Panic! Its Prevalence, Diagnosis and Treatment via the Internet

BY

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Abstract
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As evidenced by several trials, cognitive behavior therapy (CBT) is a highly effective treatment for Panic disorder with or without agoraphobia (PD). However, therapists are short in supply, and patients with agoraphobia may not seek therapy due to fear of leaving their homes or traveling certain distances. A major challenge therefore is to increase the accessibility and affordability of evidence-based psychological treatments.

This thesis is based on five studies; three treatment studies set up as randomized controlled trails (RCT), one prevalence study, and one study testing the equivalence of an Internet-administered diagnostic assessment tool with a clinician-administered interview.

Study I showed that the Swedish 12-month PD prevalence is consistent with findings in most other parts of the Western world (2.2%; CI 95% 1.0%-3.4%). There was a significant sex difference, with a greater prevalence for women (3.6%) compared to men (0.7%).

Study II showed that the validity of the computerized diagnostic interview (CIDI-SF) was generally low. However, the agoraphobia and obsessive-compulsive disorder modules had good specificity and sensitivity, respectively.

The three RCTs showed, directly or indirectly, that Internet-based self-help is superior to a waiting-list. When 10 individual weekly sessions of CBT for PD was compared with a 10-module self-help program on the Internet, the results suggest that Internet-administered self-help, plus minimal therapist contact via e-mail, is as effective as traditional individual CBT (80% vs. 67% no longer met criteria for panic disorder; composite within-group effect size was Cohen's d= 0.78 vs. 0.99). One-year follow-up confirmed the results (92% vs. 88% no longer met criteria for panic disorder; d= 0.80 vs. 0.93). The results generally provide evidence to support the continued use and development of Internet-distributed self-help programs.

Keywords: panic disorder, self-help techniques, agoraphobia, bibliotherapy, internet, randomized controlled trail, prevalence, screening

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To Sara, Alva, and Stina

List of Papers

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals.

I. Carlbring, P., Gustafsson, H., Ekselius, L., Andersson, G. (2002) 12-month prevalence of panic disorder with or without agoraphobia in the Swedish general population. *Social Psychiatry and Psychiatric Epidemiology*, 37(5): 207-211

II. Carlbring, P., Forslin, P., Ljungstrand, P., Willebrand, M., Strandlund, C., Ekselius, L., Andersson, G. (2002) Is the Internet-administered CIDI-SF Equivalent to a Clinician-administered SCID Interview? *Cognitive Behaviour Therapy*, 31(4): 183-189

III. Carlbring, P., Westling, B E., Ljungstrand, P., Ekselius, L., Andersson, G. (2001) Treatment of panic disorder via the Internet: A randomized trial of a self-help program. *Behavior Therapy*, 32(4): 751-764

IV. Carlbring, P., Ekselius, L., Andersson, G. (2003) Treatment of panic disorder via the Internet: a randomized trial of CBT vs. applied relaxation. *Journal of Behavior Therapy and Experimental Psychiatry*, 34(2): 129-140

V. Carlbring, P., Nilsson-Ihrfelt, E., Waara, J., Kollenstam, C., Buhrman, M., Kaldo, V., Söderberg, M., Ekselius, L., Andersson, G. Treatment of Panic Disorder: Live Therapy vs. Self-Help via Internet. (submitted)

Contents

Abbreviations

ACQ	Agoraphobic Cognitions Questionnaire
ANOVA	Analysis of variance
APA	American Psychiatric Association
AR	Applied Relaxation
BAI	Beck anxiety inventory
BDI	Beck depression inventory
BSQ	Body Sensations Questionnaire
CBT	Cognitive-Behavioral Therapy
CD	Compact Disc
CIDI	Composite International Diagnostic Interview version 2.1
CIDI-SF	Composite International Diagnostic Interview Short-Form
DSM-III-R	Diagnostic and statistical manual of mental disorders (3 rev ed.)
DSM-IV	Diagnostic and statistical manual of mental disorders (4 ed.)
DSM-IV-TR	Diagnostic and statistical manual of mental disorders - Text Revision (4 ed.)
ES	Effect size (Cohen's *d*)
GAD	Generalized Anxiety Disorder
HADS	Hospital Anxiety and Depression Scale
MADRS	Montgomery-Åsberg Depression Rating Scale; self-rated version
MI	Mobility Inventory for Agoraphobia
MI-Ac	Mobility Inventory for Agoraphobia – subscale: when clients are *accompanied*
MI-Al	Mobility Inventory for Agoraphobia – subscale: when clients are *alone*
OCD	Obsessive-Compulsive Disorder
PD	Panic Disorder with or without Agoraphobia
QOLI	Quality of life inventory
SCID	Structured Clinical Interview for DSM-IV Axis I Disorders, research version
Sd	Standard Deviation
SMS	Short Message Service
SSRI	Selective serotonin reuptake inhibitors
WHO	World Health Organization
WWW	World Wide Web

Introduction

Panic attacks, Panic Disorder, and Agoraphobia

Diagnosis

According to the American Psychiatric Association (APA; 2000) a *panic attack* is a discrete period of intense fear or discomfort in the absence of real danger that is accompanied by at least 4 of 13 symptoms. The symptoms can be somatic and/or cognitive in nature and include (1) pounding heart or accelerated heart rate, (2) sweating, (3) trembling or shaking, (4) sensations of shortness of breath or smothering, (5) feeling of choking, (6) chest pain or discomfort, (7) nausea or abdominal distress, (8) feeling dizzy, unsteady, light headed or faint, (9) derealization or depersonalization, (10) fear of going crazy or losing control, (11) fear of dying, (12) numbness or tingling sensations, and (13) chills or hot flashes. The symptoms must develop abruptly and reach a peak within 10 minutes. The attack is often associated with a sense of imminent danger or impending doom and an urge to escape. When asked, most patients say that their panic attacks peak within seconds or minutes, usually within five minutes. Patients further report that actual panic attacks last up to thirty minutes, but rarely longer, and are often followed by a high level of anxiety (Zuercher-White, 1997).

Although panic attacks can occur as a part of all anxiety disorders, *panic disorder* is distinguished by the occurrence of unexpected, often seemingly uncued or "out of the blue" panic attacks. This must be followed by at least one month of persistent concern about having another panic attack, worry about the possible implications or consequences of the panic attacks (e.g., having a heart attack, going crazy), or a significant behavioral change related to the attacks (e.g., more frequent medical check ups, cutting back on work). As with the other anxiety disorders, the symptoms cannot be the direct result of the effects of a substance (e.g., caffeine) or a general medical condition (e.g., hyperthyroidism, hypoglycemia).

Agoraphobia usually develops as a consequence of full or subclinical panic disorder. According to the American Psychiatric Association (APA; 2000) agoraphobia is anxiety about being in places or situations from which escape may not be available in the event of having a panic attack or panic-like symptoms. Factor analytic studies have revealed that agoraphobia is composed of several, but distinct factors including fear of public places, fear of open spaces, and claustrophobia (Taylor, 2000). People with agoraphobia tend to fear and avoid a wide range of situations, including being at home alone or being outside the home.

It should be noted that agoraphobia can be diagnosed as an individual separate diagnosis. However, since over 95 per cent of all individuals who present with agoraphobia in clinical settings also have a current (or history of) PD, the validity of the DSM-diagnosis agoraphobia without history of panic disorder has been questioned. Hedley and Hoffart (2001) reviewed research papers, including population-based as well as clinical studies, and found that inconclusiveness of the research together with methodological deficits do not constitute sufficient evidence to conclude that agoraphobia without history of panic disorder is a separate category.

Prevalence

Since panic disorder was introduced as an official psychiatric diagnosis in the third edition of the Diagnostic and statistical manual of mental disorders (DSM-III; APA, 1980), several epidemiological studies have estimated its prevalence. However, different diagnostic procedures, different samples, and different criteria in defining caseness have been used, and it is impossible to ascertain whether different prevalence rates found in various countries reflect procedural variations or true differences in prevalence.

An overview of the published prevalence studies is given in Table 1. As shown in the table, the 12-month prevalence of panic disorder ranges from a high of 2.3% in one USA study to a low of 0.2% in Taiwan. With Puerto Rico as the only exception, the female-male ratios are always greater than 1. There is often a two-to-one female-to-male ratio, which in some instances reaches statistical significance. According to White and Barlow (2002) the two-to-one female-to-male ratio is consistently found in both community and clinical studies around the world, and both in patients presenting for treatment and those participating in random samples of the population.

According to APA (2000) between 33 to 50 per cent of individuals diagnosed with panic disorder also have agoraphobia. Yonkers and colleagues (Yonkers et al., 1998) has shown that there is no difference between men and women in panic symptoms or level of severity at baseline.

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However, women are more likely to have panic with concurrent agoraphobia, while men were more likely to have uncomplicated panic.

Although PD is generally thought to be rare in children and adolescents (e.g., APA, 2000; Nelles & Barlow, 1988; Reed & Wittchen, 1998), the prevalence of PD in community samples was recently re-estimated to be between 0.5% and 5.0%, and in pediatric psychiatric clinics from 0.2% to 10% (Diler, 2003). Panic attacks were reported to be equally prevalent in boys and girls.

Onset and Course

Panic disorder is generally a disorder of adulthood, and is often described as a chronic but waxing and waning disorder. Age at onset varies considerably. Bruke, Bruke, Regier, and Rae (1990) reported that the median age of onset was 24 years. However, it has been speculated that there is a bimodal distribution. In the Epidemiological Catchment Area study (Eaton, Kessler, Wittchen, & Magee, 1994) the age of onset was either between the ages 15 and 24 or 45 and 54. In contrast, the APA (2000) put onset of PD between late adolescence and mid-30s. Only about 25 per cent of PD sufferers seek treatment (Lidren et al., 1994). For those who do, the average age is 34 years when seeking treatment (White & Barlow, 2002).

The initial panic attack typically occurs in agoraphobic situations and often in the context of some form of stressful life event (e.g., traveling on a bus when under interpersonal, financial, or occupational stress). White and Barlow (2002) reported that 70 per cent of the individuals can describe identifiable stressors at panic attack onset. Taylor (2000) emphasized that stressors do not invariably lead to panic disorder, but that stressful life events play a non-specific role in the development of psychopathology. Contrary to some beliefs (e.g., Milrod, 1995) childhood incest does not appear to be a major factor in the etiologies of panic disorder and agoraphobia (Gogoleski, Thyer, & Waller, 1993).

Seasonality may play a role in the onset of PD. Lelliott and colleagues found that more people had their first panic attacks in late spring and summer than in fall and winter (Lelliott, Marks, McNamee, & Tobena, 1989). Schmidt-Traub and Bamler (1997) have suggested that a possible explanation could be allergies. Vasodilatation (often approaching circulation collapse) is a frequently occurring allergic syndrome that is a very dramatic experience. The association between PD and allergic (vasomotor) reactions has been found to be highly significant. A functional relationship is hypothesized in terms of conditioning cognitive and vasomotor interactions during autonomic arousal. There are also documented associations between anxiety disorders and allergy in children (Kovalenko et al., 2001). Compared

to nonallergic persons with PD, allergic individuals had more full-blown situational panic attacks (Kennedy, Morris, & Schwab, 2002).

