantages of interoceptive exposure were even more pronounced at six-month follow-up. The addition of exposure to both internal and external cues did seem to increase the tendency for more improvement than exposure to external cues only in another study (Ito, Noshirvani, Başoğlu & Marks, 1996). Since this was a small study, it did not have the power required for statistical significance. A trend favoring panic provocation within CBT for agoraphobia was also observed by Page (1994). However, a later study (Ito et al., 2001) failed to support this notion, when comparing self-exposure to external interoceptive or a combination of both cues. The different treatments showed equivalent benefits.

Miscellaneous

Other ideas have included the addition of hypnosis to exposure in vivo in the treatment of PDA (Van Dyck & Spinhoven, 1997), but no additional effect was shown. Goldstein, de Beurs, Chambless and Wilson (2000) tried EMDR (Eye-Movement Desensitization and Reprocessing Therapy) for patients diagnosed with panic disorder and moderate to severe agoraphobia, in comparison to waiting list control or a credible psychological attention-placebo. Although EMDR was significantly better than the waiting-list on some measures, its difference between attention-placebo was not significant on any measure. The generally miniscule effect sizes in comparison to placebo rule out that this was only to be attributed to low power. It should be noted that this study did not contain any regular exposure condition.

Summary of additional treatment strategies

To summarize the research surveyed above, little benefit seems to have been gained by adding additional strategies to the basic exposure treatment. This has been the case for assertiveness training, relaxation and breathing retraining, to mention some strategies commonly encountered. Regarding the addition of cognitive therapy, the picture is more unclear, with some studies showing benefits, while, in others, the results have been either the same or even inferior to exposure treatment. Independent favorable reports can be found for interoceptive exposure, which basically can be considered a variant of the basic exposure paradigm. They are, however, not all in unison.

5. Determinants of Change

5.1. Prediction of outcome

The assertion that the ability to predict the outcome at pre-treatment should have a crucial value is generally common in clinical psychology. In agoraphobia treatment, this search for predictors has been stated as a quest aimed at either the ability to better adopt the treatment models for patients with comorbid conditions (Chambless, Renneberg, Gracely, Goldstein & Fydrich, 2000), or being able to reduce dropouts and treatment failures (Keijsers, Hoogduin & Schaap, 1994). It has been suggested as a way of supplying the clinician with information for designing more effective treatment, and planning treatment optimally for the individual patient (Hafner & Ross, 1983). Or, as aptly put by Sharp and Powers (1999): “Armed with such information the clinician might be more able to fine-tune treatments according to the requirements of the individual patients” (p. 336). These important and lofty goals stand in rather sharp contrast to the meager and inconclusive results that have been gained from prediction studies in this regard for the treatment of agoraphobia.

Overview

Steketee and Shapiro (1995) made an extensive review of studies regarding the prediction of the outcome for the behavioral treatment of PDA. The variables were grouped into four general categories: client characteristics, aspects of the disorder, personality traits and disorders, and family factors.

Client characteristics and demographic variables like age, gender and marital status have not proven predictive in most studies. Of the aspects of the disorder, severity of symptoms, or, more specifically, the severity of avoidance, was the most extensively studied and verified (5 studies identified). However, an equal number of studies failed to find such an association. The overall level of functioning (work, social, family, leisure) was not predictive of outcome, but some indication was found that for the long-term results, it might have some predictive utility. The duration has given inconsistent results at post-test, but was found uniformly unrelated at follow-up. Depression has also been extensively studied with mixed results, and most studies failed to find it predictive, especially the methodologically more sound ones. Regarding anxiety, no association was found between trait anxiety and the outcome in two studies, but one did at post-test, and one at follow-up. Steketee and Shapiro concluded that limited information about the impact of comorbid anxiety disorders were available, apart from the finding that a comorbid diagnosis of generalized anxiety disorder was found unrelated. Regarding personality traits and disorders, they concluded that the impact of Axis-II diagnoses was understudied, but that, in general, avoidant personality disorder and others within the anxious cluster seemed to be associated with less beneficial results. They identified four studies that indicated an incremental impact at post-treatment, but there were no studies to confirm this effect at long-term follow-up. The authors noted that marital quality has been heavily debated, but that research did not endorse the general view that marital quality was associated with an immediate treatment outcome for agoraphobics.

However, at long-term follow-up, some studies have found that improvement and dropout indeed were related to marital quality.

The general picture from the Steketee and Shapiro review was that, despite conflicting results for most variables, the vast majority of variables were not consistently associated with the outcome. Two predictors of less beneficial results stood out: severe avoidance behavior and anxious cluster personality disorder. While several studies did not distinguish between PD and PDA, no attempt to find separate predictors was made.

The general picture was quite similar when reviewing the prediction of the outcome for the pharmacological treatment of panic disorder (Slaap & den Boer, 2001). Severity of phobic avoidance appeared to be one of the most robust predictors of non-response, particularly in long-term studies. This was almost uniformly reported. Most studies investigating the role of personality disorders have reported a negative impact on outcome and this irrespective of the cluster or specific axis-II diagnosis. The authors noted that a longer duration, while not predictive of the short-term outcome, did show up in a majority of the long-term studies (along with comorbid anxiety diagnosis and comorbid depression). The authors also stated that socio-economic class, while not widely studied, may be the best demographic predictor. Three long-term studies found that lower socioeconomic class predicted a non-response.

Criticism of prediction studies

The Steketee and Shapiro review used a liberal inclusion of studies and comprised studies with no limitation due to quality. Their explicit intention was to identify predictors that were consistently associated with the outcome over several studies. The prediction literature has been criticized for several methodological weaknesses (Keijsers, Hoogduin & Schaap, 1994; Sharp & Power, 1999). Among the methodological flaws noted are: some studies use simple between-group designs, where patients were defined as successes or failures according to criteria applied to post-treatment response, with *post hoc* comparisons between these two groups made for a variety of pre-treatment measures. Other studies have employed multiple bivariate correlations between pairings of pre- and post-treatment variables or separate individual regression analyses, thereby not controlling the inter-correlation between predictors. Another common flaw has been performing regression analyses with small sample sizes employed to support too many variables, thus increasing the risk of sample-bound, non-replicable findings. Studies have been criticized for choosing too narrow dependent variables. Another line of criticism is the clinical meaningfulness of prediction studies. Sharp and Power (1999) stated that, while regression techniques are suitable for identifying relationships between predictor variables and outcome variables, they can give no indication of whether these relationships have any real clinical significance.

The later studies

Aspects of the disorder

Some of the later studies are worth looking at a little more thoroughly, since they have generally used methodologically sounder approaches, and have special relevance to study II. However, they do not escape criticism (Dressen & Arntz, 1997; Sharp & Power, 1999).

Keijsers et al. (1994) investigated the prognostic utility of several pre-treatment variables in 60 patients receiving behavioral treatment for panic disorder (where the majority of patients also were agoraphobic). Of these variables, severity of avoidance, depression, motivation, personality pathology and catastrophic cognitions were predictive of the outcome. The quality of the therapeutic relationship and marital dissatisfaction did not predict the outcome. In a study of 144 PDA-patients, treated with alprazolam vs. placebo, and exposure vs. relaxation in combination (Basoglu et al., 1994), duration and severity were found to be negatively related to the immediate outcome as well as maintaining treatment gains at follow-up. Neither self-rated anxiety nor the level of depression at pre-treatment were related to outcome, although a history of depression along with old age were found to be the negative predictors at follow-up.

Sharp and Power (1999) studied a sample of 149 patients, whose panic disorders were with and without agoraphobia. They underwent 12 weeks of treatment with fluvoxamine, placebo and CBT, alone or in combination. They studied a variety of predictors like demographic variables, personality and social variables, panic attacks, and other complaint-related variables. Underscoring the clinical utility of the prediction task, they dichotomized subjects whether or not they had reached the criteria for a clinically significant improvement (CSI; Jacobson & Truax, 1991) in four variables: anxiety, panic attacks, agoraphobic avoidance, and a composite. In these respective outcome variables, lower levels of self-rated symptoms, and higher levels of extroversion at pre-treatment predicted a greater likelihood of CSI for anxiety. Lower frequency of panic episodes and lower levels of self-rated symptoms at pre-treatment predicted a greater likelihood of achieving CSI for self-rated symptoms. Less pre-treatment severity of avoidance predicted a greater likelihood of achieving CSI for agoraphobic avoidance. For the composite measure, higher panic frequency, self-rated symptom intensity and social maladjustment predicted a greater likelihood of achieving CSI for post-treatment. At six-month follow-up, the prediction capacity was reduced compared to end-point, but similar predictors were noted for panic frequency and avoidance, as at end point. Regarding anxiety, they found that initial therapist rated depression predicted a lower likelihood of achieving CSI at follow-up. A lower likelihood of achieving CSI for the composite at follow-up was predicted by social maladjustment.

The finding that social maladjustment might have an adverse effect on the treatment response has received additional support (Wade et al., 1993). In a group highly symptomatic at pre-treatment, subjects, who reported chronic stressors of marked to moderate severity, evidenced significantly less improvement, irrespective of the type of stressor, and a greater likelihood of showing moderate to severe symptoms at post-treatment.

Comorbidity

The impact of additional axis I or II diagnoses was studied using 51 patients with PDA or AWOPD, who underwent a 2-week intensive outpatient treatment program (Chambless, Renneberg, Gracely, Goldstein & Fydrich, 2000). In contrast to the findings of Basoglu et al. (1994), concomitant mood disorder did seem to have an impact on outcome. Comorbidity for dysthymic disorder was associated with less of an improvement in the panic frequency at post-treatment, and comorbid major depression was associated with less of an improvement in a behavioral approach test at follow-up. In a trial of 22 sessions of behavior therapy for obsessive-compulsive disorder and PDA, major depression was found predictive of poorer results both at post-test and follow-up (Steketee, Chambless & Tran, 2001). A comorbid diagnosis of GAD was associated with a smaller treatment gain regarding target fear at 6-month follow-up. Hoffart and Martinsen (1993), on the other hand, reported that a comorbid diagnosis of depression was associated with a greater improvement from post-treatment to follow-up.

Personality pathology has been of special interest in the treatment of agoraphobia. Mavissakallian and Hamann (1987) found that patients, who scored higher on pathological personality traits, were less likely to be classified as responders after combined pharmacological and behavioral treatments. Avoidant personality disorder is the axis-II disorder most frequently reported in agoraphobic samples (Chambless et al., 2000) and it is also the one that has attracted the most research in this line of research. Patients with a comorbid diagnosis of avoidant personality disorder have been found to improve less on agoraphobic avoidance, social phobia and depression after treatment (Chambless et al., 1992), or show detrimental progress during follow-up (Hoffart & Martinsen, 1993).

Dressen and Arntz (1998), on the other hand, caution against relating personality disorders to inferior treatment outcome in Axis I disorders, partly due to the methodological flaws of many studies. They reviewed the literature using a best-evidence procedure, where the selection criteria were that the study had a prospective design using a self-report questionnaire or an interview appropriate for diagnosing axis-II disorders. Only half of the identified studies of the impacts of axis-II comorbidity on the treatment of panic disorder met these criteria. Their conclusion was that, in general, it could not be concluded that personality disorders negatively affect the treatment outcome of anxiety disorders.

The complexity of this picture is further emphasized by the finding that comorbid axis-II pathology was associated with deleterious effects at post-treatment, but not at follow-up (Steketee et al., 2001). Furthermore, in the treatment of agoraphobia, a concurrent diagnosis of avoidant personality disorder was found predictive of less reduction in panic attacks at follow-up, but no impact on agoraphobic avoidance was found (Chambless et al., 2000). It should also be noted that the scores reflecting personality pathology themselves have been found positively influenced by treatment not specifically designed to address this issue (Mavissakallian & Hamann, 1987).

Dropout

Dropouts are one of the more serious problems in psychotherapy practice (Keijsers, Kampman & Hoogduin, 2001). The ability to predict and address dropout in therapy could be considered just as important as the non-response issue.

Findings have been contradictory regarding the relationship between dropout and symptom severity in panic disorder. An increased risk of dropout has been found associated with milder symptom severity (Barlow, Craske, Cerny & Klosko, 1989; Emmelkamp & van der Hout, 1983), higher symptom severity (Grilo et al., 1998), or not significantly associated with symptom severity at all (Burke, Drummond & Johnston, 1997, Keijsers et al., 2001). The findings regarding comorbidity and dropout are likewise inconclusive. Depressive symptoms were found indicative of the risk of higher dropout in one study (Burke et al., 1997), but not in others (Grilo et al., 1998; Keijsers et al., 2001). Personality pathology has failed to predict dropout (Grilo et al., 1998; Keijsers et al., 2001), whereas, in one study, a comorbid diagnosis of GAD was associated with a risk of higher dropout (Steketee et al., 2001).

On the other hand, lower socio-economic status, household income and lower levels of education represent a group of predictors fairly consistently associated with the risk of higher dropout in the treatment of panic disorder (Grilo et al., 1998; Keijsers et al., 2001), even though contradictory findings have been reported (Carter, Turovsky, Sbrocco, Meadows & Barlow, 1995). Likewise, lower motivation for treatment has also been found to predict dropout (Grilo et al., 1998; Keijsers et al., 2001).

5.2. Process-related determinants of change

Compliance and homework

Incorporating homework-assignments into therapy is a distinctive feature of cognitive-behavioral therapies (Blagys & Hilsenroth, 2002). Generally, the literature supports a position that stresses the importance of this. Michelson, Mavissakalian, Dancu and Greenwald (1986) found a strong relationship between end-state functioning and the number of self-directed exposures between sessions. A study of the group-treatment of moderate to severe agoraphobia did not confirm that a greater success would be achieved by more between-session practice (Barlow, O'Brien & Last, 1984). However, this is a study carried out with limited statistical power, and yielded a non-significant correlation of $r = .36$.

Edelman and Chambless (1993) found in agoraphobic patients, treated with exposure and anxiety management techniques, that those, who were more compliant with the application of these techniques, showed greater improvement in a behavioral approach test, but not in other outcome variables. Furthermore, clients, who spent more time doing self-directed exposure, reported larger changes in the decrement of fear and the self-report of avoidance behavior. However, when doing a quasi-experimental comparison of homework and non-homework conditions in therapy, no differences were obtained. It was also noted that the degree of compliance was negatively related to the pre-treatment levels of symptoms. The

relation to pre-treatment symptoms parallels the findings from CBT for depression that compliance with homework was related to outcome as well as premature termination (Persons, Burns & Perloff, 1988). This effect was especially pronounced in those patients that showed high pre-treatment levels of depression.

An indication of a more complex relationship between compliance and outcome came from a study of CBT protocol for panic disorder with and without agoraphobia (Schmidt & Woolaway-Bickel, 2000). Patients' estimates of compliance were not significantly associated with most outcome measures. However, therapist ratings of compliance significantly predicted positive changes in most outcome measures. And, most notably, the estimates by the therapist and the independent assessor of the quality, relative to the quantity of the work, were better predictors.

Expectancy and motivation

Steketee and Shapiro (1995) noted that treatment motivation, as a predictor in exposure treatments, was not largely studied. In an early study of behavioral treatment of agoraphobia (Mathews et al., 1976), the factors to predict outcome were emotional stability and expectancy of performance ($r = .34$). Southworth and Kirsch (1988) made an experimental comparison of two exposure conditions, where expectancy was manipulated. Although subjects in the low-expectancy group reported an equal improvement regarding experienced anxiety, the subjects in the high expectancy group made a better improvement regarding avoidance behavior. Other studies have failed to find a relationship between expectancy and outcome (Basoglu et al., 1994), or that treatment preference should be a powerful mediator of treatment effect (Van Dyck & Spinhoven, 1997). Keijsers and co-workers (1994) did find that motivation, as measured by the "willingness to participate" factor of the Niemegen Motivation List, significantly predicted the outcome for the behavioral treatment of PDA. In general though, research on motivation is scarce in this area.

The therapeutic relationship

"Those who wish to make use of learning theory to treat their patients should not ignore the relationship between the patient and the therapist. The two ideas are not incompatible."

(Meyer & Gelder, 1963, p. 27)

When drawing up the guidelines for how to conduct this new behavior therapy with agoraphobic patients, Meyer and Gelder assumed that the relationship with the client would be a critical factor for success: "Feelings which the therapist forms in the relation to the patients influence the course of treatment just as the counter-transference does in psychotherapy." (p. 26). In fact, the early work, which laid the ground for exposure in vivo treatment, focused specifically on the socially reinforcing properties of the therapist (Agras et al., 1968). But it would be uncontroversial to say that the further development has traditionally focused more on elaborating the technical aspects of exposure treatment, than the relational ones.

The argument for behavioral therapies has often been made in opposition to those stressing the relational aspects as curative factors per se.

Therapeutic style in behavioral therapies

The image of the behavior therapist as a technical expert with little skill or interest in managing the therapeutic relationship is not confirmed by the available empirical research. Early studies of the therapeutic style of proponents of different schools in psychotherapy revealed that outside observers rated behaviorally oriented therapists as displaying significantly higher levels of empathy, genuineness and interpersonal contact than psychoanalytically oriented therapists, and rated them equally regarding warmth (Sloane, Staples, Cristol, Yorkston & Whipple, 1975). Behavior therapists were found to use more supportive communication such as reassurance, praise, and sympathy than psychoanalytic therapists (Brunink & Schroeder, 1979). While clearly differential verbal behavioral styles were found between cognitive-behavioral and insight-oriented therapists, acknowledgement (i.e., active listening) was the most frequent therapist behavior mode, and occurred at about the same rate in both conditions (38% vs. 40% of all responses; Stiles, Shapiro & Firth-Cozens, 1988).

Furthermore, early data tended to indicate that the elements that were appreciated by the patients were not merely the technical skills of the therapist. In one study of flooding and exposure treatment, patients attributed the effects of treatment at follow-up mainly to the interaction with the therapist as a person that showed encouragement and sympathy, and, to a lesser extent, to the practice component or learning to cope with panic (Mathews et al., 1976). Similar results were found in phobic and obsessive-compulsive patients successfully treated with exposure in vivo. They rated their therapists at follow-up significantly higher with regards to respect, understanding and interest, but lower concerning the tendency to gratify dependence. Regarding the therapeutic style, they rated their therapists as significantly more encouraging and challenging, but gave them lower ratings with regards to permissiveness, tolerance and neutrality (Rabavilas, Boulougouris & Perissaki, 1979).

Therapist – client perceptions and the outcome of exposure treatment

At a measurement level, the concept “therapeutic relationship” has often been equated with clients’ perception of the therapist, or their perception of each other. Since this line of research, in the behavioral tradition, has special relevance to study III, it will be reviewed somewhat more in detail. Emmelkamp and van der Hout (1983) found a positive significant relationship between the outcome of the group exposure treatment for agoraphobia and the perception of the therapist’s characteristics as being that of positive regard and empathic at post-treatment. They also found a significant negative relationship between outcome and “directivity”. This might sound an odd finding, since directivity has been considered a key feature of cognitive and behavioral therapies (Blagys & Hilsenroth, 2002). But here “directivity” was defined from a client-centered perspective in the instrument used,

i.e., as a negative characteristic of therapists. This illustrates the conceptual difficulties that may occur when instruments are borrowed from other therapeutic traditions, and the definitions are impregnated with theoretical issues.

With this in mind, the Therapist Client Rating Scale (TCRS) was developed with the purpose of studying the interpersonal process, specifically in behavioral therapies (Bennun, Hahlweg, Schindler & Langlotz, 1986). This instrument has versions for the therapist and the client respectively, which allow them to rate their impression of the other on a number of items in a semantic differential-like fashion. The initial factor structure, proposed by Bennun et al., contained three factors for the therapist and client each. Therapists were assessed on (i) positive regard, (ii) competency, and (iii) direct guidance. Client factors were (i) positive regard, (ii) self-disclosure, and (iii) cooperation. The authors reported high internal consistencies but varying degrees of independence for the factors in a cross-cultural sample of in- and outpatients treated with behavioral methods for various disorders. The correlations with outcome were generally positive, but it should be noted that ratings were carried out at post-treatment, and thus the influence of treatment outcome is obvious. In a later study of phobic patients (various, but mainly agoraphobia) treated with exposure and cognitive interventions, TCRS-ratings were carried out at the second session (Bennun & Schindler, 1988). The ratings seemed to capture a mutual understanding between client and therapist and were highly correlated with outcome.

Keijsers, Hoogduin and Schaap (1992) failed to replicate the factor structure of Bennun and co-workers and proposed a somewhat different structure.

Therapist perceived by the patient:

- (i) Supportive
- (ii) Expertise
- (iii) Trustworthiness

Client perceived by the therapist:

- (i) Active participation
- (ii) Goal direction
- (iii) Attractiveness

When employing this solution with a sample of patients diagnosed with various anxiety disorders, high inter-correlations between factors were found, but the therapists' and clients' ratings of each other were uncorrelated (Keijsers, Schaap, Hoogduin & Peters, 1991). They also failed to find any correlations between TCRS and outcome, whereas the clients' perception of the relationship as accepting, empathic and supportive, as measured with another rating instrument, did show positive correlations with outcome.