Heredity

Reviews of studies examining the genetic etiology of panic disorder show the familial nature of the disorder and clearly demonstrate genetic influence. Strong evidence for vertical transmission in family studies led to molecular genetic studies, among which association designs appear promising, particularly when based on trait markers (van den Heuvel, van de Wetering, Veltman, & Pauls, 2000).

   According to the DSM-IV-TR source book, twin studies suggest a genetic contribution to PD. In a meta-analysis by Hettema, Neale, and Kendler (2001) of all available large-scale twin studies for panic disorder, heritability was estimated at 0.43. The remaining variance in liability was attributed primarily to nonshared environment.

   Furthermore, first degree biological relatives of individuals with PD are up to 8 times more likely to develop PD. Should the age at onset of PD be before 20, first relatives have been found to have a twenty-fold risk of having PD (APA, 2000). Anxiety sensitivity, which has a familial-genetic influence, has been proposed as one contributor to the higher risk of PD in certain families (van Beek & Griez, 2003).

Table 1. The prevalence of panic disorder with or without agoraphobia.

Location/Study	Prevalence (%)				Female/Male ratio	Diagnostic criteria	Assessment	Sample size (response rate)	Reference (first author only)
	Life	12 mo	6 mo	1 mo					
Africa									
Lesotho				4.2	9.1**	DSM-III	DIS	456 (78%)	Hollifield, 1990
America									
Canada (Edmonton)	1.2-1.4 [A]	0.7-1.2 [A]	0.7	0.4	2.1* / 2.5	DSM-III	DIS	3258-4550 (72%)	Newman, 1994; Dick, 1994; Bland, 1988a,b; Weissman, 1997
Puerto Rico	1.7		1.1		1.2 / 0.8	DSM-III	DIS	1701 (91%)	Canino, 1987
Nationwide USA		1.2			3.6	DSM-III	SCL[B]	3161 (76%)	Uhlenhuth, 1983
USA (ECA[C])	1.6			0.5	2.1 / 2.0	DSM-III	DIS	19501 19498	Eaton 1995
USA (All ECA[C] sites)	1.6		0.8	0.5	2.3*	DSM-III	DIS	18571 (68-79%)	Regier, 1988
USA (48 states)	3.5	2.2-2.3 [A]		1.5	2.5-2.7 [A] / 2.5 / 2.5	DSM-III-R	CIDI	8098 (82-84%)	Kessler, 1994; Eaton, 1994; Weissman, 1997
USA (New Haven, Conn)	1.4		0.6	0.4	3.0-3.5 [A]	DSM-III	DIS	3058 (76-80%)	Myers, 1984; Regier, 1988; Wittchen, 1992; Von Korff, 1985

Table 1. (Continued)

Location/Study	Prevalence (%)				Female/ Male ratio	Diagnostic criteria	Assess ment	Sample size (response rate)	Reference (first author only)
	Life	12 mo	6 mo	1 mo					
America Cont…									
USA (Baltimore)	1.5		1.0	0.7	1.5	DSM-III	DIS	3481 (76-80%)	Myers, 1984; Regier, 1988; Wittchen, 1992
USA (St Louis)	1.5		0.9	0.6	1.4	DSM-III	DIS	3004 (76-80%)	Myers, 1984; Regier, 1988; Wittchen, 1992
USA (Los Angeles)	1.5		0.9	0.6	2.6-4.8[D]	DSM-III	DIS	3132 (68%)	Karno, 1987; Burnam, 1987; Regier, 1988
USA (Piedmont & Durham, NC)			0.7	0.5				3921 (77-79%)	Burnam, 1987; Regier, 1988
USA (San Antonio, Tx)	3.8				2.7*	DSM-III-R	SCID	1683 (78%)	Katerndahl, 1993
Asia									
Korea	1.7	1.5			5.8	DSM-III	DIS	5100 (83%)	Lee, 1990; Weissman, 1997
S Korea (Seoul)	1.1					DSM-III	DIS	N/a	Wittchen, 1992
Taiwan	0.2-0.4[A]	0.2			1.6-3.7[E]	DSM-III	DIS	11004 (90-99%)	Hwu, 1989; Weissman, 1997

Table 1. (Continued)

Location/Study	Prevalence (%)				Female/ Male ratio	Diagnostic criteria	Assessment	Sample size (response rate)	Reference (first author only)
	Life	12 mo	6 mo	1 mo					
Australia									
New Zealand (Christchurch)	2.1-2.2 [A]	1.3-1.4 [A]	1.1	0.4	3.7**-4.7 [A]	DSM-III	DIS	1498 (70%)	Wells, 1989; Weissman, 1997; Wittchen, 1992; Oakley-Brown, 1989
					3.4				
Europe									
France (Savigny)	2.2	0.9			2.3	DSM-III	DIS	1746 (63%)	Weissman, 1997
Germany (Munich)	2.4		1.1		1.7	DSM-III	DIS	657 (74%)	Wittchen, 1992
Germany	2.6	1.7			2.7	DSM-III	DIS	481 (76%)	Weissman, 1997
Italy (Florence)	2.9	1.3			3.2	DSM-III	DIS	1100 (100%)	Weissman, 1997
UK (Leicester)				3.2	N/a	DSM-III-R	Postal survey [F]	1500 (54%)	Stirton, 1988
Sweden		2.2			5.1*	DSM-IV	CIDI	1000 (63%)	Study I
Middle East									
Lebanon (Beirut)	2.1	2.1			2.8	DSM-III	DIS	234 (77%)	Weissman, 1997

Differential diagnosis and Co-morbidity

The diagnosis of PD rarely occurs in isolation. According to White and Barlow (2002) more than 50% of the individuals with PD suffer from at least one other comorbid disorder. In 1994 Kessler and colleges (1994) conducted a large National Comorbidity Survey (NCS). The NCS was administered to 8,098 respondents (aged 15-54 yrs) in face-to-face interviews in a nationally representative survey of the prevalences and correlates of major Mental Disorders-III-Revised (DSM-III-R; APA, 1987) disorders in the US population. Strong lifetime and current comorbidity were found between panic and depression.

About half of the subjects with lifetime panic attack and panic disorder also met lifetime criteria for depression, whereas about one fifth of the subjects with lifetime depression reported a lifetime panic attack and one tenth met lifetime criteria for panic disorder. Temporally primary depression predicted onset of panic attacks, and temporally primary panic attacks with or without panic disorder predicted onset of depression.

Comorbidity was associated with greater symptom severity, persistence, role impairment, suicidality, and help-seeking, with many findings persisting after controlling for additional comorbid diagnoses. Findings did not differ according to which disorder was chronologically primary (Kessler, Stang et al., 1998; Roy Byrne et al., 2000). It has been suggested that PD and depression share well-defined disturbances in hypothalamic-pituitary-adrenal axis function, serotonergic neurotransmission, and growth hormone response to pharmacological challenge (Gorman & Coplan, 1996).

Other common psychological disorders comorbid with PD included other anxiety disorders, substance use disorders, and personality disorders (Chantarujikapong et al., 2001). It has been estimated that between 25 and 64 per cent of individuals with PD also meet the criteria for an axis II personality disorder, usually dependent, avoidant, or histrionic personality disorder (White & Barlow, 2002).

Although initial studies suggested that patients with comorbid panic disorder and depression have a poorer treatment outcome, recent data show

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similar outcomes for patients with both disorders and for those with panic disorder uncomplicated by depression (Gorman & Coplan, 1996).

In a replication and extension of Brown, Antony, and Barlow's study (1995), Tsao and colleagues examined the effects of CBT for panic disorder on comorbid conditions (Tsao, Lewin, & Craske, 1998). Following CBT, there was a significant reduction in the number of patients with at least one additional diagnosis. The greatest declines were found in comorbid social phobia and generalized anxiety disorder. Severity ratings also declined significantly from pre- to posttreatment for comorbid social phobia, generalized anxiety disorder, and posttraumatic stress disorder and were marginally significant for depression. However, there was a trend for axis I comorbidity to reduce the likelihood of reaching substantial improvement in panic disorder following treatment. According to Hecker, Losee, Fritzler, and Fink (1996) the presence of a comorbid axis II personality disorder is also associated with poorer outcome in studies of panic disorder and agoraphobia.

Recently, Zvolensky and colleagues have found that a disproportionate number of persons with PD smoke cigarettes compared to individuals with other anxiety disorders and people in the general population (Zvolensky, Schmidt, & Stewart, 2003). At the onset of their illness, 51.6% of persons with PD were smokers and 36.8% were regular smokers (Zvolensky, Schmidt, & McCreary, 2003). Currently, there is little theoretical or empirical understanding as to how smoking impacts those with PD. However, it has been suggested that anxiety sensitivity may moderate the relation between level of smoking and prototypical panic psychopathology variables (panic attacks and agoraphobic avoidance) even after controlling for the theoretically-relevant factors of alcohol abuse and negative affect (Zvolensky, Kotov, Antipova, & Schmidt, 2003). Hence, there is a need to assess smoking among persons with panic disorder and a potential need for specialized treatment approaches.

Psychological models of PD

According to the National Institute of Health, the Panic Disorder Practice Guideline Work Group, and the Steering Committee on Practice Guidelines of the American Psychiatric Association, PD can be treated effectively with either cognitive-behavioral therapy or pharmacological therapy (APA, 1998; National Institute of Health, 1991). These two treatments represent very different theoretical views. Pharmacotherapy is based on the premise that disturbed biochemical and physiological mechanisms in the brain cause PD. Accordingly, brain chemistry is targeted with medication. In contrast, cognitive behavior theory proposes that some individuals greatly fear anxiety

symptoms and thus interpret them catastrophically. Although the explanations are different, the neurofunctional changes underlying effective antianxiety treatments appear to be common to both when measured with regional cerebral blood flow (cf. Furmark et al., 2002).