Consecutive TCRS-ratings were taken after each session (15 sessions in total) in a study of patients in behavior therapy for obsessive-compulsive disorder (Blaauw & Emmelkamp, 1994). They found that ratings tended to be severely skewed towards positive evaluations, especially from the clients, and that the ratings showed considerable stability over time. The correlations with outcome were generally low

and only reached significance between the therapists' positive regard of the client and the benefit from therapy regarding anxiety discomfort. Williams and Chambless (1990) used a different instrument, the Therapist Rating Scale, during in vivo exposure treatment with agoraphobic patients after the fourth session. They found significant correlations with outcome and factors: (i) perceiving the therapist as caring/involved and (ii) the therapist modeling self-confidence. The authors also noted a striking restriction of range towards the positive evaluations of the therapists. While most studies do contain some aspect confirming the general hypothesis of the importance of these relational aspects, one study found that the relationship contributed conversely to what was expected. There was a greater chance of being classified as "treatment failure" for patients highly satisfied with their therapists, when rated at the 3rd session (Keijsers et al., 1994).

In a study of the importance of more clearly specified therapeutic strategies, some support was received for the hypothesis that in establishing a therapeutic relationship within behavioral treatment programs for panic disorder and agoraphobia, it would be important to maintain an empathic and non-directive stance during the early phases (Keijsers, Schaap, Hoogduin & Lammers, 1995). The authors used observer ratings of patient- and therapist behaviors, and found them related to outcome.

At a superficial level, the above-mentioned studies could be confirmative in that they do suggest the importance of the interpersonal factors in behavioral therapies. But they also contain several confounds that hamper any conclusions from being drawn. The earlier studies were based on post-treatment ratings; they used diagnostically heterogeneous samples; treatment methods were not always defined and a multitude of computations were performed. The later studies have used more homogeneous samples, but they either explicitly used inexperienced therapists or did not state the therapists' training levels in behavior therapy.

Therapist variables

The possible confounds mentioned above lead further into the question of the therapist's contribution. Generally, the more experienced the therapists are, the better the outcome is expected to be, although the differences tend to be modest (Christs-Christoph et al., 1991). And especially important when considering outcome prediction is that more experienced therapists had smaller between-therapist differences than did less experienced therapists. Clinicians, who were more accustomed to principally using psychosocial methods, were found to be classified as more effective in treating depression, regardless whether they were cognitive or interpersonal therapists (Blatt, Sanislow, Zuroff & Pilkonis, 1996). Clinical experience has also been found to predict significantly greater change in manualized CBT for panic disorder (Huppert et al., 2001). These differences were evident in clinical ratings and anxiety sensitivity, but not in a range of other measurements. However, years of experience in CBT specifically, were not significantly related to outcome. The obtained differences were evident even though there were no differences in adherence and competency, when comparing those with the most favorable outcome with those with the least. Regarding both competency and adherence, all therapists

were, in fact, given a high rating. The authors concluded that, even in accordance with a well-structured format, individual therapist factors make a significant, though modest contribution.

Working alliance

From a generic psychotherapy perspective, the concept “working alliance” has probably received most attention. It has been called “the quintessential common ground shared by most psychotherapies” (Horwath & Bedi, 2002). A modest, but consistent correlation with outcome is reported over a range of different therapeutic practices. Horwath and Bedi reported an average correlation with outcome of .21 (weighted for sample size).

Historically, the concept “working alliance” can be traced back to Freud’s idea of forming a coalition with the patient (Horwath & Bedi, 2002). His main interest was in the transference aspects of the relationship, which can be defined as the relocalization of affect from one person to another. But he also held that there was an “unobjectionable positive transference” that should not be analyzed, since it provided the patient with motivation to cooperate with the analyst. The importance of an alliance in counseling and psychotherapy has become generally accepted, but the definition of the construct has varied greatly (Tichenor & Hill, 1989). Bordin’s tripartite conception of the working alliance, comprising of the mutual agreement regarding goals, tasks and the interpersonal bond is probably the one that has gained the most widespread acceptance (Horwath, 1994). It has also provided the basis for one of the most commonly used measures of the alliance; namely, The Working Alliance Inventory (WAI; Horwath, 1994; Tracey & Kokotovic, 1989).

Studies of the relationship between working alliance and therapies within the cognitive-behavioral tradition are scarce, but confirmative findings have been reported in the treatment of depression (Raue & Goldfried, 1994) and “partner violent men” (Taft, Murphy, King, Musser & DeDeyn, 2003). DeRubeis and Feeley (1990), on the other hand, failed to show that alliance predicts outcome in CBT for depression. In a group-treatment for social phobia, the client-rated working alliance increased during treatment, but no relationship to outcome was found (Woody & Adessky, 2002).

Generally, the empirical evidence indicates that cognitive-behaviorally oriented skills of therapists in establishing this working alliance have been rated at the same level as the skills of psychodynamic therapists (Raue, Goldfried & Barkham, 1997). The CBT therapy sessions also displayed less variability regarding alliance than the psychodynamic sessions.

Moreover, one study (Faller, Wagner, Weiss & Lang, 2002) found that cognitive-behaviorally oriented therapists themselves perceived the quality of the working alliance to be better and their feelings of sympathy for the patients to be stronger than did psychodynamically oriented therapists, when this was rated at an intake interview. Moreover, they perceived patients’ motivation and several prognostic factors more favorably. This study does contain several confounds, but it is in agreement with the results of Raue, Putterman, Goldfried and Wolitzky (1995),

where psychodynamically oriented therapists rated alliance lower, irrespective of the type of therapy.

The question whether alliance should be considered a unitary concept in all therapies, i.e., involving identical processes, or whether the alliance building processes are specific for different therapies, remains unanswered. As stated by Horwath and Bedi (2002), the research on working alliance is based more on attempts to develop reliable measurements of this concept, than exploring the validity of these measurements and elaborating the theoretical positions. Different methods to measure the working alliance generally show high inter-correlation between different sub-scales (Tichenor & Hill, 1989). Researchers have tended to adopt the view of treating alliance as a unitary concept (Tracey & Kokotovic, 1989), thus considering only the general factor.

However, in an exploratory factor analysis of observer rated working alliance in a group of depressed patients treated with standard CBT (Andrusyna, Tang, DeRubeis & Luborsky, 2001), a two-factor structure was found. This challenged the commonly accepted single general factor of alliance. Their results suggested a first factor, "agreement/confidence", roughly comparable to Bordin's task and goal factors. The second factor, "relationship", is portrayed more by emotional elements such as mutual liking, trust, and appreciation between the therapist and client. This closely resembles the distinction made by Gelso and Hayes (1998) between a *working bond* and a *liking bond*. It also gives an indication of the need for a more fine-grained understanding of the therapeutic relationship, than that of a general alliance factor.

5.3. Aspects of change

Generalization of symptoms

As stated previously, the diagnostic concept "panic disorder with agoraphobia" entails two principal aspects: panic attacks and avoidance. However, we have learnt that it is a complex disorder with several features of dysfunction and ill-being. This raises the question of the change processes intrinsic in treatment; to what extent is change in these areas mutually dependent and how is change generalized over different areas?

Early treatments of agoraphobia favored ratings of anxiety and phobia as outcome, and panic attacks were seldom assessed specifically (e.g., Hand et al., 1974; Emmelkamp et al., 1978; Michelson et al., 1986). Questions have been raised whether in vivo exposure would have an effect in itself on these attacks (Mattick et al., 1990; van den Hout et al., 1994). The subordination of agoraphobia under the concept "panic disorder" has also emphasized the attacks themselves as the key pathological element (Klein, 1981). Consequently, reports of outcome, in the area of panic disorder, came to favor the frequency of panic attacks and results are often referred to in percentage of panic-free subjects.

Later studies in the psychological field have accepted this subordination and subsequently focused on the change in panic per se. And, indeed studies have shown large and substantial treatment effects on panic attacks from CBT (Barlow, 2002). However, the debate cannot be put to rest with this. As shown earlier, the development of agoraphobia is associated with greater debility, but it must also be

remembered that the mere presence or severity of recurring panic attacks, per se, does not seem closely linked to the level of agoraphobia (Cox, Endler & Swinson, 1995). Barlow (2002) points to the fact that the well-established cognitive-behavioral treatments for panic disorder have frequently focused on subjects with minimal or no agoraphobia, thereby limiting their scope to those patients within a less serious spectrum of the disorder. This raises serious questions about the generalization of these treatments for the full spectrum of panic disorders.

In vivo exposure has been found to not only address the problem of agoraphobic avoidance, but it has also been found to have a substantial impact on panic frequency, even in the absence of interventions specifically targeting these attacks (Cox et al., 1992; Williams & Falbo, 1996). The literature does seem consistent with a change route where a decrease in panic follows reductions in avoidance. Craske, DeCola, Sachs and Pontillo (2003) set out to try panic control treatment with interoceptive exposure, in absence of explicit situational exposure work in a group of PDA patients. Thus, testing the hypothesis that controlling panic attacks may determine the reductions in agoraphobia, and, therefore, panic control treatment alone may be sufficient in ameliorating agoraphobia. Their results were consistent with this hypothesis and they found that a reduction in panic attacks, but not a variety of other panic related measures, predicted a change in agoraphobia. Now, this study has limitations in that panic was rated retrospectively, which is often considered to yield inflated measures, as compared with prospectively assessed panic attack variables (Sharp & Power, 1999). Also, agoraphobia was either rated by a clinician, or assessed by way of a behavior approach test, which solely looked at a small enclosed space and not typical agoraphobic situations. These limitations set boundaries for the external validity of these results.

Now, while the relationship of the change in panic and in avoidance is of both theoretical and clinical interest, the pervasiveness of PDA as a clinical disorder is not fully accounted for in this relationship. And, indeed, the successful treatment of agoraphobia has been found associated with altered depression (Chambliss, 1985) and general anxiety (Cox, 1992). Findings also indicate that psychological treatment for panic disorder is accompanied by a decline in other comorbid anxiety disorders or mood disorders (Brown, Anthony & Barlow, 1995).

Quality of life

Apart from aspects of psychopathology, there is a growing recognition of quality of life (QOL) as a treatment outcome variable in its own right (Maisson et al., 1993). In a group of patients with DSM-III-R diagnosis of panic disorder with agoraphobia, Telch et al. (1995) noted a significant impairment in QOL at intake. They found that cognitive-behavioral treatment had a significant beneficial impact on this impairment. But QOL was neither related to panic frequency at baseline, nor was change in QOL related to change in panic after treatment or at follow-up. Instead, anxiety and phobic avoidance were related to indices of QOL at baseline, and changes in anxiety, the most potent predictor of changes in QOL.

6. Statement of the Problem

The behavioral treatments of PDA are based on solid empirical ground regarding the ability to show immediate and long-term results. This development of treatments has continuously strived towards incorporating new auxiliary treatment techniques. When planning the treatment project, from which the present data comes, no randomized controlled treatment trials that explicitly assessed the potential beneficial effects of adding cognitive therapy for panic attacks to exposure in vivo were available. In spite of the stated potential promise of these methods, this applied to this population (e.g., Michelson & Marchione, 1991).

Apart from the addition of auxiliary treatment techniques, the identification of pre-treatment predictors is often stated as crucial knowledge for the further improvement of treatment approaches. However, in the area of PDA, little has been found and the clinical implications are not evident.

While the learning processes involved in the development of panic disorder have been the focus both of research and theoretical advancements, the beneficial learning processes of therapy remains an area, where there has been far less research. From a learning theory perspective, what therapies provide are ultimately contingencies for learning. The therapeutic relationship can be understood as such contingencies, but, in the behavioral tradition, this is an area, where research must be considered as being only in its infancy.

Panic disorder with agoraphobia is a complex disorder. This implies that a success story for a treatment would have to show effects in a broad spectrum of the areas that are afflicted, and that singular symptoms may be of less interest. It also paves the way for the study of how change processes in different areas relate to each other. Understanding these relationships may increase the ability for behavioral treatments to target the most central and pivotal aspects of change.

7. Summary of Empirical Studies

7.1. General outline of the project

The patients in paper I (n=73), paper II (n=62), paper III (n=59), and paper IV (n=62) were all included in the sample of a treatment study conducted at the Department of Psychology at Stockholm University between 1995 and 1998, and led by Professor Lars-Göran Öst. The staff involved a research assistant, and three therapists, who were clinical psychologists, with licenses as psychotherapists, carried out treatments. The project was approved by Karolinska Institute's Ethical Research Committee.

Participants

The participants were referred by their physicians in the County of Stockholm, Sweden. To be included in the treatment study, the patient had to fulfill the following criteria:

1. A primary diagnosis of panic disorder with agoraphobia of moderate to severe magnitude (severity rated at least 4 on the 0-8 scale);
2. Aged between 18-60;
3. A minimum of one year for the duration of the disorder;
4. If simultaneously treated with psychotropic medication, having been on a constant dose for at least 4 months and having agreed to keep this dosage constant throughout therapy;
5. No diagnosis of primary major depression (i.e., onset before the PDA), no current alcohol or substance abuse, or psychotic or organic symptoms;
6. No ongoing psychotherapy.

A total of 128 subjects went through the diagnostic interview by the independent assessor using the Anxiety Disorders Interview Schedule-IV (ADIS-IV; Brown, DiNardo & Barlow, 1994), and 48 of these were excluded. Reasons for exclusion were failure to fulfill any diagnosis at all ($n=2$). 13 had cases of agoraphobia considered too mild, 3 had a severity that made them unable to come to the therapist for treatment and another 4 were hindered due to miscellaneous problems. For 26 subjects, other DSM-IV disorders were the principal diagnoses. Of them, 3 had a primary major depression, 2 had alcohol abuse, and 1 had ongoing psychotherapy. Of the remaining 80 patients, 7 never started treatment; 3 of them did not complete the three-week self-observation period and 4 did not accept randomization and decided to obtain treatment outside the project. This left 73 patients, all of whom had been diagnosed with panic disorder with agoraphobia (PDA) according to DSM-IV (APA, 1994). 11 patients dropped out, and a full data set was collected for 62 patients. For 3 of them, too much of the process data (see below) was missing in order for a meaningful estimate to be made. They were, therefore, dropped in the analysis in study 3.

Procedure

Pre-treatment

Once a patient was referred to the project for treatment they were first mailed a number of self-report scales to fill in. Upon returning these the patient was contacted by telephone in order to book the diagnostic interview. An independent research assistant not involved with the treatment performed all the diagnostic interviews and ratings. The main purpose of the first interview was, using the ADIS-IV interview format, to ascertain that the patient fulfilled the project's inclusion criteria. To assess the diagnostic reliability, 20% of the audio taped interviews (both of included and excluded patients) were randomly selected and rated by independent clinicians. A kappa coefficient of 0.78 was achieved, which is very satisfactory.

Table 1. Sample characteristics

Gender distribution	50 females, 23 males
Average age	36.1 years (SD = 10.3; range 18-58)
Average age at panic onset	26.9 years (SD = 9.0; range 12-53)
Average age at agoraphobia onset	28.6 years (SD = 8.9; range 12-53)
Marital status	36 (49%) of the patients were married/living together with a steady partner, 24 (33%) were single and 13 (18%) divorced.
Occupational status	51 (70%) of the patients worked or studied full-time, 6 (8%) part-time, while 16 (22%) were unemployed or on sick leave.
Interference	According to the ADIS-IV interview, all of the patients were moderately-severely handicapped by their agoraphobia in their daily lives or work.
Axis-I comorbidity	27 (37%) of the patients had at least one comorbid Axis-I disorder (major depression, 9; social phobia, 8; generalized anxiety disorder, 6; specific phobias, 2, and obsessive-compulsive disorder, 2).
Axis-II comorbidity	17 (23%) of the patients fulfilled the DSM-IV criteria (APA, 1994) for personality disorders (avoidant, 9; dependent, 3; both avoidant and dependent, 2, and antisocial, 3).
Medication	38 (52%) of the patients were taking psychotropic medication for their PDA at the start of treatment (SSRIs, 37%; Tricyclic Ads, 24%; BZDs, 31% and a combination of a neuroleptic and a BZD, 8%).
Previous treatment	Only 11 (15%) of the patients had not been previously treated for PDA. 24 (33%) had received psychotherapy alone, 8 (11%) pharmacotherapy alone, and 30 (41%) both types of treatment. Of the 54 patients who had received psychotherapy, 51 had had psychodynamic therapy and 3 cognitive-behavior therapy. The mean length of previous psychotherapy was 22.5 months (SD = 27.8, range 1-150).

The patients were given detailed instructions to record each time they experienced panic symptoms in a specific panic diary. This diary contained a description of what constitutes a panic attack according to the DSM-IV criteria. The patient recorded date, situation, what symptoms were present, and the intensity (0-100) of the panic attack. They also classified it as a panic attack or a limited symptom attack. This was measured for a 3-week base-line period. Along with this diary, the patients were instructed to perform two types of behavioral approach tests (BAT) during the baseline period. One individualized test consisted of 10-15 individually chosen situations relevant to the individual patient, and rank ordered for perceived difficulty. The patient then had three weeks to try to approach as many of the situations as possible. Along with the patient's rated expected and experienced anxiety level in these trials, the percentage of achieved situations was registered. There was also a standardized test that consisted of riding a subway train for 10

stations, and then back again. Anxiety and percentage of achieved situations were registered. Specific diaries were used to record these tasks. A multitude of self-report inventories were gathered to assess a wide range of topics relevant to the clinical condition.

A week after the first interview the patient returned for a second one, with the primary purpose of assessing the personality disorders by means of the Structured Clinical Interview for DSM-IV Axis-II (SCID-II; Spitzer, Williams, Gibbon & First, 1987).

After the pre-treatment assessment, when the baseline data had been gathered, the patients were randomly assigned to three conditions: (1) exposure in vivo (n=25), (2) cognitive-behavior therapy (n=26), and (3) waiting list for 4 months (n=22). After the post-assessment of the waiting-list, two patients dropped out. The remaining patients were randomized to the two treatment conditions with 10 in each.

The therapy sessions were audio-taped and three randomly selected sessions for every patient were assessed for treatment integrity and competency by independent psychotherapists blind to the patient's treatment condition.

Process data

At session 1, when the patient had met with the therapist and been provided with a treatment rationale, yet before any of the actual treatment had started, the client rated the perceived treatment credibility and motivation. At sessions 4, 8 and 12, the therapist and client rated their perceptions of each other, and at session 8 the patients rated the working alliance.

Post-treatment assessment

Closely after the last therapy session, the patient was contacted by the independent assessor for an interview. This interview was an abbreviated version of the ADIS-IV. Self-report scales were administered once again, and the instructions for a new self-observation period were given (panic diary and BAT).

Follow-up assessment

One year after the post-treatment assessment the patients were again contacted for a follow-up assessment, which was identical to that done at post-treatment.

7.2. Study 1

Purpose

The primary purpose of study 1 was to investigate whether the combination of cognitive therapy and exposure in vivo (called CBT) would be more effective than exposure alone for PDA-patients with moderate to severe agoraphobia. Based on earlier research showing the efficacy of CT for PD (Clark et al., 1994), it was predicted that CBT would be more effective than exposure, and that the effects would be maintained at the 1 yr follow-up.

The second purpose was to investigate whether, by increasing the number of sessions to 16, a higher proportion of patients would achieve clinically significant

improvement compared to the previous studies that used 12 sessions (Öst et al., 1984; Öst et al., 1993). In the 1984 study, exposure treatment resulted in 59% being clinically significantly improved at post-treatment and 71% at follow-up, and, in the 1993 study, this proportion was 64% and 65% respectively.

The third purpose was to study whether the treatments led to significant improvements in a broader spectrum of outcome, rather than just observations strictly related to the areas of panic and agoraphobia, on which the treatments were focused. We wanted to assess the impact on measures of complications such as general anxiety, depression, quality of life and social adjustment.

Method

As described earlier, the patients were randomly assigned to exposure in vivo, cognitive-behavior therapy and waiting-list control.

Exposure in vivo (E)

Patients with this condition received an individualized exposure in vivo treatment based on a brief behavior analysis of the individual case. The exposure exercises were carried out following a fear and avoidance hierarchy and were, at least initially, therapist-assisted. Homework assignments were used throughout and gradually the responsibility for the exposure work was to be taken over by the patient. Cognitive interventions were explicitly proscribed in this condition. If a patient brought up the topic of their cognitions, the therapist just listened politely, but treated them as epiphenomenal to the exposure work.

Cognitive Behavior Therapy (CBT)

This condition was a combination of exposure as described above and cognitive therapy based on the cognitive theory of panic (Clark, 1988). Both cognitive and behavioral techniques were used and cognitive content was explicitly treated as having a causal role in the patients' fears. The emphasis was on using behavioral experiments to challenge the validity of the patients' catastrophic interpretations of bodily sensations and entering phobic situations. Generating more realistic perceptions was stressed and encouraged when re-entering the situations.

The clients perceived the treatments as equally credible and both integrity and quality were judged to be good. Neither of the therapies followed a strict manual, but they were to be applied in a clinically sensitive way depending on the needs of the individual patient. This implementation was left to the clinical decisions by the therapists, and team supervision with the senior author. Sessions lasted 60-90 minutes and were scheduled once a week for a total of 12-16 sessions. The decision to terminate treatment between sessions 12-15 was made unanimously by the therapist together with the patient. Apart from the offer during the last session to follow a maintenance program, no treatment took place between post-treatment and the 1-year follow-up assessment in agreement with the patient at pre-treatment. The maintenance program included a total of 60-90 minutes of telephone contact with the therapist for the 6 months following the termination of the therapy if they wished to. Patients were generally appreciative of this offer, but few adhered to the program.

Results and discussion

Both treatments yielded significant improvement vis-à-vis the waiting-list control on all outcome variables. CBT was significantly better than E only on one out of 32 outcome measures: self-rated distress from panic attacks and this at post-test only. Improvement was well maintained at follow-up. On none of the 32 measures did E or CBT show a significant deterioration from post- to follow-up assessment. On the contrary, the E-group showed significant improvements from post- to follow-up assessment on 7 measures and the CBT-group displayed further improvements on four measures. So the main conclusion that can be drawn from the present study was that there were significant effects for both active treatments, but basically no difference between E and CBT, replicating that of a number of previous studies.