There are many other theories, models and suggested treatments of PD. Some examples are *Psychoanalytic theory* (e.g., Milrod, 1995), *Psychodynamic* (e.g., Hoffart, 2001; Milrod et al., 2001; Schwartz, 1994; Shear, Cooper, Klerman, Busch, & Shapiro, 1993; Grant, 1997), *Hypnosis* (e.g., Stafrace, 1994; Van Pelt, 1975; Wild, 1994), *Japanese Kampo herbal* (e.g., Mantani et al., 2002), *Humanistic-existential* (e.g., Matheson, 1998), *Holistic* (e.g., Alfonso & Dziegielewski, 2001), *Eye movement desensitization and reprocessing* (EMDR; e.g., Feske & Goldstein, 1997), *Interpersonal Psychotherapy* (e.g., Weissman & Markowitz, 1998), *Rational Emotive Therapy* (e.g., Singh & Banerjee, 2002), *Mindfulness meditation* (e.g., Kabat Zinn, Massion, Kristeller, Peterson, & et al., 1992; Miller, Fletcher, & Kabat Zinn, 1995), *Acceptance and Commitment Therapy* (e.g., Eifert & Heffner, 2003; Lopez, 2000), *the Match-mismatch model* (e.g., De Beurs, Chambless, & Goldstein, 2002; Rachman & Lopatka, 1986a, 1986b), *Classical conditioning* (e.g., Sanderson & Beck, 1989; Wolpe & Rowan, 1988, 1989), *Psychobiological* (e.g., Ashcroft, Walker, & Lyle, 1993), *Psychophysiological* (e.g., Margraf & Ehlers, 1989), *False suffocation* (Klein, 1993), *Ley's model* (e.g., Moynihan & Gevirtz, 2001), *the Neuroanatomical hypothesis* (e.g., Gorman, Kent, Sullivan, & Coplan, 2000), and *Beta-Adrenergic* (e.g., Pohl, Yeragani, Balon, Ortiz, & Aleem, 1990).

However, the treatment tested in this thesis is limited to the major cognitive behavioral models. This is because the effect of the treatment that has sprung from the CBT-models is empirically well established[1]. Today, the two dominating models are Clark's cognitive model (Clark, 1986) and Barlow's biopsychosocial model (Barlow, 2002). Actually the two models are not vastly different, and can be seen as variations of the same model,

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[1] It should be noted that objections have been raised that the exclusive reliance on randomized clinical trials has generally favored CBT and that there is reason to evaluate alleged empirical support with caution (e.g., Sandell, 2001). Sandell (2001) argued for a suitability matching approach to empirical validation, where each treatment is tested, as powerfully as feasible, on samples based on self-selection. On the other hand, voices have also been raised (e.g., Rosen & Davison, 2003) that the current systems for listing empirically supported therapies (ESTs) provide recognition to treatment packages, many of them proprietary and trademarked, without regard to the principles of change believed to account for their effectiveness. Rosen and Davison's (2003) position is that any authoritative body representing the science and profession of psychotherapy should work solely toward the identification of empirically supported principles of change (ESPs). As challenging as it is to take this approach, a system that lists ESPs is suggested to keep a focus on issues central to the science and practice of psychotherapy while also insulating the profession from undue entrepreneurial influences.

with slight dissimilarity in the emphasis of different components. As both models stress that panic attacks are the result of a combination of stress, arousal, biological and psychological vulnerability factors, hyperventilation, conditioning processes, and avoidance behaviors, only one model will be described (i.e. Clark's Cognitive Model).

Clark's Cognitive Model

In 1986, Clark published a cognitive model trying to explain the process by which panic attacks occur (see Figure 1). Within this model, Clark argued that panic attacks result from the catastrophic misinterpretation of certain benign arousal-related bodily sensations. The sensations which are misinterpreted are mainly those involved in normal anxiety responses (e.g., pounding heart or accelerated heart rate, sensations of shortness of breath or smothering, feeling light headed or faint) but can also include some other sensations (e.g., sensations produced by physical activity or caffeine; Uhde, 1995).

The catastrophic misinterpretation involves perceiving these sensations as much more dangerous than they really are (Clark, 1986). That is, when a person experiences palpitations, for example, it is taken as evidence of an impending heart attack, or unusual thoughts are perceived as a sign of impending loss of control or insanity. This causes the person to become further alarmed, convinced that the catastrophe is imminent. In a vicious cycle the interpretations feed the anxiety which in turn gives rise to more physiological symptoms which boosts the conviction of a forthcoming disaster.

According to operant theory (e.g., Thompson, Iwata, Hanley, Dozier, & Samaha, 2003) extinction would eventually correct a non reinforced behavior. However, the enduring tendency to interpret certain bodily sensations in a catastrophic fashion is maintained by two processes; selective attention and avoidance and safety behaviors (Clark & Ehlers, 1993).

Because the person is frightened of certain sensations (as they signal danger) he/she becomes hypervigilant and repeatedly scans his/her body (Richards, Cooper, & Winkelman, 2003). This internal focus of attention allows him/her to notice sensations more readily. Often the patient tries to avoid situations where the likelihood of eliciting these symptoms is heightened. However, if the sensations cannot be avoided they are taken as further evidence of the presence of some serious physical or mental disorder. In order to minimize the risk of a bad outcome the person often engages in safety behaviors (Clark, 1997). An example of a safety behavior is having a bottle of water near by to drink to avoid suffocating. Another example is only doing things with a safe person. This is because individuals suffering from PD often have a basic concern to have other people available to help

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them if they should have a panic attack. Research has shown that there indeed is a recognition bias for safe vs. neutral faces in panic patients (Lundh, Thulin, Czyzykow, & Öst, 1998).

Clark and Ehlers (1993) reviewed the research on the efficacy of cognitive approaches in the treatment of panic (e.g., Sanderson, Rapee, & Barlow, 1989). Experiments testing the main predictions of the cognitive theory provided good support for the model.

Further, the literature indicates that the proposed model is consistent with the major features of panic. In particular, it is consistent with the nature of the cognitive disturbance in panic patients, the perceived sequence of events in an attack, the occurrence of 'spontaneous' attacks, the role of hyperventilation in attacks, and the effects of sodium lactate (see Otte et al., 2002; Peskind et al., 1998; Reschke, Mannuzza, Chapman, Lipsitz, & et al., 1995; Salkovskis & Clark, 1990; Sloan et al., 1999; Westling & Öst, 1993). Moreover, questionnaire studies show that panic patients, compared to normal controls, are more likely to make catastrophic interpretations of arousal related bodily sensations (Clark et al., 1997; Kamieniecki, Wade, & Tsourtos, 1997). However, following treatment this dysfunctional interpretation of bodily sensations is normalized (Westling & Öst, 1995). There are also subliminal studies confirming that panic patients, as opposed to normal controls, have a preattentive bias for panic-related information (Lundh, Wikström, Westerlund, & Öst, 1999).

As always, there are a few reports that fail to support the cognitive model (Austin & Richards, 2001). For example, Schniering and Rapee (1997) found no evidence for a stronger association between somatic sensations and threat in people with panic disorder compared with nonclinical controls.

Nonetheless, Clark's model has been the theoretical backbone on which the treatment in study III, IV and V has been based. In fact, the participants in the treatment studies have generated their own personal vicious circles as homework during the treatment. Generally, the model has rung true to the patients and has been well received.
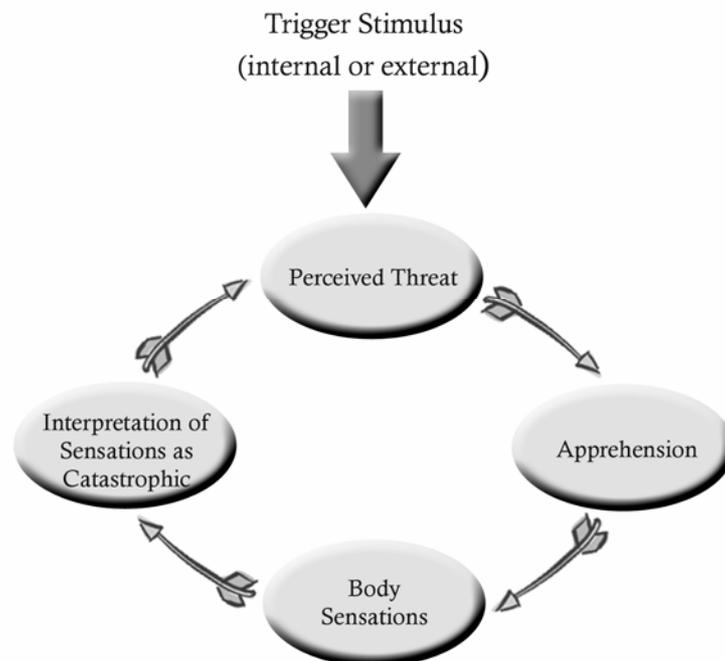
Figure 1. The suggested sequence of events in a panic attack according to Clark's cognitive model[2]. A range of events can provoke attacks. The stimuli are often internal (e.g., body sensation, thought or image), but can also be external (e.g., a supermarket). If these stimuli are perceived as a threat, a state of mild apprehension results. This state is followed by a wide range of body sensations (e.g., palpitations). If these anxiety-produced sensations are interpreted in a catastrophic fashion (e.g., impending heart attack), a further increase in apprehension occurs. This produces a further increase in body sensations and so on in a vicious circle, which culminates in a panic attack.

Treatment of PD

The first effective treatments of PD arouse from the pioneering work by Klein in 1964 (Klerman, 1990). His research suggested that panic attacks could effectively be treated by a tricyclic antidepressant (imipramine) and

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[2] The figure is reprinted from Clark, D. M. (1986). A cognitive approach to panic. Behaviour Research and Therapy, 24, 461-470. Copyright (1986) by Elsevier Science Ltd, Amsterdam (NL). Reprinted by permission.

that agoraphobia best was treated with exposure. Since then evidence has established exposure as among the best treatments (Taylor, 2000). However, exposure is not always effective and, similarly, imipramine also fails to eliminate panic in many cases. Accordingly, researchers have sought to develop new and more effective treatments.

The research regarding treatment outcome of PD is voluminous. More than 100 outcome studies have been conducted to evaluate treatments for PD. According to two consensus conferences PD is presently best treated with either CBT or medicine (American Psychiatric Association, 1998; National Institute of Health, 1991).

Medical treatment of PD

There are four classes of medications that have been shown to be effective: selective serotonin reuptake inhibitors (SSRI), tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), and benzodiazepines. Medications from all four classes have roughly comparable efficacy (American Psychiatric Association, 1998). Hence, considerations of adverse effects and the physician's understanding of the patient's personal preferences guide the choice of a particular medication class (Bakker, van Balkom, & Spinhoven, 2002; Bruce et al., 2003). SSRIs and TCAs are equal in efficacy in the treatment of panic disorder, but SSRIs are tolerated better (Bruce et al., 2003).

Both SSRIs and TCAs suffer from a long latency period, possibly as long as 12 weeks before maximal benefit is obtained, which is in contrast to the benzodiazepines that produce almost instant symptom relief. The dependency potential of the benzodiazepines, however, limits their usefulness (Wade, 1999).

Despite efforts aimed at increasing the use of SSRIs in patients with panic disorder, only a modest increase in their use has occurred. Treatment patterns for psychotropic drugs appear to have remained stable over the past decade, with benzodiazepines being the most commonly used medication for panic disorder (Bruce et al., 2003).