The percentage of those clinically significantly improved was assessed for three measures, and was in the present study 67% for E and 79% for CBT at post-test. At follow-up these figures were 74% and 76%. It was concluded that both the E- and the CBT-group had better effects than the E-groups in the two previous studies, perhaps due to the increased possibility of a longer duration of therapy.

A third purpose was to study if the treatments led to significant improvements in measures associated with areas of disturbance, such as general anxiety, depression, quality of life and social adjustment. The results clearly showed significant effects on these measures. Moreover, at follow-up, these results were maintained, or were further improved. Thus, it can be concluded that the impact of behavioral treatments for PDA has favorable and lasting effects that are not restricted to the panic attacks and agoraphobic avoidance that the treatment is focused upon.

7.3. Study 2

Purpose

The second study is concerned with predicting outcome at post-treatment and follow-up using pre-treatment variables. The predictor variables were chosen to represent complaint-related (severity, duration), personality (axis-II disorder, state anxiety) and cognitive factors (motivation, perceived treatment credibility) that would be expected to influence outcome. We were also interested in studying the possible diversity that could arise between considering outcome as a categorical or continuous variable. The impact of variables pertaining to poor pre-treatment functioning could be thought to be especially associated with outcome, when regarded as a category defined in relation to the dysfunctional population. Other variables might be believed to have a larger impact on outcome defined by the degree of individual change.

Method

Two approaches to the task of prediction were compared: (i) predicting class membership as clinically significantly improved at post-test and 1-year follow-up and (ii) predicting individual change from the same variables.

For the outcome a composite score was constructed from (i) the independent assessor's rating of clinical severity and (ii) the agoraphobia scale (Öst, 1990), which

has two parts assessing agoraphobic anxiety and avoidance, and (iii) an index score reflecting the percentage of performed situations and experienced anxiety during the behavioral approach test. From this composite score, each individual was classified if they had reached the criteria for clinically significant improvement (CSI; Jacobson & Truax, 1991); thus, giving a dichotomous outcome variable. Individual residualized change scores were calculated by conducting linear regression analyses for the composite scores from pre-treatment to post-treatment, and pre-treatment to follow-up. The residuals were used as a continuous measure of individual change, which was uncorrelated with the pre-treatment values.

The predictors were:

- a. Duration of agoraphobia;
- b. Severity of agoraphobic avoidance assessed by the Mobility Inventory – Alone subscale (MI-A; Chambless, Caputo, Jasin, Gracely & Williams, 1985);
- c. Trait Anxiety assessed by State-Trait Anxiety Inventory (STAI-T; Spielberger, Gorsuch & Lushene, 1971);
- d. Motivation assessed by the Nijmegen Motivation List (NML; Keijsers, 1994);
- e. Perceived treatment credibility as assessed by the Credibility-Scale adopted from Borkovec and Nau (1972);
- f. SCID-II diagnosis of anxious cluster personality disorder.

Logistic regression analyses were carried out for predicting CSI as a dichotomous variable. The continuous predictors were standardized before entering the equation to increase interpretability of odds ratios. Multiple regression analyses were calculated to predict individual change scores from the same predictor variables. Semi-partial correlations were used to estimate the impact of individual predictor variables.

Results and discussion

Agoraphobic severity was the only individual predictor to reach statistical significance, when predicting CSI. It was found to be a significant predictor at post-treatment (Exp. $\beta = .19, p < .01$) as well as at follow-up, although to a lesser extent (Exp. $\beta = .42, p < .05$). Severity was also found to be a significant predictor of change scores at post-treatment ($sr = -.30, p < .05$), though not as influential as when predicting CSI. However, severity was not a significant predictor of change at follow-up. Instead the duration of the disorder was found to be a significant predictor of change at follow-up ($sr = -.29, p < .05$). Perceived treatment credibility, motivation, anxious cluster personality disorder or trait anxiety were not identified as significant predictors of outcome, when perceived either way.

The results did indicate that pre-treatment severity of avoidance has a substantial impact on outcome. However, when predicting CSI, it may well be estimated to have a larger impact on the treatment of PDA than individual change. If the ultimate criterion for treatment benefit is regarded as individual

long-term change, the present study indicates that this may not be equally influenced by the level of pre-treatment severity.

7.4. Study 3

Purpose

The purpose of the third study was to investigate factors pertaining to the therapeutic relationship in the behavioral treatment of panic disorder. In vivo exposure is a rather unique practice of the behavioral tradition, whose efficacy is well established. It is also a practice that diverges from the prototypical picture of psychotherapy, i.e., it takes place in primarily a verbal and office-based environment. This raises the question of the broader interest than just studying the relationship in this special methodological variety. For the therapeutic factors that are alleged to be “common factors” (Gelso & Hayes, 1998) to demonstrate that they are truly common, they need to demonstrate influence not only over different labels of therapeutic practices, but also over treatments that show clear topographic diversity.

We were interested in whether there were patterns in the interpersonal relationship identifiable in the therapists’ and clients’ mutual perceptions of each other during the treatment. We were also interested if there would be a correlation between these perceptions of each other and outcome. The third purpose was to investigate whether the common factors’ concept “the working alliance” would be related to the ratings of the therapist’s and client’s qualities, and if it would influence outcome.

Method

Therapists’ and clients’ perception of each other

The Therapist Client Rating Scale (TCRS; Bennun et al., 1986) consists of two versions, each with 29 semantic differential-like items. The scale was administered at sessions 4, 8 and 12. The clients’ ratings were blind to the therapists’, and vice versa. In interpreting the ratings we followed the proposed factor structure from Keijsers et al. (1992). The therapist factors (as perceived by the client) were: (1) support; (2) expertise; (3) trustworthiness, and the client factors (as perceived by the therapist) were: (1) active participation; (2) goal direction; (3) attractiveness.

Working alliance

An abbreviated form of the Working Alliance Inventory (WAI; Tracey & Kokotovic, 1989) was administered after the eighth session. This scale relies on the tripartite conception of the working alliance, comprising the mutual agreement regarding goals, tasks and the interpersonal bond and is one of the most commonly used measures of the alliance (Horvath, 1994).

Outcome

Residualized change scores and the classification of clinically significant improvement on a composite variable, which were identical to that in study 2, were calculated for each patient.

Results and discussion

No significant differences were found between therapists regarding outcome. Neither were there significant differences between therapists regarding the clients' ratings of the therapist factors or working alliance. The ratings of therapists were generally very positive, and showed some increase during treatment. There was initially a low correspondence between therapist and client perceptions, but a growing consensus during treatment. This was most pronounced regarding high ratings of therapist qualities and the perception of the client as "attractive". Thus, the data seemed to capture a sense of growing mutual positive regard between the two.

The clients' perceptions of therapists showed virtually zero correlation with outcome, regardless of time. Regarding the therapists' perceptions of the client, we found, at session 4, significant correlations between "active participation" and "goal direction", and change scores at post-treatment ($r = .29$; $p < .05$) and follow-up ($r = .32$; $p < .05$) respectively. At session 8, these factors showed significant correlations in the same range, with change scores at post-treatment and follow-up, as well as with clinically significant improvement at post-treatment. These correlations were further strengthened at session 12. The factor "attractiveness" did not correlate significantly with outcome at any point. An interpretation could be that the process of growing mutual positive regard, as hypothesized above, was separate from this process that did affect outcome.

Ratings of working alliance were not significantly correlated with client- or patient factors in TCRS at mid-treatment. No significant relationship between working alliance and outcome was found, apart from the fact that the mean rating of the working alliance of those who improved during follow-up was significantly higher than those who remained not clinically significantly improved. (4.41 vs. 3.36; $t(16) = 2.124$, $p < .05$). This does lead to an intriguing interpretation; namely, the working alliance can affect the advent of further improvement after the end of actual treatment. However, this must be considered speculative, since it could equally well serve as a basis for questioning what the inventory, in its Swedish translation, actually measures.

7.5. Study 4

Purpose

The diagnosis of PDA contains by definition the principal features of panic attacks (and associated fear) and agoraphobic avoidance. However, the often rather complex clinical picture involves several associated areas of distress. While the etiological relationship between the two principal areas has been documented, their relationship regarding the maintenance of the disorder is less clear. Behavioral treatments for PDA have shown to be effective, not only regarding panic attacks and avoidance, but also for a wide array of clinical problems that tend to be present in the clinical picture. But the question is still open as to whether change in these interrelated clinical areas occurs in a unitary fashion during therapy.

The purpose of the fourth study was to investigate the relationship between the change in panic attacks and the change in agoraphobic avoidance after therapy and at follow-up. We also wanted to investigate the relationship between change in these two aspects and change in two further areas of special interest: (i) general

negative affect, since this posits a central role in modern theorizing on panic disorder (Barlow, 2002); (ii) the perceived quality of life.

Method

The frequency of panic attacks was measured during a three-week baseline period in a specific panic diary. A behavioral measure of agoraphobic avoidance was calculated from the behavioral approach test. An overall measure of agoraphobic avoidance and anxiety was constructed from the percentage of situations achieved and the mean rating of experienced anxiety. Both of these baseline measurements were carried out at pre-, post-treatment and follow-up.

Along with the self-observation and behavioral test, self-rating scales were administered: Panic Attack Scale (PAS; Clark et al., 1994); Mobility Inventory (MI; Chambless et al., 1985); Beck Depression Inventory (BDI; Beck et al., 1961); State-Trait Anxiety Inventory – Trait form (STAI- T; Spielberger, Gorsuch & Lushene, 1971); Quality of Life Inventory (QOLI; Frisch, Cornell, Villanueva & Retschlag, 1992).

For the study of change in different aspects of the disorder, residualized change scores from pre- to post-treatment and pre-treatment to follow-up were calculated. To obtain more robust indices of change, these were compiled into composite scores for the central aspects of the disorder: (i) change in panic (Panic frequency and PAS); (ii) change in avoidance (BAT and MI); (iii) change in negative affect (BDI and STAI-T). Change scores were also calculated for quality of life (QOLI), but not compiled.

Results and discussion

The treatment resulted in substantial effects on panic attacks and agoraphobic avoidance that were well maintained and increased at one-year follow up. Patients were classified as panic-free if they reported zero regular panic attacks during the three-week self-observation periods. 21% of the patients did not report any panic attacks during pre-treatment self-observation. When comparing these patients with the group that did report panic attacks, they only differed by scoring significantly lower on the BDI. They did not score significantly different on any of the other measures, including the retrospectively rated panic frequency.

At post-treatment, 64.5% of the subjects were panic-free. Again, they scored significantly lower on the BDI, but also on the PAS. However, on the other variables, there were no differences. At follow-up, when 75.8% were panic-free, there were significant differences on all measures between the two groups.