A major problem is that patients with PD have been reported to be one of the most difficult groups of patients to treat with medication (e.g., Katon, 1994). The reason is believed to be that all psychopharmacological treatments have side effects, and that these patients are already hypervigilant about bodily sensations. The idea of taking medication that will have side effects and alter their central nervous system makes some people feel even more out of control and frightened. It is far too common that patients take their medication for only a few days and then stop – reporting that it causes for example nervousness and palpitations, which can be the very symptoms

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they fear. An alternative to medication is CBT, which is a treatment that PD patients tend to be more willing to accept than drug therapies (Hofmann et al., 1998).

Psychological treatment of PD

Since the earliest treatments for PD, CBT has evolved from a simple single component therapy to a complete treatment package. Today treatments for panic disorder typically require 8-16 weeks. According to APA (American Psychiatric Association, 1998), 12 weeks is roughly the duration required for most therapies to realize there full benefits. The most often used ingredients are psychoeducation, breathing retraining or relaxation, cognitive restructuring, interoceptive exposure, in vivo exposure, and finally relapse prevention (Carlbring, Westling, & Andersson, 2000).

Psychoeducation

The term psychoeducation refers to the first and educational part of the therapy (Dannon, Iancu, & Grunhaus, 2002). This component provides the information and rationale for the treatment. The patient is taught the physiology of fear and anxiety (e.g., the fight/flight response). Moreover, panic and anxiety are demystified and normalized. The patient learns that panic attacks are a response to physiological, cognitive, and behavioral components, and that the goal is to change the catastrophic view via cognitive and behavioral methods.

Breathing Retraining or Relaxation

Breathing retraining is, at least until recently, commonly used in the treatment of panic disorder (Taylor, 2001). It involves teaching the client slow, diaphragmatic breathing, the idea being that PD sufferers might be chronic hyperventilators, or that the panic attacks are caused by acute hyperventilation. Diaphragmatic breathing is thought to offer quick somatic management. It is a helpful coping skill even for those who do not hyperventilate (Zuercher-White, 1997).

Although several studies (e.g., Berger, 2001; Griegel, 1995; Ley, 1993) suggest that this intervention is effective in reducing panic frequency, concerns have been raised about its routine use (e.g., Schmidt et al., 2000). For example, research suggests that hyperventilation plays a limited role in producing panic attacks (e.g., Craske, Rowe, Lewin, & Noriega Dimitri, 1997; Garssen, de Ruiter, & Van Dyck, 1992). This suggests that breathing retraining may only be useful for a minority of patients, for whom hyperventilation (or chest breathing) plays a role in producing panic symptoms.

Griegel (1995) goes further and calls breathing retraining a rational placebo. He argues that the specific mechanisms of action may be psychologically based via (1) perceived controllability, (2) distraction, (3) meditation/relaxation, or as (4) a credible placebo. After empirical studies he concluded that it is a placebo. However, Ley (1993) disagreed and maintained that there is neither an empirical nor logical basis for questioning the rationale underlying breathing retraining.

In opposition, Schmidt and coworkers (Schmidt et al., 2000) conducted a dismantling study questioning the utility of breathing retraining. The CBT theory implies that PD can be cured. Hence, coping techniques such as breathing retraining should be avoided as they might interfere with effective exposure. Some data suggested that the addition of breathing retraining yielded a poorer outcome. However, findings were generally more consistent with treatment equivalence, questioning whether breathing retraining produces any incremental benefits in the context of other CBT interventions for PD. The theoretical concern that breathing retraining may be a safety behavior, and consequently counterproductive, is strengthened by the fact that clients like it and attribute great gains to it (Zuercher-White, 1997).

In a recent review article, Taylor (2001) concludes that breathing retraining can play a useful role in the treatment of panic disorder, although clinicians must exercise care to ensure that it is not misused by patients as a means of escaping or avoiding feared sensations. This is echoed by Meuret and coworkers, who also strongly argue that more studies are needed before breathing training can be rejected (Meuret, Wilhelm, Ritz, & Roth, 2003).

Relaxation, often progressive muscle relaxation, has been suggested to be useful for treating the general anxiety associated with panic disorder (Taylor, Kenigsberg, & Robinson, 1982), sometimes almost as effective as cognitive therapy (Beck, Stanley, Baldwin, Deagle, & et al., 1994). However, Marks et al. (1993) claimed that relaxation is "…a good psychological placebo in agoraphobia/panic, despite some beliefs in its value" (p. 784). Again, the cognitive theory implies that PD can be cured; hence, one should not try to minimize tension.

Another relaxation technique is applied relaxation (Öst, 1987). Applied relaxation builds on progressive muscle relaxation in various ways. However, there is a big difference, as applied relaxation also includes interoceptive and situational exposure. As a consequence the results have been better, with 82 to 100 per cent clinically significant improvement at follow-up (Öst, 1988a, 1988b; Öst & Westling, 1995a; Öst, Westling, & Hellström, 1993). However, the good results of applied relaxation seem to be specific to the Swedish population, as a British (Clark, Salkovskis, Hackmann, Middleton, & et al., 1994) and a Dutch (Arntz & van den Hout, 1996) research team have failed to replicate the good results. Even though

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there has not been any research done on applied relaxation on PD since 1996, this multi component protocol is less demanding on the therapist. Furthermore, if the patient has a comorbid generalized anxiety disorder, using applied relaxation as a joint treatment might be very promising since recent studies suggest that applied relaxation is equally as effective as cognitive therapy (Arntz, 2003; Öst & Breitholtz, 2000). Besides affecting generalized anxiety, the treatments also yield marked and lasting changes on ratings of worry, cognitive and somatic anxiety, and depression.

Cognitive Restructuring

Several studies have indicated that people with PD tend to overassociate fear-relevant stimuli and aversive outcomes, i.e., they show a covariation bias. Such a bias seems to be a powerful way to confirm danger expectations and enhance fear (De Beurs et al., 2002; Wiedemann, Pauli, & Dengler, 2001). Thoughts and beliefs concerning the perceived dangerousness, unpredictability, and uncontrollability of panic need to be challenged with the use of cognitive restructuring techniques (for an introduction see Wells, 1997). One of the first steps is using a recent panic attack to illustrate the relationship among arousal-related sensations, catastrophic misinterpretations, and emotions.

The goal of cognitive restructuring is to modify the client's catastrophic misinterpretations of the bodily sensations produced by anxiety and panic. Over the course of treatment, by learning how to access corrective and helpful information, patients increasingly substitute logic for catastrophic misinterpretations of the bodily sensations and thereby decrease rather than increase anxiety symptoms. The cognitive changes are achieved via verbal challenges and behavioral experiments (Hecker, Fink, Vogeltanz, Thorpe, & Sigmon, 1998).

Cognitive restructuring tends to be more effective when catastrophic misinterpretations of the bodily sensations are challenged than when other sorts of cognitions are targeted (Taylor, 2000).

Interoceptive Exposure

After the patient has learnt to identify catastrophic thoughts it is time to replace the maladaptive beliefs with more realistic thinking. That is partly achieved by interoceptive exposure. Usually the two components are practiced hand-in-hand; the client challenges any negative cognition that may arise during exposure training.

Interoceptive exposure exercises are often framed as behavioral experiments to test a patient's belief about consequences of arousal-related sensations. Interoceptive exposure involves the repeated, intentional elicitation of physical sensations that produce anxiety. The feared sensations

are elicited through specific physical exercises, and these exercises are repeated over several trials until the client habituates to the sensations. The process of interoceptive exposure aids in breaking the connection between physical sensations and fear by providing the client with concrete experiences indicating that the physical sensations do not lead to the feared consequences (Beck, Shipherd, & Zebb, 1997).

For a person who fears a heart attack, an example of an interoceptive exposure experiment is testing the idea of palpitations always leading to a cardiac infarction by running up and down stairs and observing what happens. Usually the patient does a variety of tests including sensations of shortness of breath, accelerated heart rate, sweating, feeling of choking, feeling dizzy, unsteady, light-headed or faint, derealization, and numbness or tingling sensations (Carter & Barlow, 1993).

In Vivo Exposure

One cannot assume that cognitive shifts automatically result in decline of avoidance behavior (Van den Hout, Arntz, & Hoekstra, 1994). Hence, something more is needed. In vivo exposure is used primarily for reducing agoraphobia, and requires the patient to repeatedly encounter a feared external stimulus in order to challenge maladaptive beliefs about the object or place and possible catastrophic outcomes (Soechting et al., 1998; Zarate, Craske, & Barlow, 1990). Typical situations are those in which the person believes he/she would panic, or situations in which he/she thinks it would be embarrassing or dangerous to panic in (Cox, Endler, Lee, & Swinson, 1992).

In vivo exposure tends to be most effective when patients are encouraged to refrain from using safety behaviors (Taylor, 2000).

Relapse Prevention

Many patients achieve high end-state functioning following CBT treatment (Rayburn & Otto, 2003). However, presently the exact relapse rate is unclear. It is known from long term follow-up studies on the clinical course of PD that following *pharmacological* treatment the relapse rates are high. Yonkers and coworkers (Yonkers, Bruce, Dyck, & Keller, 2003) found that this is especially true for women, who have been reported to relapse three times more often than men (64% vs. 21%). In contrast, there are other studies concluding that, over a period of 11 years, there is a good chance of recovery from panic attacks and disabilities, and full remission is also possible (Swoboda, Amering, Windhaber, & Katschnig, 2003). Regardless, symptoms may reoccur, even when PD is successfully treated (Rayburn & Otto, 2003). The important issue is not whether the symptoms return, but how the patient deals with them. Hence, strategic planning for relapse is nowadays part of the treatment. Provisions need to be made for setbacks,

recurrence and relapse. Accordingly, a maintenance program should be written down for the patient to consult. Öst (1989) has developed and tested a maintenance program that yielded a larger percentage of improvement during follow-up, a lower proportion of patients needing further treatment, and fewer relapses. If the patient begins to experience problems with panic he/she should remind himself/herself that the setback is not a catastrophe, but a temporary failure to manage the situation that one has managed before. One should analyze the situation, practice the exercises used in the therapy, and learn from it. Also, one should restrict the setbacks by not letting it spread to other situations and try to return to situations one started to avoid. Finally, if nothing works, the patient is encouraged to contact the therapist as soon as possible to discuss the problem or arrange further therapy sessions.

Important ingredients

As with all therapies, even pharmacological, there is also a nonspecific component that includes factors that facilitate therapeutic alliance (e.g., therapist warmth, genuineness, empathy), and factors that mobilize hope and foster expectations (Andrews, 2001; Rapaport, Pollack, Wolkow, Mardekian, & Clary, 2000; Shepherd, 1993; Shepherd, 1993; Cox, Swinson, & Endler, 1991). CBT has been found to be more effective than nonspecific treatments (Taylor, 2000). Consequently, there must theoretically be specific benefits from some, or all, of the components in modern CBT for PD.

The relative efficacy of cognitive restructuring and interoceptive exposure procedures for the treatment of panic disorder, as well as the differential effects of the order of these interventions, have been studied (e.g., Hecker et al., 1998). It has been suggested that exposure reduces agoraphobia but not panic, and cognitive therapy reduces panic but not agoraphobia (Van den Hout et al., 1994). Certain studies favor cognitive techniques over exposure (e.g., Zarate et al., 1990), others go in the opposite direction (e.g., Soechting et al., 1998 Craske et al., 1997). There are also indications of the equivalence of the two components (Bouchard et al., 1996).

However, there are reports that cognitive techniques and interoceptive exposure utilize different change mechanisms (Arntz, 2002). Hence, if given the possibility, the average client would probably benefit most from a combined treatment package.

Meta-Analyses and Treatment Outcome

To date, eight meta-analyses have been conducted on panic disorder; three on pharmacotherapy (Bakker et al., 2002; Boyer, 1995; Wilkinson, Balestrieri, Ruggeri, & Bellantuono, 1991), three on psychotherapy (Clum,

Clum, & Surls, 1993; Gould, Otto, & Pollack, 1995; Westen & Morrison, 2001), and two on the comparison between pharmacotherapy and psychotherapy (Cox et al., 1992; van Balkom et al., 1997).

The interpretation of the results is not straightforward, since all meta-analyses suffer from a number of shortcomings that sometimes severely undermine the strength of the conclusions (Aikins, Hazlett Stevens, & Craske, 2001). Also, the studies that the meta-analyses are based on are relatively old, sometimes using less effective treatment methods. Since 1998 no studies have been included in a meta-analysis for PD. However, using the same search words as Gould and coworkers did in 1995 ("panic" in the title together with "outcome", "clinical", "comparative", "long-term" or "short-term") generated 75 new studies never included in a meta-analysis. Although far from all search engine hits are randomized controlled treatment trials, a compilation and analysis of the results is not within the scope of this thesis.

However, it seems that both pharmacotherapy and psychotherapy are generally well-tolerated, and at least moderately effective (Taylor, 2000). The treatments appear to influence most of the major symptom domains. According to Goldberg (1998) around 85% of patients are panic-free at posttreatment and improvements are maintained at follow-up. However, 26% of waiting-list controls are also panic-free, making the net percentage of panic-free treated patients 59%. Across most studies the proportion of female participants are around 75 per cent (Gould et al., 1995), and the drop out rate between 5.6 and 22 per cent (White & Barlow, 2002).

In conclusion, the current empirical findings point in the direction of CBT being an effective treatment for PD. What is more uplifting is that the results from the empirical findings seem to be transportable to community mental health centers. Hence, despite differences in settings, clients, and treatment providers, both the magnitude of change from pretreatment to follow-up and the maintenance of change from posttreatment to follow-up in the community mental health centers were comparable with the parallel findings in the efficacy studies. For example, in a naturalistic study by Stuart and coworkers 89% clients were panic free at follow-up, and a substantial proportion of the sample successfully discontinued benzodiazepine use (Stuart, Treat, & Wade, 2000).

Treatment of PD normally involves 12-15 one hour sessions (Clark et al., 1999). However, attempts to develop more economical treatments have been made. The briefer treatments make extensive use of between-sessions patient self-study modules. The outcome data are generally impressive (Alford, Freeman, Beck, & Wright, 1990; Clark et al., 1999; Craske, Maidenberg, & Bystritsky, 1995; Newman, Kenardy, Herman, & Taylor, 1997; Westling & Öst, 1999), but further research is needed (Stein, Norton, Walker, Chartier, & Graham, 2000; Taylor, 2000).

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What is the treatment of choice?

Both CBT and medications have been shown to be effective treatments for PD (American Psychiatric Association, 1998; Otto, Pollack, & Maki, 2000). Since CBT besides dealing with current symptoms also teaches patients self-help strategies for future use it is believed that CBT has a long-term protective effect (e.g., Bakker, van Balkom, Spinhoven, Blaauw, & van Dyck, 1998; Gould et al., 1995; Milrod & Busch, 1996; Otto, Gould, & Pollack, 1994; Swoboda et al., 2003). This would give CBT a considerable advantage over medication management of panic disorder, as patients often relapse when they are tapered off their medications. Furthermore, in a meta-analysis by Gould and colleges (Gould et al., 1995) CBT was found to yield the smallest attrition rates and to be cost-effective.

In a recent review of the literature on the long-term effectiveness of CBT a modest protective effect of CBT was found in comparison with medicine (Nadiga, Hensley, & Uhlenhuth, 2003).

It has been suggested that psychological and pharmacological treatments affect different facets of the anxiety condition (Schmidt, Koselka, & Woolaway Bickel, 2001). Hence, a combination could in theory be beneficial. However, the knowledge regarding combined treatments for panic disorder is limited and the results are conflicting (American Psychiatric Association, 1998; Barlow, Gorman, Shear, & Woods, 2000; Sharp et al., 1996; van Balkom et al., 1997; Westra & Stewart, 1998). It has been suggested that combined treatment for panic disorder seems to provide an advantage over CBT alone at posttreatment, but is associated with greater relapse after treatment discontinuation (Foa, Franklin, & Moser, 2002). Currently it is not possible to identify which patients might benefit from a combination therapy.

In conclusion, there is no convincing evidence that one modality is superior for all patients. The choice between CBT and/or medication depends on an individualized assessment of the efficacy, benefits, and risks of each modality and the patient's personal preferences. In every case, the patient should be fully informed by the health professional about the availability and relative advantages and disadvantages of CBT, anti-panic medications and other forms of treatment.

Bibliotherapy

As evidenced by several trials there are highly effective treatments available for panic disorder (Taylor, 2000). However, only about 25 per cent seek any kind of treatment (Lidren et al., 1994).

Barriers to accessing expert assistance include shortage of skilled therapists, long waiting lists, and cost (National Institute of Health, 1991). These barriers particularly disadvantage geographically isolated people such as those in regional and rural areas where travelling time is an added burden (Richards, Klein, & Carlbring, 2003). Another problem is that those with agoraphobia may not seek therapy due to fear of leaving their houses or travelling certain distances (Newman, Erickson, Przeworski, & Dzus, 2003). A major challenge therefore is to increase the accessibility and affordability of evidence-based psychological treatments.

Printed self-help manuals have been developed to assist people with mental health problems who are unwilling or unable to access professional assistance, although until recently there has been little evaluation of their efficacy (Rosen, 1987, 1993; Kurtzweil, Scogin, & Rosen, 1996; Rosen, Glasgow, & Moore, 2003).

To date, four empirical trials (Hecker et al., 1996 Gould & Clum, 1995; Gould, Clum, & Shapiro, 1993; Lidren et al., 1994) have been published on the use of bibliotherapy in the treatment of people meeting the DSM criteria for panic disorder[3]. The results are encouraging, although methodological issues limit the inferences that can be drawn from them (Febbraro et al., 1999; Hecker et al., 1996).

In the first study, Gould et al. (1993) compared bibliotherapy to individual therapy and to a waiting list control. A therapist saw individual therapy clients for one hour twice a week. Participants in the bibliotherapy condition were asked to read the self-help book *Coping with Panic* (Clum, 1990) at their own pace, and to apply the strategies described. Both treatments were applied over a 4-week period and involved the same CBT procedures. The results indicated that participants in the bibliotherapy group, in general, showed significantly more improvement than those in the waiting-list control, and were not significantly different from those in the individual therapy group. Seventy-three percent of the subjects in the bibliotherapy condition, 56% in the individual therapy condition, and 36% in the waiting-list condition, were panic-free at the post-treatment assessment. The averaged ES across all dependent measures was $d = 1.5$ post-test for the bibliotherapy condition compared to the waiting-list condition. According to Cohen (1988), an ES of 0.8 or higher constitutes a large ES.

In a replication and extension of their original study, Gould and Clum (1995) compared self-help treatment to a waiting-list control. In addition to reading *Coping with Panic,* self-help clients watched a brief videotape explaining the etiology of panic disorder, the spiraling and circular

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[3] Studies on the use of bibliotherapy where the participants did not have to meet DSM criteria for panic disorder are omitted (e.g., Febbraro, Clum, Roodman, & Wright, 1999).

relationship between panic symptoms and cognitions, and modelled diaphragmatic breathing. They were also provided with an audiotape of progressive muscle relaxation. Gould and Clum (1995) reported that the evidence strongly supported the effectiveness of the self-help treatment relative to the waiting-list condition both post-treatment and at a 2-month follow-up. The proportions of panic-free patients were 46% for the self-help treatment and 25% for the waiting-list at post-treatment, and 69% and 25% at follow-up, respectively. This study showed a medium effect ($d = 0.5$) at post-treatment and a large effect ($d = 0.8$) at the 2-month follow-up.

In a third study using *Coping with Panic*, Lidren et al. (1994) compared bibliotherapy and group therapy to a waiting-list control. Lidren et al. (1994) reported that both bibliotherapy and group therapy treatments were more effective than the waiting-list condition in reducing frequency of panic attacks, severity of physical panic symptoms, catastrophic cognitions, agoraphobic avoidance, and depression. These two conditions were also more effective in increasing self-efficacy. The efficacy of both treatments was maintained throughout the follow-up periods (3 and 6 months) and produced clinically significant levels of change among the majority of treated subjects. The proportion of panic-free patients at post-treatment assessment and 6-month follow-up were 83% (75%) for bibliotherapy, 83% (92%) for group therapy, and 25% for waiting-list. A post-test comparison between the bibliotherapy condition and the waiting-list condition across all dependent measures showed a large ES ($d = 1.5$).

In a study by Hecker et al. (1996), two approaches to providing CBT for panic disorder were investigated: self-directed and therapist-directed. All participants were provided with Barlow and Craske's (1989) *Mastery of Your Anxiety and Panic*. The therapist-directed participants met with a therapist for 12 weekly sessions, during which material covered in the book was discussed and worked through. The self-directed participants also met with a therapist, but only on three occasions, and the therapist was not allowed to deliver any therapeutic interventions. Instead, the sessions consisted of the therapist answering questions about the material covered thus far, and assigning new readings. In both conditions participants improved with treatment and maintained their gains at the 6-month follow-up. There were no differences between the two treatment conditions on the outcome measures. Forty percent of the clients who completed self-directed treatment met conservative criteria for high end-state functioning. The proportions of panic-free self-directed patients were 60% at post-treatment and 80% at 6-month follow-up, and 63% for the therapist-directed at post-treatment and 71% at 6-month follow-up.

In a thorough review of published bibliotherapy studies it is suggested that bibliotherapy for PD can be effective, with a medium to large effect size, ranging from $d = 0.5$ to $d = 1.5$ (Carlbring et al., 2000).