Change in panic and avoidance were related to each other at post-treatment ($R^2 = .12$, $F(1,60) = 7.83$, $p < .01$), and more so at follow-up ($R^2 = .26$, $F(1, 60) = 21.34$, $p < .001$). However, change in avoidance was more related to change in negative affect at both pre-treatment ($\beta = .38$, $p < .01$) and post-treatment ($\beta = .44$, $p < .001$), than change in panic was. Change in quality of life was also more related to change in avoidance at post-treatment ($\beta = .30$, $p < .05$). At follow-up, however, this picture was reversed, and the relationship to change in panic was the more influential ($\beta = .38$, $p < .01$).

The results from the present study would suggest that, for this group of patients, a “panic-free status” was a more isolated aspect of outcome at post-test.

Change in avoidance seemed to affect a broader range of the clinical aspects studied here, especially negative affect. It should be noted that at one-year follow-up change in panic was more closely associated with change in QOL. The mean QOL for the patients, who still reported panic attacks at follow-up, was close to the pre-treatment value.

8. General Discussion

Treatment efficacy

Agoraphobia, the “fear of the marketplace”, is a serious health problem with profound consequences for the individual. But, it is also a health problem, where the behavioral tradition has been successful. Among the psychological treatments, exposure-based variants have been consistently supported in the literature. The effect of behavioral treatments on panic has been questioned, but, in the last decades, cognitive and behavioral treatments have been successfully launched for the treatment of panic attacks (Barlow, 2002). Since the early days of struggling with long and tedious treatments like graded retraining and systematic desensitization, the behavioral tradition has gone a long way in establishing treatments that are efficacious, amenable and achieve results that seem to be well maintained – hence, a “success story”. Nevertheless, it is a story, where several parts are still waiting to be written.

The primary purpose of the first study was to investigate whether the addition of cognitive techniques to exposure in vivo (CBT) would give better treatment effects than exposure (E) alone for PDA-patients with moderate to severe agoraphobia. Since CBT was only significantly better than exposure on one out of the 32 outcome measures, and at post-test only, this hypothesis cannot be considered validated. Clinically, there seems to be an advantage for the CBT-condition; however, this is only evident at post-treatment. When the mean for a combination of three important outcome measures was used to assess clinically significant improvement in the present study, it was 67% for E and 79% for CBT at post-test. At one-year follow-up, the corresponding figures were 74% for E and 76% for CBT. The results were generally well maintained and further improved on the outcome variables during follow-up. Neither of the groups showed any significant deterioration. The main outcome of the present study can be summarized as achieving significantly better effects for the active treatments than the waiting-list control, but basically there was no difference between E and CBT.

An additional purpose was to study if the treatments led to significant improvements to a broad range of measures, such as general anxiety, depression, quality of life and social adjustment. The results clearly showed significant time effects on these measures. Again, the follow-up assessment also indicated that the initial improvements to these measures were not temporary, but remained, or were increased one year later.

Our results do fall in line with previous research, which generally has failed to support the hypothesis that adding cognitive techniques aimed at panic attacks should prove to add substantial treatment effects, more than that achieved by exposure only (Bouchard et al., 1995; Burke et al., 1997). Only one study has found more substantial beneficial effects (Michelson et al., 1996), and one study (Williams & Falbo, 1996) showed inferior results in the cognitive condition. This failure should also be considered in the light of high expectations for this approach (e.g., Michelson & Marchione, 1991) and the possibility of allegiance effects.

The reasonable conclusion from the above mentioned studies would be that the addition of CT has over a number of studies failed to add any consistent significant and substantial effects than that achieved by exposure itself. Actually, when going through the literature, a broader picture is conveyed. Additional methods like assertiveness training (Emmelkamp et al., 1983; Thorpe et al., 1985), relaxation (Öst et al., 1984; Michelson et al., 1996), breathing retraining (de Ruiter et al., 1989; de Beurs et al., 1995; Schmidt et al., 2000), or hypnosis (Van Dyck & Spinhoven, 1997) have not been found to bolster treatment effects. Thus, the conclusion could be stated more generally: very little has been gained by adding auxiliary components to the basic exposure treatment.

However, these findings would be equally consistent with the verdict that all treatments are equal and above those non-specific features provided in the general therapeutic framework, only trivial variation is to be found (e.g., Wampold, 2001). Exposure has been found superior to non-specific treatment procedures like group-discussion (McDonald et al., 1979), or the behavioral approaches that did not include exposure (Mattick et al., 1990). Mattick et al. calculated expected pre- to post-effect sizes from placebo treatment for PDA on measures of phobia ($d = -.02$) and panic ($d = .32$). Comparing them to the corresponding mean effect sizes of behavior therapies that included exposure (phobia: $d = 1.7$; panic: $d = .96$), they concluded that placebo effects are unlikely confounds in the treatment of PDA. Now, one problem is that of assessing the importance of specific ingredients, when comparing with “placebo treatments” in psychology. Wampold asserts that the target of investigation must be “bona fide therapy”, i.e., therapies intended to be therapeutic. The earlier behavioral treatments of graded retraining and systematic desensitization explicitly claimed the importance of avoiding anxiety. However, they were definitely intended to be therapeutic, but with rather poor results (Mathews et al., 1976; Mattick et al., 1990). But these studies are old and the understanding of the disorder in question has been further advanced. There were two studies identified during recent years that have examined what could be essentially considered “non-exposure treatments”. The study by Goldstein et al. (2000) on EMDR concluded that the effect sizes of both EMDR and their non-specific treatment were poor and within the expected limits of a placebo. Therapists were reported to favor the active approach in EMDR, so allegiance should not be considered a serious threat to this conclusion. The study of Bouchard et al. (1995) is noteworthy because the cognitive therapy condition contained instructions that explicitly told the patients that the essential components of exposure were unnecessary and of no use in the treatment of PDA. If researchers’ allegiance should be considered here, an indication is given when the authors’ main conclusion was that treatments were equivalent, even though exposure was

significantly superior on one measure and a substantial difference, in percentage of subjects reaching high end-state, was noted in favor of exposure at post-test.

Table 1 shows pre- to post-effect sizes for three measures used in both trials and our main study. The picture of negligible effect sizes for EMDR and the attention and relaxation therapy are easily detected. But while exposure has produced substantial effects in the Bouchard et al. study, the CT-condition is closer to the placebo range. A more reasonable conclusion from the Bouchard et al. study than treatment equivalence would be that which Goldstein et al. explicitly caution their study against; namely, the conclusion that the study failed to detect potentially meaningful differences due to low power.

Table 2. Pre- to post-treatment effects for panic and phobia measures (Cohen's d)

<i>Study</i>	<i>Treatment condition</i>	<i>ACQ</i>	<i>BSQ</i>	<i>MI-A</i>
Goldstein et al. (2001)	EMDR	-0.06	0.26	0.37
	ART	0.16	0.14	0.01
Bouchard et al. (1995)	Exposure	1.77	1.43	1.90
	Cognitive Therapy	0.49	0.63	0.50
Öst et al. (2004)	Exposure	1.32	0.95	1.30
	CBT	1.38	1.16	1.88

ACQ (Agoraphobic Cognition Questionnaire); BSQ (Body Sensation Questionnaire); MI-A (Mobility Inventory – Alone subscale); EMDR (Eye-Movement Desensitization and Reprocessing Therapy); ART (Attention and Relation Therapy).

In this context, it also worth considering the study of Telch et al. (1985) on the relative role of exposure and imipramine in a group of patients diagnosed with DSM-III agoraphobia with panic attacks, who were considered severely disabled. Their study contained a condition, where medication was combined with anti-exposure instructions. While this group showed improvement in anxiety and dysphoria, no improvement in panic attacks or phobia was observed. When reversing the anti-exposure instruction, improvement was achieved over more variables.

Thus, it does seem reasonable to conclude that exposure is a necessary and essential ingredient in the treatment of PDA, and that adding auxiliary components have not provided a demonstrated efficacy.

The exception from this seems to be interventions not directed at individual psychopathological features, but rather at the social context of the patient by forming socially supportive groups (Hand et al., 1974; Sinnott et al., 1981) and intervening in spousal relationships (Jones, Sinnott & Fordham, 1980; Barlow et al., 1984; Arnow et al., 1985).

There has also been the hypothesis that the length of treatment is a critical variable, and that especially severely disabled agoraphobics would benefit from

longer treatments (Keijsers, Hoogduin & Schaap, 1994). While not providing a formal investigation, this topic could perhaps be the target of at least an indirect assessment when the percentage of patients that reached CSI on the Agoraphobia scale (Öst, 1990) is compared with the earlier studies that contained exposure treatment for PDA (Öst et al., 1984; Öst et al., 1993) and the present one. In the 1984 study, the proportion for the exposure group was 59%, and in the 1993 study it was 64%. In the present study, the exposure condition outperformed the earlier ones. Thus, both the E- and the CBT-group had better effects than the E-groups in the two previous studies, which could be due to a longer treatment (16 sessions à 60-90 minutes versus 12 sessions à 60 minutes). This does establish some credibility regarding treatment time as a crucial variable.

Prediction of outcome

Predicting outcome has an intuitive attraction for the clinician, and the goals that can be achieved from this process are often highly stated, as exemplified earlier (p. 29). But, in the area of behavioral treatments for PDA, few predictors consistently turn up. The basic dimension of severity of avoidance seems to be an exception (Basoglu et al., 1994; Keisers et al., 1994; Sharp & Power, 1999; Steketee & Shapiro, 1995). However, the ability to predict outcome itself bears no necessary implications of clinical relevance for designing treatment. Slaap and den Boer (2001) point out that socioeconomic class might be the most important predictor from pre-treatment observations. Does this imply that treatment of panic disorder should include interventions that help the patients to obtain better household incomes and education? Or perhaps to adopt the treatment in some other way for those economically disadvantaged? Neither of these propositions were raised by the authors, and understandingly so. Predictors need not by necessity inform us of what to do different in treatment.

Sharp and Power (1999) clearly pointed out the clinical utility as the ultimate purpose of prediction studies. The solution they proposed as a remedy was the use of a generally accepted criterion for clinically significant improvement (Jacobson & Truax, 1991), and using this as a categorical outcome divided at cut-off. This seems, at least by a statistical definition, reasonable in the sense of identifying those who get well and those who do not. But apart from losing statistical power, by using categorical outcome in prediction tasks (Hunter & Schmidt, 1980), it might otherwise influence the results in a predictable manner.

In our second study, we found that when predicting class membership as clinically significantly improved, agoraphobic severity was a significant negative predictor, and more substantially so at post-test than at follow-up. But if we then turn to the prediction of the magnitude of individual change during treatment, severity was a significant, though less influential predictor at post-test, but not at follow-up. Instead, duration was a significant negative predictor of change at follow-up.

Actually, when examining the results of Sharp and Power (1999), whose work is a larger study with greater statistical power, a similarity is evident. The four outcome variables: (i) anxiety; (ii) panic attacks; (iii) agoraphobic avoidance and (iv) a composite were predicted at post-treatment by (i) self-rated symptoms and higher

levels of extroversion; (ii) frequency of panic episodes and level of self-rated symptoms; (iii) severity of avoidance, and (iv) panic frequency, self-rated symptom intensity and social maladjustment for the composite. Basically, the variables predict themselves at post-test, in that those patients, who score higher at pre-treatment, show less likelihood of scoring outside the dysfunctional population at post-treatment. At six-month follow-up, the prediction capacity was reduced compared to end-point, but similar predictors were noted.

This is very much in line with our results, where a composite highly reflecting agoraphobia was used as outcome. Generally, the severity of a variable was the predictor of CSI for that variable. But, if the question instead is whether patients with a more severe condition gain less from behavioral treatment, then our study does not give an unambiguous confirmation, especially not regarding long-term follow-up. In terms of clinical usefulness, it is far from evident that a categorical criterion of this kind is more informative.

What did not emerge as important predictors in our second study might be somewhat surprising. We found no effect, whatsoever, from cluster C personality disorder, which could be expected from several studies (Chambless et al., 1992; Hoffart & Martinsen, 1993; Steketee & Shapiro, 1995). It should, however, be remembered that the detrimental effects of a simultaneous diagnosis of avoidant personality disorder is far from evident and the results are inconclusive (Dressen & Arntz, 1998; Chambless et al., 2000). Our study did use a structured interview by an independent assessor, which qualifies as one of the possible methods to meet the criteria set by Dressen and Arntz for "best evidence". Nevertheless, they also note that this is a method that tends to indicate less personality pathology, than when using self-rating instruments.

This line of reasoning does, however, risk falling prey to the same criticism that can be raised against trying to explain agoraphobic avoidance (which renders a more severe disorder with increasing level of dysfunction) with an increased frequency of responses in other variables that are closely connected to that which is to be explained. As demonstrated by Sturt (1981), more diagnostic features and more unusual responses are to be expected with increasing severity.

The conceptual difficulties with a diagnosis like avoidant personality disorder have been pointed out by Salkovskis and Hackman (1997), especially since it can be assumed to show a great deal of overlap with the concept "agoraphobia". It can never be an explanation of behavior to cite additional diagnostic signs, when no causal relationship is demonstrated. It gives no more than a further description. But, in the case of prediction, we also run the risk of merely ending up with another version of the basic dimension of pre-treatment severity as the key predictor.

Neither did we find that motivation or perceived credibility had any impact on outcome. From a common sense perspective, the assertion seems obvious that patients have to be motivated to change and believe in the treatment. However, motivation is, from a learning theoretical point of view, a problematic concept, in that it posits some kind of hypothetical inner construct that is subject neither to direct observation nor manipulation, but often used for giving an explanation. The concept "motivation" has also been problematic in behavioral therapies from an operational point of view. The Niemegen Motivation List (NML; Keijsers, 1994) tries to avoid any

mystical conceptions when regarding motivation for therapy as the joint product of (i) the extent of suffering; (ii) willingness to participate in treatment; (iii) pressure from others. However, the psychometric properties of the instrument are questionable. Likewise, perceived treatment credibility did not have any impact on outcome in our study, but here we have a problem with the restriction of range. The treatments were considered highly credible thus reducing variance and the likelihood of finding significant correlations.

Our study does support the view that severity of avoidance is a key determinant of outcome. But what does it inform us regarding the future development of behavioral treatments for PDA? Despite being a critical question based on clinical frequency and importance, Fava et al. (1997) noted that the issue of panic disorder being resistant to treatment has attracted little research. Their important study also gave an indication that the answer might be quite simple. They studied 21 patients with a DSM-IV diagnosis of panic disorder with agoraphobia, who failed to respond to a standard course of individual behavioral treatment based on exposure in vivo. Three modalities of additional treatment were compared: exposure alone, exposure with the addition of imipramine, and cognitive therapy supplementing exposure. The treatments were administered in a controlled crossover design. Twelve of the patients achieved clinical remission, 8 of these after exposure and two cases each for the other treatments. The two cases treated with imipramine relapsed 1 year after having discontinued the drug.

The logical step of being able to acquire a fuller picture of the effectiveness of exposure in vivo for panic disorder with agoraphobia could simply be to flexibly extend the time in therapy offered; thus, allowing for “late improvers” in the same vein as shown by de Hahn and co-workers (1997) for the treatment of OCD. A suggestion for future research would be to conduct effectiveness studies with flexible time limits in order to test the simple hypothesis that a greater level of pre-treatment severity is merely an indication of the need for a longer duration of therapy.

The therapeutic relationship

Related to the interest in developing treatments, according to the individual patient's requirements, lies the interest in studying the therapeutic relationship. Within the behavioral tradition the alleged interest for studying the therapeutic relationship has risen tremendously during recent years. Follette, Naugle and Callaghan (1996) noted that it had become customary in book chapters to state the importance of the therapeutic relationship in CBT, but without any kind of analysis of why and how this relationship is important. Two main objectives for the study of interpersonal factors in CBT can be stated: on a practical level, interpersonal strategies may be developed to enhance outcome, and, on a theoretical level, to develop the understanding of relational factors in CBT (Keijsers, Schaap & Hoogduin, 2000). Our main questions, in the third study, have emerged from an interest in the latter. We have chosen here to focus on the global trends in the material, but it should, of course, be acknowledged that the approach is correlational and mainly interpretative. The basic question bears some resemblance to Freud's struggle with the question as to what keeps the analysand in therapy in the face of

the psyche's unconscious fear and rejection of repressed material (Horwath & Bedi, 2002): what makes agoraphobic patients persist with exposure treatment, where they are confronted with stimuli that they have built a lifestyle around trying to avoid?

While we can confidently state that exposure treatment works, this treatment cannot be regarded as a mere technique. As every clinician that has worked this kind of therapy knows, it is a type of therapeutic work that is interpersonally demanding and requires effort to form a supportive and encouraging relationship with the patient. The concept "relationship" is often equated on a measurement level with the rated impression of the behavior of the other (therapist or patient) in therapy (e.g., Keijsers et al., 1991; Blaauw & Emmelkamp, 1994). We have chosen to refer to the observations as clients' and therapists' perceptions of each other. This is, of course, indeed a crucial factor in the relationship, but it is dubious to reduce the concept "relationship" to these perceptions.

Our study replicates a finding that seems consistent with several studies from the cognitive-behavioral area; namely, clients' ratings of their therapists tend to be severely skewed towards the positive end from early on in treatment (Williams & Chambless, 1990; Blaauw & Emmelkamp, 1994). As mentioned before, reduced variance regarding alliance has been noted in CBT in comparison to psychodynamic therapy (Raue et al., 1997). But it should also be noted that we used experienced therapists, who could be expected to show smaller between-therapist differences than less experienced therapists (Crits-Christoph et al., 1991).

This reduced variance poses a problem, which may account for moderate correlations to outcome. But, as Keijsers et al. (2000) have theorized, it might also indicate an important characteristic of how this relationship is formed based on high initial expectations largely established prior to therapy. And, as long as the therapist behaves within reasonable limits of these expectations, this positive view is kept intact and later successively replaced by a relationship based on the perceptions of the actual therapist. They point out that empirical evidence suggests that patients that are dissatisfied with their therapists do not merely respond poorly; they drop out of treatment.

We were able to observe a growing consensus between the respective ratings of the therapist and client throughout the therapy process. This was most pronounced between the client factor "attractiveness" and the therapist factors. It seems reasonable to interpret this as a process of growing mutual positive regard between client and therapist, which develops during the treatment process.

But if we instead look at the correlations with outcome, the clients' ratings were almost impressively unrelated. Moreover, the client factor that was least correlated with outcome was "attractiveness". So it seems that a mutual positive regard developed, but that this development was independent of the processes that did affect treatment outcome. In contrast, the therapists' ratings of the degree to which the client showed "goal direction" and "active participation" were, from session 4 onwards, rather consistently related to outcome.

Ultimately, we do not know exactly what behaviors the therapists assessed in these ratings. Was it an early treatment response regarding avoidance? This has previously been shown to be a strong predictor of the global improvement in treatment (Basoglu et al., 1994). Was this simply what could be regarded as

compliance with the treatment? As discussed earlier (p. 33), the estimation of compliance and its relation to outcome in behavioral treatments are not as self-evident as might be assumed. The findings from a structured treatment of panic disorder was that the therapists' and independent assessors' estimate of qualitative aspects of homework were good predictors of outcome (Schmidt & Woolaway-Bickel, 2000). This suggests a somewhat different direction than the passive connotations implied in the concept "compliance". But there is no way of conceptually making a clear-cut differentiation, in observational terms, between the working relationship, compliance with the idea of exposure or an early engagement in breaking avoidance in this process of change. Either way, it is a process of change that occurs in relation to a therapist.

The pattern we observed, in some ways, resembles the findings from Andrusyna et al., (2001), when analyzing observer ratings of working alliance in CBT for depression. They also studied experienced therapists and found that working towards mutually agreed goals and tasks in therapy represented a factor that was separate from the affective bond between therapist and client. The distinction between *a liking bond* and *a working bond* (Gelso & Hayes, 1998) might be more distinct in behavioral therapies.

Suggestions for future research would include studying the formation of the relationship in behavioral treatment. For instance, how this relationship relates to factors that are present before the patient enters therapy, like knowledge and expectancy of treatment. There is a need to develop valid means of assessing these relational factors and ultimately interventions designed to address these issues, when they pose a problem.

Turning to the estimate of the working alliance (WAI) at mid-treatment, it was basically unrelated to the ratings of therapist qualities. That could, at least, be taken as an indication that the scale did not merely capture a halo effect of the general appreciation of the therapist. The lack of relationship between WAI and outcome is in line with the results of Woody and Adessky (2002), who studied an exposure-based treatment approach for social phobia. These findings could, of course, be interpreted as an indication that working alliance, as conceptualized in the WAI, might have less importance in exposure-based therapies. This would be a notable exception in what has been the generic variable most consistently found related to outcome (Horwath & Bedi, 2002). However, caution should be taken with such conclusions from our study: the Swedish translation of the scale is of unknown psychometrical properties, and the variance between ratings was restricted in a positive direction. It is a notable finding in the present study that the "late improvers" did rate the working alliance higher than those who did not improve. But any interpretation must be considered speculative. It could, of course, reflect that a higher degree of perceived alliance served as a motivator to keep up the exposure work after having terminated the therapy. But it is not self-evident using Gelso and Hayes' (1998) more limited definition of the working alliance that the scale reflected the mutual alignment between therapist and client to observe, understand and do therapeutic work.

Regarding the two objectives stated for studying the therapeutic relationship in cognitive-behavioral therapies, our study does not suggest an immediate need to

include additional special ingredients that would exclusively focus on the interpersonal relationship between therapist and client. This is in line with the available empirical research, which suggests that therapists within the cognitive-behavioral tradition do show a great deal of skill in managing the therapeutic relationship (Keijsers et al., 2000).