Internet and Psychological Treatment Aspects

A modern alternative to printed self-help manuals is computers (Andersson & Carlbring, 2003; King & Moreggi, 1998; Smith & Senior, 2001; Ström, 2003). Computerized programs have been used for a number of years for assessment, diagnosis, and education (Newman, Consoli, & Taylor, 1997), but most controversial has been their use for psychological treatment (Proudfoot et al., 2003). Until recently, computer mediated therapies have been offered without any patient-therapist interaction (Marks, Shaw, & Parkin, 1998). However, there now seems to have been a shift toward using the World Wide Web (WWW; Zuckerman, 2003) to inexpensively administer self-help treatment instructions, in conjunction with some sort of text-based human interaction (e.g., e-mail). However, there does not yet seem to be any golden standard for the delivery of these novel minimal therapist contact therapies (Ragusea & VandeCreek, 2003).

Internet-based psychological interventions, recently referred to as "Interapy" (Lange et al., 2000; Lange, van de Ven, & Schrieken, 2003; Lange, van de Ven, Schrieken, & Emmelkamp, 2001), can be divided into four categories: (1) self-administered therapy or pure self-help, (2) predominately self-help (i.e. therapist assesses and provides initial rationale, and teaches how to use the self-help tool), (3) minimal contact therapy (i.e. active involvement of a therapist, though to a lesser degree than traditional therapy), and (4) predominantly therapist administered therapy (i.e. regular contact with therapist for a number of sessions, but in conjunction with self-help material (Scogin, 2003). Most of the randomized controlled trails on Internet-based treatment have been done on minimal contact therapy. Although an early review of articles indexed in Medline up until 2001 concludes that the methodological quality of many Internet-based studies was poor (Bessell et al., 2002), and that there was almost a complete lack of evidence of any effects this may have on health outcomes, there are a number of more recent studies indexed in PsycINFO. The latter programs have been used successfully in the treatment of headache (Andersson, Lundstrom, & Ström, 2003; Ström, Pettersson, & Andersson, 2000), insomnia (Ström, Pettersson, & Andersson, 2004), the distress associated with tinnitus (Andersson, Strömgren, Ström, & Lyttkens, 2002; Kaldo, Larsen, & Andersson, 2003), depression (Christensen, Griffiths, & Jorm, 2004; Clarke et al., 2002; Andersson et al., 2004; Marks et al., 2003), social

phobia (Carlbring et al., 2004), stress (Zetterqvist, Maanmies, Ström, & Andersson, 2003), posttraumatic stress (Lange et al., 2003), chronic pain (Buhrman, Fältenhag, Ström, & Andersson, 2003), reducing risk factors for eating disorders (Winzelberg et al., 2000; Zabinski et al., 2001), weight loss (Tate, Jackvony, & Wing, 2003), smoking (Brandon, Collins, Juliano, & Lazev, 2000; Jerome, Fiero, & Behar, 2000), and jet lag symptoms (Lieberman, 2003).

Generally, according to Wright and Wright (1997), computer-assisted therapy has been well accepted by patients. In fact, patients are more likely to disclose suicide plans to a computer than to a human being (Proudfoot et al., 2003).

According to Zabinski and coworkers (Zabinski, Celio, Wilfley, & Taylor, 2003), on-line interventions also offer practical advantages. Time constraints are removed and communication can be done asynchronously. Winzelberg (Winzelberg, 1997) found that participants in an electronic support group for eating disorders posted more than half of the messages between 18.00 h and 07.00 h, times when traditional therapy is unavailable. Furthermore, treatment compliance can be easily and accurately monitored through computerized tracking devices, the use of aliases can reduce social barriers to self-disclosure, and finally, computerized interventions can be disseminated easily in a cost-efficient manner.

Despite promising findings and the advantages discussed, the drawbacks of the Internet must also be acknowledged. One obvious problem is computer ownership and Internet access, which, though rapidly expanding, is still not available to everyone. According to a report by Official Statistics of Sweden (SCB; Statistics Sweden, 2002) slightly less than 70 per cent of the Swedish population aged 16-64 used the Internet. People aged 16 to 19 used the Internet most frequently (90%). Generally, the older the person the less likely he/she is to use the Internet. Most of the users spend one to five hours a week, only 21% of the women and 33% of the men use the Internet more than six hours a week (SCB, 2004). Furthermore, the technology is imperfect. Differences in computer software can interfere with communication and determined hackers may be able to infiltrate even secure servers. A good way to counter these potential problems is using SSL-certificates, encrypted storage in databases, anonymous log-in names, automatic timed log-off and not caching the web content on the local computer (Nosek, Banaji, & Greenwald, 2002).

Another obvious potential problem is the lack of visual cues and facial expressions that can aid in understanding words and phrases in face-to-face contact (Bloom, 1998; Childress, 2001; Childress & Asamen, 1998; Mallen, Day, & Green, 2003). However, it has been suggested that it is possible to overcome this limitation by adding in parenthetical remarks (i.e. "smilies" or

"emotional bracketing") to express implied undertones that would have been more easily understood in person (Zabinski et al., 2003). The therapist can also actively check in with participants with follow-up questions to comments that may cause concern.

According to Kraut and coworkers (Kraut et al., 1998), there is a potential risk for Internet use to decrease communication with family members and decrease the size of one's social network and increase isolation. However, a 3-year follow-up of the same respondents found that negative effects dissipated (Kraut et al., 2002). In fact, the sample generally experienced positive effects of using the Internet on communication, social involvement, and well-being. However, consistent with a "rich get richer" model, using the Internet predicted better outcomes for extraverts and those with more social support but worse outcomes for introverts and those with less support.

Perhaps the most critical point is how psychological crises are to be identified and managed in Internet-delivered interventions. The need for a thorough assessment is particularly important because PD itself is associated with an increased risk of suicide attempts (Weissman, Klerman, Markowitz, Ouellette, & et al., 1989). When combined with significant depression as it often is (Gorman & Coplan, 1996), PD is also associated with a substantially increased risk of suicide completions (Hirschfeld, 1996). Consequently, there is always the possibility of a psychological crisis occurring for people with PD in psychotherapy. When therapy is conducted on a face-to-face basis, the therapist is usually on hand to assess and manage it, but because of their remoteness from the therapy center, this is usually not possible for participants who are enrolled in Internet-based programs. It is therefore also important to have details of each participant's primary care physician in the event of a psychological emergency (e.g., threatened suicide). One way to counter this is to at an early stage exclude potential participants who are suffering from other psychiatric disorders needing immediate attention, who are significantly depressed, and/or who seem at risk of suicide. However, the patients' status can change during the course of the treatment. It is important to monitor the participants, preferably on a weekly basis (e.g., using the Hospital Anxiety and Depression Scale, HADS; Zigmond & Snaith, 1983). If a weekly monitoring score reaches a cut-off (e.g., 15 or above on HADS) the therapist should get an automatic e-mail prompting him or her to call the participant and his/her primary care physician.

As Rosen (1987) pointed out, it is very important that professional standards, not commercial considerations, influence the development and use of self-help materials. If proper assessment is not done before commencing treatment, there is a significant risk that someone with panic disorder symptoms, but who actually has a physical disorder (e.g., hyperthyroidism), tries psychological self-help without any success. Other

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problems Rosen pointed out are the possible problems with a client misunderstanding or misapplying instructions or failing to comply with therapeutic regimens. In the more comprehensive treatment programs, compliance, understanding, and progress are monitored on a weekly basis (e.g., Andersson et al., 2004; Carlbring et al., 2004). However, should treatment failure occur, there are still potential risks of negative self-attributions, and of reduced belief in today's therapeutic techniques.

In conclusion, the Internet is being used as a source of mental health information as well as structured treatment programs for people with mental health concerns or problems. Although promising as a form of intervention, there is a need for more research on the efficacy of Internet-based treatment for PD and on comparisons with evidence-based face-to-face therapies. This thesis is an attempt in that direction.

The Empirical Studies

Participants in the empirical studies

All participants, except those in study I, were self-recruited. In study III, which was chronologically the first study, participants were recruited by means of newspaper articles in national and regional papers, notes in health magazines, and by an Internet link from the home page of the Swedish National Association for people suffering from PD.

In Studies II, IV, and V, participants were recruited from a waiting-list of people who had expressed an interest in taking part of the Internet-administrated self-help program for panic disorder. Originally they were recruited by means of newspaper articles or other media coverage.

In Study I a total of 1000 subjects aged 16-79 years were randomly selected from the Swedish population and address register (SPAR).

Table 2. *Descriptive data for the participants in the five studies.*

	Study I n=591	**Study II** [a] n=60	**Study III** n=41	**Study IV** n=22	**Study V** n=49
Age (*sd*)	48 (17)	39 (9)	34 (8)	38 (9)	35 (8)
Female	52%	58%	71%	68%	71%
Years with PD (*sd*)	-	-	>1	10 (5)	9 (9)
Agoraphobia	-	-	38%	91%	51%
Diagnosis	CIDI	Computerized and SCID	Computerized and e-mail	SCID	SCID
Medication	-	-	64%	50%	31%
On-going psychotherapy (not CBT)	-	-	2%	14% [b]	0%
Daily anxiety (*sd*)	-	-	30% (15%)	23% (12%)	29% (20%)
Attacks / week (*sd*)	-	-	2.2 (3.5)	2.9 (2.7)	3.3 (4.7)
Drop out	37%	12%	12% [c]	23% [c]	12% [c]
Modules completed	-	-	-	56% (23%)	82% (56%)
Treatment time (weeks)	-	-	7-12	10-28 [d]	10
Treatment credibility (0-50)	-	-	43 (6)	34 (8)	37 (7)

[a] The participants in study II who met criteria for PD according to SCID were later included in study IV.

[b] In the original paper the figure is 27.3, but the correct figure is 13.7.

[c] In accordance with the intention to treat paradigm (e.g. Nich & Carroll, 2002; Newell, 1992) post-treatment and follow-up data were collected from all drop-outs. However, when that was not possible the last observation was carried forward.

[d] No time limit was set for completing each module. Post-treatment assessment was conducted after 28 weeks.

Study I: *12-month Prevalence of Panic Disorder with or without Agoraphobia in the Swedish General Population*

Aims

The prevalence of DSM-IV- defined (APA, 1994) panic disorder in Sweden was unknown. However, Halldin (1984) found a 12-month prevalence of 0.8% using the anxiety neurosis criteria in the International classification of diseases, eighth edition (ICD-8; World Health Organization, 1967), on an urban population in central Sweden (Stockholm County).

The aim of the first study was to investigate the 12-month prevalence of panic disorder in a representative Swedish sample.

Method

A total of 1000 subjects, aged 16-79 years, were randomly selected from the Swedish population and address register (SPAR).

A questionnaire, described below, was mailed to each subject together with a stamped return envelope and an explanatory letter, in which the aim of the study was described and participant anonymity and integrity was guaranteed. After 2 weeks, questionnaires and stamped return envelopes were sent out to the non-responders only ($n = 580$).

Fifty-three individuals (5.3%) could not be reached by mail and their questionnaires were returned undelivered. The replies from nine subjects were impossible to interpret. Thus, with a response-rate of 63%, a total of 591 subjects were eligible for analysis (281 men, 310 women, median age = 48, mean age = 47.9, $SD = 17.1$).