An obvious weakness of the study was the failure to collect meaningful TCRS-data among dropouts. This could be explained by the fact that attrition occurred early, or that patients, who eventually dropped out, failed to return the rating scales to the therapist. Another key limitation is that it was made in an exploratory fashion, without theoretically derived specific hypotheses.

Like the observation made by Follette et al. (1996), it has become customary to state the importance of the therapeutic relationship at a superficial level that conveys very little sensible information and is compatible with almost any outcome and any theory. Another danger is that of reification (Rosenfarb, 1992), i.e., treating the relationship or alliance as though it were a thing or separate entity capable of causing outcome. Instead of reifying the relationship, in that sense, it could be considered as a context of learning and behavioral change.

Such a contextual analysis was provided by Follette et al. (1996). They suggested a learning theory account on how the therapeutic relationship can provide direct contingencies for learning functional behavioral repertoires that generalize a wide variety of situations. However, this is exemplified with patients seeking professional help for explicit difficulties in relationships. PDA has important social features (Pollard & Cox, 1988; de Jong & Bouman, 1995), but can never be understood without considering the established aversive functions of stimuli like public transportation, elevators, bridges, etc., which need not have an essential interpersonal component. Bouton et al. (2001) assert that contextual factors can have important determining functions of reducing the ambiguity of aversive stimuli. To paraphrase that assertion, the therapeutic context could have an important function by introducing ambiguity, not only by stressing the possibility of approaching avoided stimuli, but also stressing the outright desirability of this approach. It does so, not only by direct social reinforcement, but also largely by establishing new verbal functions through planning goals and providing instructions and an explanation. The comprehensive behavioral account for these contingencies of therapeutic learning is, as far as is known, still waiting to be laid out.

Aspects of change

The hypothesis that panic attacks do have an etiological function in the development of agoraphobia, at least in clinical samples, must be considered well validated (Thyer & Himle, 1985; Craske & Barlow, 1988). But it must be borne in mind that for maintaining the disorder, a clear-cut relationship between panic and avoidance has not been demonstrated (Street et al., 1989; Telch et al., 1989; Cox et al., 1994). Instead, avoidance seems more closely linked to general anxiety and expectancy of panic (Craske et al., 1988). This expectancy has showed signs of being rather general (Cox et al., 1995) and displaying trait-like features (Rodebaugh et al.,

2002). Still, since the development of CBT for panic attacks has progressed, it has often been the panic-attacks that are the focus of outcome research (e.g., Gould et al., 1995). And, as Barlow (2002) noted, much of this research has routinely excluded agoraphobic subjects from trials on panic disorder; thereby, not only limiting the generality of these results, but also excluding the majority of patients that would come under the concept "panic disorder". Williams and Falbo (1996) did find that those with greater agoraphobic avoidance achieved less of an effect on panic than those with more circumscribed avoidance.

The elimination of panic attacks and panic-related avoidance has been described as the desired results of treatment of PDA (Gould et al., 1995). Behavioral treatments of PDA have been shown to affect these two areas, and a broad range of outcome variables that cover diverse additional areas (e.g., Telch et al., 1995; Study I). However, the mutual dependency of panic and avoidance is still far from evident, and it is neither apparent that these processes change together during treatment, nor which one of them is of greatest clinical importance.

Our study contained during a three-week baseline period the detailed prospective registration of panic-attacks, which is considered more accurate than retrospective estimates (Sharp & Power, 1999). During pre-treatment baseline observation, a substantial proportion of the patients, who all fulfilled the DSM-IV diagnosis of PDA, did not report any panic attacks (21%). Apart from a difference in mood ratings, no significant differences were obtained between "panickers" and "non-panickers" at pre-treatment. Of special importance was that "non-panickers" did not rate their agoraphobic avoidance as significantly less, and nor did they perform better on the BAT. This is in accordance with the rather common finding that the mere presence of panic attacks is loosely related to the degree of agoraphobic avoidance (Cox et al., 1995). This also gives an indication that reporting not experiencing panic was simply not due to a more extensive avoidance of situations associated with them. It is especially noteworthy that the retrospective ratings of panic attacks in the weeks before the baseline measurement period were not significantly different between these two groups. This could, of course, be taken as an indication that there was a difference that became visible during the measurement period and the task of performing behavioral approach tests. But it seems implausible that this would be a condition that would reduce panic in some subjects. It seems more reasonable to take this as a serious reminder of the uncertainty that is inherent in data based on retrospective ratings.

At post-treatment the percentage reporting panic attacks was drastically decreased, but again, there was a significant difference in the mood of "panickers" and those who were panic-free. At this point, there was also a significant difference regarding the retrospectively rated panic attacks. Since a significant component in treatment could be considered as training in the discrimination of panic attacks, this might account for the fact that the retro- and prospective ratings were more coherent. Nevertheless, regarding the rest of the variables, there were no significant differences between those who were panic-free, and those who were not. However, at 1-year follow-up, there was a much more complete picture of the different aspects of the results. While being panic-free seemed to be a more isolated aspect of outcome at

post-treatment that conveyed relatively limited information of the more generalized aspects of the disorder, it seemed to be more pervasive at follow-up.

The convention of letting the results focus on percentage of panic-free individuals has been criticized (Telch et al., 1995). Our results do fall in line with the argument that it might not be the ultimate way to convey information of clinical change in this group of patients, at least not directly after treatment.

Regarding the amount of change that could be predicted from panic to avoidance, our study basically replicates the findings of Craske et al. (2003). They reported that 12 % of the variance of change in agoraphobia at post-treatment and 21 % at follow-up was predicted by change in panic frequency. In the present study, these figures were 12 % and 26 % respectively. While no causal direction can be demonstrated, this gives, at least, an indication that these two change processes are not independent. However, it does not tell us anything about the other aspects of the disorder, and the change processes in these. When looking at change in the more generalized negative affect, this was more closely linked to change in avoidance, both at post-treatment and follow-up. Furthermore, change in panic was not related to change in quality of life at post-treatment, while change in avoidance was significantly so. In the Telch et al. (1995) study, impairment in quality of life (QOL) was neither related to panic frequency at baseline, nor was change in QOL related to change in panic after treatment or at follow-up. Instead, anxiety and phobic avoidance were related to indices of QOL, and changes in anxiety were the most potent predictor of changes in QOL. Our results are in agreement with the view that change in panic does not correlate with change in QOL at post-treatment. However, at 1-year follow up, this picture had changed. It should be noted that the Telch et al. study had a shorter follow-up period (6 months). As noted earlier, at follow-up there was a much more complete picture regarding outcome and the patients that reported panic attacks at follow-up, some of which should be considered “relapsers”, did rate their quality of life very low. The limitations of study 4 should readily be pointed out. The study is correlational and does not establish the causal direction in the relationships studied. The limited statistical power also prevents a more thorough study of some of the complexities of these relationships.

However, in line with Telch et al. (1995), the clinical implications of the present study would suggest that the mere elimination of panic attacks might not be the most crucial clinical target for this group of patients. Change in avoidance seems to affect a broader range of the clinical aspects studied here, especially negative affect. This would be quite logical considering that the severity of avoidance has been found to be associated with generally more clinical distress, but not with the frequency of panic attacks (Cox et al., 1995). It is also reasonable given the experimental research that does support the view that avoidance is not only an ineffective, but also a toxic strategy in managing unwanted private experiences that are associated with increased anxiety (Levitt et al., 2004; Eifert & Hefner, 2003).

It is important to note that this is not an argument that counters the assertion of the etiological function of panic attacks for agoraphobic avoidance. On the contrary, our data is consistent with the hypothesis that for long-time maintenance, the management of panic attacks might have a more crucial role. Early on, Gelder and Marks (1966) noted that a single panic attack might well undo weeks of training.

For the vast majority of PDA subjects who relapse, panic has been identified as the first symptom to reach the levels of intensity necessary for relapse classification in naturalistic follow-up (Keller et al., 1994). Also, in a clinical trial, panic attacks were found to precipitate relapse (Michelson et al., 1996).

But reasoning in line with the theory of Bouton et al. (2001), where panic attacks are considered non-specific stress reactions quite commonly expected in the population, the focus on the mere presence of panic attacks, per se, as outcome criteria, makes little sense. Rather, the disruptive features of a panic attack on the person's behavior would seem more crucial. Or, as insightfully stated by Ferster (1972): "Thus behaviorally and clinically, a phobia is not so much one kind of behavior as it is a change in a substantial part of the person's total repertoire. (...) The patient that can react differentially and specifically to that part of his natural environment that is upsetting him is a step away from acting on it to free himself from the disruption." (p. 5). Indeed, one of the difficulties for agoraphobic patients that Goldstein and Chambless (1978) observed clinically was appropriately attributing the source of the distressing feelings. These aspects could be assumed to be crucial for long-term outcome. Recommendations for future research would be to conduct studies that involve the close monitoring of panic attacks, avoidance and related features during the treatment process and follow-up. This would allow taking the temporal sequence into consideration and change processes could be subject to a closer scrutiny.

When the goals for behavioral therapies are set as the elimination of panic attacks and panic-related avoidance (Gould et al., 1995), it fosters a perspective, where treatment essentially seems to be considered an eliminative process (Forsyth, 1999). This is in a way a strange position, from a behavioral point of view, that the learning process in therapy should result in less, rather than more behavior. The study of what kind of changes people do in their lives at large, during and after therapy, is sadly neglected in the field of behavioral treatment of PDA. Our study gives an indication that the post-therapy process is rather profound and generally beneficial. However, a more thorough description of these changes in peoples' lives would be an important topic of investigation. We need to remind ourselves that the change processes that occur after the termination of the therapy are the ultimate test of our ability to write a "success story".

Conclusions

To briefly summarize, the main findings in this thesis are as follows:

- The addition of cognitive techniques did not add a substantial beneficial effect to the basic exposure treatment for patients with panic disorder with moderate to severe agoraphobia. Treatment effects were observed over a wide variety of measurement areas, and were well maintained at one-year follow-up.
- Pre-treatment severity of avoidance was a significant predictor of outcome. This was especially evident when outcome was considered in terms of

clinically significant improvement as a categorical variable. When considering the degree of individual change as a continuous variable, severity did not significantly predict outcome at follow-up.

- Clients generally rated their impressions of the therapists very favorably during the treatment and a growing consensus between clients' and therapists' ratings of each other was observed during treatment. This could be understood as a process of mutual positive regard. This process was not related to variations in outcome. Instead, the therapists' perception of clients showing goal-direction and active participation was related to outcome from early on in the treatment.
- The change in panic and in phobic avoidance was, to some extent, related to each other after treatment, and more so at follow-up. When categorizing subjects as panic-free or not, these groups failed to show a significantly different outcome on a number of variables at post-treatment. Rather, change in avoidance seemed to be related to a broader spectrum of clinical change, than change in panic at post-treatment. At one-year follow-up, clinical change showed a more unitary picture.

9. References

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