The postal survey contained three different sections. The first evaluated sociodemographic variables such as sex and age.

The second section contained a Swedish translation of the panic disorder module from the World Health Organization's (WHO) Composite International Diagnostic Interview version 2.1 for 12-month prevalence (CIDI; WHO, 1997). The CIDI is a fully structured interview that maps the symptoms elicited during the interview onto DSM-IV diagnostic criteria and reports whether the diagnostic criteria are satisfied.

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The third section of the questionnaire assessed if treatment for panic disorder had been sought, and the reasons for not seeking help when this was the case.

Questions were also asked if there was a history of treatment, and how that treatment was perceived.

In order to validate the questionnaire (CIDI), it was administered to 53 subjects (22 male, 31 female, mean age 38.6 years, $SD = 8.9$) who volunteered for a treatment study on an Internet based self-help program targeting panic disorder. These individuals were interviewed with the Structured Clinical Interview for DSM-IV Axis I Disorders, research version (SCID; First, Gibbon, Spitzer, & Williams, 1997). Using the SCID interview as a reference there was a 75% agreement between the CIDI and SCID for the diagnosis of panic disorder. Cohens Kappa was .48, which is fair (Robson, 1993). The sensitivity was 76% and the specificity 74%.

Results

A total of 13 (2.2%) respondents met the DSM-IV criteria for panic disorder with or without agoraphobia. The 95% confidence interval for the point estimate was 1.02% - 3.38%. There was a significant sex difference, with the highest prevalence for women (3.6% vs. 0.7%; $\chi^2_{(1)} = 5.51$, $p<.05$)[4]. There was no age difference; three (23%) respondents categorized as having panic disorder with or without agoraphobia were between 16 and 29 years old. Six (46%) were 30-49, and four (31%) were 50-79 years old.

Median number of attacks during the past twelve months were 4 ($m = 7.9$; $sd = 12.2$; min 2; max 50). Median time for an attack to reach its peak was 3 minutes ($m = 3.5$; $sd = 2.7$). The three most frequent symptoms during a bad attack were palpitations, pounding heart, or accelerated heart rate (87%), fear of losing control or going crazy (82%), and nausea or abdominal distress (55%).

Respondents categorized as suffering from panic disorder used significantly more medication in general ($\chi^2_{(1)} = 12.31$, $p<.001$).

Discussion

The 12-month prevalence of panic disorder with or without agoraphobia in the Swedish general population was estimated to 2.2%, with a female-male ratio of 5.1 to 1. The result from this study strengthens Wittchen and Essau's (1993) conclusion that being female is associated with higher prevalence of

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[4] The original paper contained an error, the sentence should read *"(3.6% vs 0.7%; $\chi^2_{(1)}=5.51$, $p<.05$)"*, and not *"5.6% vs 1.0%; $\chi^2_{(1)}=10.59$, $p<.05$"*. Hence, the ratio should be 5.1 and not 5.6.

panic disorder, whereas age is not a consistent powerful factor. Making comparisons between different countries' prevalence rates is problematic since different diagnostic procedures, different samples, and different criteria in defining caseness have been used. Most studies have relied on the Diagnostic Interview Schedule (DIS) for DSM-III administered by a lay interviewer. It has been argued that the DIS may dismiss panic disorder too easily, due to an overly stringent screening question (Katon, Vitaliano, Russo, Jones, & Anderson, 1987). That could explain the relatively higher prevalence rate in the present and the Kessler et al. (1994) study, both using the CIDI.

There are limitations to this study. Rather than a careful diagnostic interview in person, such as the SCID (First et al., 1997) or the Anxiety Disorders and Interview Schedule for DSM-IV (ADIS-IV; Di Nardo, Brown, & Barlow, 1994), this study depended on retrospective self-reporting. Furthermore, there were no attrition analyses, and the sample was comparatively undersized.

While the sample size was relatively small, it is comparable to prevalence studies conducted in Italy, Germany, and Lebanon. In contrast, in the largest prevalence study to date – the epidemiological catchment area research project (ECA) with close to 20,000 respondents (Regier et al., 1984) – the instrument used (DIS) has been described as having poor reliability (McNally, 1994). For panic disorder the obtained Kappa, when psychiatrists conducted clinical reappraisal interviews, was -.02 (Anthony et al., 1985). That is considerably lower than the Kappa of .48 that the instrument used in the present study obtained.

The most frequent symptom during a bad attack according to the present study is palpitations, pounding heart, or accelerated heart rate. The same has been reported in several other studies, such as the ECA (Von Korff et al., 1985), and a survey questionnaire data on panic attacks gathered using the Internet (Stones & Perry, 1997). All respondents categorized as suffering from panic disorder had been in contact with a health professional as a consequence of their attacks, with varying degree of satisfaction. They used significantly more medication than non-panic respondents. This is consistent with reports that people suffering from panic disorder have an unusually high health service utilization (e.g., Boyd, 1986; Salvador Carulla, Segui, Fernandez Cano, & Canet, 1995).

Katerndahl and Realini (1993) argued that the SCID detects more true cases of panic disorder than does the relatively insensitive DIS. Hence, in the next wave of cross-national epidemiological studies there is a need to seriously reconsider what instrument to use. Although costly, we would like to see studies that assess DSM-IV criteria, preferably with the SCID administered by trained professionals.

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In conclusion, the present study suggests that the prevalence of panic disorder in Sweden is consistent with the prevalence rates found in previous international studies.

Study II: *Is the Internet-Administered CIDI-SF Equivalent to a Clinician-Administered SCID-Interview?*

Aims

Finding suitable participants for clinical trials is time-consuming and costly. The aim of this study was to evaluate the efficacy of the Composite International Diagnostic Interview Short-Form (CIDI-SF; Kessler, Andrews, Mroczek, Ustun, & Wittchen, 1998) as a substitute for a human diagnostic interview. The CIDI-SF was developed from the larger CIDI by the World Health Organization (1990) to evaluate hierarchy-free diagnoses according to the definitions and criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM). It evaluates seven DSM-IV (APA, 1994) mental disorders and two DSM-III-R (APA, 1987) substance disorders: major depression, generalized anxiety (GAD), specific phobia, social phobia, agoraphobia, panic attack, obsessive-compulsive disorder (OCD), alcohol dependence, and drug dependence. The CIDI-SF uses a stem-branch logic in which a small number of initial diagnostic stem questions are used in each section to eliminate respondents who are least likely to be cases before they are asked further symptom questions. The CIDI-SF yields a probability-of-caseness ranging from 0.0 to 1.0 for each disorder.

Method

Sixty participants[5] volunteered for a treatment study of an Internet-based self-help program targeting PD (see Study IV). One person was rejected because of a too high depression total score and a clear suicidal ideation. Six people declined to participate after initially showing interest. This left 53 subjects eligible for analysis (see Table 2 for demographic data).

Two days before the scheduled human interview the participants were instructed to complete a computerized interview via a web page. The

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[5] In the original paper the number of participants initially showing interest in the study can easily be misinterpreted. Sixty participants volunteered, but only 53 agreed to be interviewed. Out of those 53 people 22 was later included in study IV.

computerized interview consisted of demographic questions, the CIDI-SF, and the self-rated version of the Montgomery Åsberg Depression Rating Scale (MADRS; Svanborg & Åsberg, 1994). In addition, it was decided that the panic disorder module from the long CIDI also be included. This was done because the CIDI-SF does not fully cover all panic disorder criteria.

Two days after the Internet assessment the participants were interviewed with the Structured Clinical Interview for DSM-IV Axis I Disorders, research version (SCID; First et al., 1997) by one of two trained research assistants, who were blind for the results in the computerized interview. All interviews were recorded on a 120-minute audiotape that was assessed for inter-rater reliability (Kappa = .81).

In connection with the SCID-interview the following questionnaires were administered to the participants; Mobility Inventory for Agoraphobia (MI; Chambless, Caputo, Jasin, Gracely, & Williams, 1985), Anxiety Sensivity Index (ASI; Reiss, Peterson, Gursky, & McNally, 1986), and Cardiac Anxiety Questionaire (CAQ; Eifert et al., 2000).

Results

The average time for CIDI-SF completion on the Internet was 19.9 minutes (SD = 8.3, min = 6.8, max = 47.6). The agreement between CIDI-SF and SCID was generally low. In none of the diagnoses did Cohen's Kappa reach the suggested cut-off for fair agreement (K = .40; Robson, 1993). The sensitivity and specificity were generally low, except for the agoraphobia and OCD diagnoses. However, the panic disorder module from the long version of CIDI rendered a fair Kappa (K = .48) with an agreement of 75% with the SCID diagnosis.

An analysis of variance was conducted to explore the discriminative ability of the CIDI-SF, SCID, and the panic module from the larger CIDI. There were no differences in questionnaire responses between participants categorized as suffering from PD or not according to CIDI-SF. However, there was one significant difference and one trend in the scores between subjects categorized as suffering from PD or not according to the panic module in the larger CIDI (CAQ; $F_{(1,51)}$ = 4.34, p = .042, MI-alone; $F_{(1,51)}$ = 3.69, p = .06). For the SCID, all responses from participants categorized as suffering from PD or not were significantly different (MI-accompanied; $F_{(1,51)}$ = 8.68, p = .005, MI-alone; $F_{(1,51)}$ = 11.19, p = .002, ASI; $F_{(1,51)}$ = 4.16, p = .046, and CAQ; $F_{(1,51)}$ = 9.08, p = .004). Furthermore, there were clear differences between participants diagnosed as agoraphobics according to SCID compared to those not diagnosed as agoraphobics on both the MI-scales (all p's<.001). The same result was found for CIDI-SF.

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Discussion

Although the results need to be replicated before the idea of using CIDI-SF as a substitute for a human SCID-interview is completely dismissed, it is safe to say that the agreement between the Internet-administered CIDI-SF and a subsequent in-person SCID-interview seems to be generally low with PD patients.

The explanation is not straightforward. It could be that CIDI-SF has low validity, or that the response pattern is uniquely different on the Internet as opposed to in-person interviews. There could also be an interaction, or a problem with the reference used (the research assistants' diagnostic precision).

Another possible source of disagreement could be due to the fact that people have been reported to be more honest on the Internet (Joinson, 1999). The fact that CIDI-SF reported 60% more diagnoses than SCID could be an indication of this. In contrast, the CIDI-SF is hierarchy-free, which means that both social phobia and agoraphobia could be diagnosed, even though agoraphobia could theoretically be better accounted for by social phobia, or vice versa. The different scores on panic relevant questionnaires between probable panic cases and non-probable panic cases for the SCID, but not for the CIDI-SF, strengthen the validity of the SCID-interview. Furthermore, the inter-rater reliability was excellent. However, as evident from the DSM field trials the agreement between two clinicians is less than perfect (Kappas of .63 and .72; Peters & Andrews, 1995). As the established diagnostic procedure is imperfect, this raises the difficult methodological question of how to measure a new diagnostic procedure when the standard it is compared to is imperfect.

However, for agoraphobia and OCD two interesting results emerged. These two diagnostic modules could potentially be used as acceptable screening instruments. When CIDI-SF dismisses an agoraphobia diagnosis it is uncertain if it is actually correct. However, if CIDI-SF classifies a person as having agoraphobia, the chances are high that it is a valid decision (hence, it has a high specificity). The opposite is true for the OCD module. A probable CIDI-SF diagnosis of OCD is uncertain, but a non-probable case is likely not to be suffering from OCD (i.e. high sensitivity). However, due to the inadequate sample size and the low number of cases the calculated Kappas are unstable and making clear recommendations impossible. Use of CIDI-SF on the Internet is cautioned against until more data is available.

The panic module from the long version of CIDI proved to have an acceptable Kappa. Hence, if a cost effective and easily administered screen for panic disorder is preferred it could be of some value.

In conclusion, CIDI-SF is probably inadequate for screening for entry into panic disorder treatment study. Explanations as to where and why the CIDI-SF performs poorly must await additional research.

Study III: *Treatment of Panic Disorder via the Internet: A Randomized trial of a Self-Help Program*

Aims

Study III was designed to investigate the feasibility of providing a self-administrated assessment instrument on the Internet, and to test the effects of a self-help program while reducing the therapist contact to e-mail messages only. By not having any personal contact with the participants, neither at assessment nor during treatment, we hoped to attract those normally too shy to seek treatment and those without access to CBT. Furthermore, since the amount of therapist contact was substantially reduced, this study is an addition to the literature investigating cost-effective treatments for panic disorder (e.g., Botella & Garcia Palacios, 1999; Clark et al., 1999; Westling & Öst, 1999).

Method

To be included in the study, participants had to meet the following criteria: fulfil the DSM-IV (APA, 1994) criteria for PD; duration of at least 1 year, age between 18 and 60 years; not suffer from any other psychiatric disorder in immediate need of treatment; have a depression point total on the self-rated version of the MADRS (Svanborg & Åsberg, 1994) of less than 21 points and less than 4 points on the suicide question (Item 9); PD as the primary problem; at least one full-blown panic attack or one limited symptom attack during the pretreatment baseline (a limited symptom attack is an attack that meets all other criteria but has fewer than four somatic or cognitive symptoms.); if on prescribed drugs for panic disorder, (a) the dosage had to be constant for 3 months before the start of the treatment, and (b) the patient had to agree to keep the dosage constant throughout the study; if in therapy, this must have been ongoing for more than 6 months and not be of CBT type; previous contact with a physician, psychologist, or other health professional as a consequence of panic attacks; no epilepsy, kidney problems, strokes, organic brain syndrome, emphysema, heart disorders, or chronic high blood pressure.

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During the 2-week baseline period, participants made daily diary ratings of anxiety. In addition, the participants recorded their panic attacks in a specially designed panic diary (Clum, 1990). Participants recorded the date, situation, intensity, duration, and symptoms of every attack, and whether the attacks were expected or unexpected.

The main treatment component in this study was a self-help manual that was adapted for use via the WWW and to be suitable for Swedish conditions. About 80% of the text was a translation of the self-help book *An End to Panic: Breakthrough Techniques for Overcoming Panic Disorder* (Zuercher-White, 1998). The remaining 20% was largely inspired by and modified from *Mastery of Your Anxiety and Panic II* (Barlow & Craske, 1994) and *Overcoming Panic: A Complete Nine-Week Home-based Treatment Program for Panic Disorder* (Franklin, 1996). The material was divided into six modules. Each module ended with five to eight questions. Participants were asked to explain, in their own words, the most important sections of the module they had just completed. The questions were intended to encourage learning and to enable the therapists to assess whether the participants had assimilated the material. Individual feedback was given within 24 hours of the participants sending their answers via e-mail. On the basis of these e-mails, an assessment was made to judge whether the participant was ready to continue; if so, the password to the next module was sent. If not, the participant received instructions on what needed to be completed to be able to get to the next step. After randomization, five people dropped out during the course of the study. There were four dropouts from the treatment group and one from the waiting-list group. In the treatment group, lack of time was given as the main reason for discontinuing ($n = 3$). One patient dropped out because of a newly discovered cancer. The person who left the waiting-list group gave no reason. In the statistical analysis, pre-assessment data for applicants who were allocated to one of the two study groupings but who did not complete the treatment were brought forward and used as post-assessment data. This was done on the basis of an intention-to-treat evaluation of the results, which is a more conservative approach compared to only including completers of treatment. Hence, it was assumed that the condition of the participants who dropped out neither improved nor deteriorated during the course of treatment.

Results

The two groups did not differ significantly on any of the measures at pretreatment. Two-way repeated measures ANOVAs showed that significant interactions (Time X Treatment) were found for the daily anxiety and for all full-blown panic attack measures (frequency, duration, and intensity).

Moreover, the treated participants differed significantly from the untreated controls at post-assessment on all measures (all p's<0.05).

Significant interactions (Time X Treatment) were found for all scales, except for one subscale on the MI (the accompanied scale), where only a trend was identified. Subsequent post-hoc Tukey analyses showed that the treated participants had improved on all self-report scales during treatment, including MI "accompanied" (all p's <0.05). Moreover, the treated participants differed significantly from the untreated controls at post-assessment on all self-report measures (all p's <0.05).

Clinical significance of the Internet self-help treatment was investigated to determine the rate of improvement on an individual basis. Clinically significant improvement of panic attack frequency was defined as no occurrence of full-blown panic attacks, and no limited symptom attacks during the 2 weeks posttreatment. Beck et al.'s (1961) cutoff score for affective functioning was used for BDI. Cutoff scores on the remaining questionnaires were determined on the basis of data from our sample and the normal population, according to the formula provided by Jacobson and Truax (1991). Differences between the two groups in terms of clinically significant improvement were investigated by means of chi-square analyses. Results showed that the groups differed on BSQ (81 vs. 20%; $\chi^2_{(1)}$ = 15.23, $p<$ .001), ACQ (81 vs. 45%; $\chi^2_{(1)}$ = 5.71, $p<.05$), BAI (86 vs. 30%; $\chi^2_{(1)}$ = 13.10, $p <.001$), BDI (90 vs. 40%; $\chi^2_{(1)}$ = 8.31, $p<.01$), MADRS (67 vs. 15%; $\chi^2_{(1)}$ = 11.27, $p<.001$), Daily Anxiety (57 vs. 10%; $\chi^2_{(1)}$ = 10.12, $p<.01$), and frequency of panic attacks (33 vs. 5%; $\chi^2_{(1)}$ = 5.24, $p<.05$). Only a trend was identified on MI when alone (52 vs. 25%; $\chi^2_{(1)}$ = 3.23, $p<.10$). No difference was identified on the MI when accompanied (52 vs. 30%; $\chi^2_{(1)}$ = 2.11, $p>.10$) and the QOLI (48 vs. 30%; $\chi^2_{(1)}$ = 1.34, $p>.10$).

Even though there were no face-to-face contacts or phone calls, most participants considered the self-help program and the included advisory service to be personal. Furthermore, the lack of eye contact was reported as highly valuable by the majority of participants, as it facilitated the sharing of sensitive and important issues, such as the focal fear of losing control. Almost all participants mentioned the advantage of being able to get the treatment in the comfort of their own homes and at times that suited them.

Discussion

The results from the present study support the hypothesis that Internet administered self-help plus minimal therapist contact via e-mail is a promising new treatment approach for people suffering from PD. Participants improved significantly on the self-report scales used, whereas the waiting-list subjects did not. Specifically, the treated participants

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achieved significant improvement on diary measures of frequency of panic attacks, total intensity of each attack, total duration of each attack, and daily anxiety. Moreover, bodily sensations associated with the arousal accompanying anxiety were reduced, as well as anticipatory and catastrophic thoughts, agoraphobic avoidance, severity of anxiety symptoms, and depression. Finally, overall quality of life was increased. With the exception of two dependent measures, the treated participants reached a significantly higher degree of clinical significance compared to the waiting-list group.

The proportion of panic-free participants in this study might seem a bit lower than in previous bibliotherapy studies (cf. Gould & Clum, 1995; Gould et al., 1993; Hecker et al., 1996; Lidren et al., 1994). Interestingly, it has been argued that the number of panic attacks is not especially important as a treatment outcome measure (e.g., Zuercher-White, 1997). From a cognitive behavioral perspective, it could be argued that what matters the most are (a) the interpretation of symptoms and (b) the amount of fear associated with a panic attack. However, the results of the present study did show that the intensity and duration of the panic attacks were significantly reduced following treatment. In addition, although participants avoided significantly fewer situations posttreatment, the daily anxiety was reduced and did not increase as a consequence of the increased exposure. Some researchers have abandoned panic attack frequency as an outcome measure (e.g., Barlow et al., 2000; Clark et al., 1999). This is supported by the latest edition of the DSM (American Psychiatric Association, 1994), which puts a greater emphasis upon worry about attacks, and has eliminated panic frequency as a diagnostic criterion.

Because the therapists never met the participants in person, there was a risk of including those with too extreme suicidal tendencies. To minimize this risk, a decision was made to exclude those who, according to the depression inventory MADRS (Svanborg & Åsberg, 1994), were severely depressed. Hypothetically, this might have led to a sample of people who were less depressed compared with other studies. The other three bibliotherapy studies that used BDI as a measure of depression had average pretreatment assessments of 14, 15, and 18 points, respectively (Gould et al., 1993; Hecker et al., 1996; Lidren et al., 1994). In this investigation the treatment group had an average BDI score of 11 points, which raises the question of how the treatment would have worked on patients who were more severely depressed.

However, comparisons with standardized face-to-face therapy are imperative. An attempt should also be made to identify the characteristics of the subgroup of people with PD who would be most likely to benefit from this simple and cost-effective treatment. In sum, this was probably the first controlled study investigating the efficacy of a self-help treatment program

on the Internet for panic symptomatology. The results from this experiment generally provide evidence for the continued use and development of Internet-based self-help programs for PD.

Study IV: *Treatment of Panic Disorder via the Internet: A Randomized trial of applied relaxation vs. cognitive behavior therapy*

Aims

In an attempt to provide a cost-effective treatment for people suffering from PDA, Carlbring and coworkers (Study III) developed an Internet-delivered self-help program and provided minimal therapist contact via e-mail. A question that came up was if the time the therapist spent on each subject (approx. 90 minutes in total) could be reduced even more, and how important therapist monitoring of the patient's progress was. Study IV deliberately minimized the time spent on each subject by using one of about 25 different standardized e-mail messages in response to questions. Furthermore, no time limit for the completion of the different treatment steps was set.

Instead of using a waiting-list control, which in an earlier study showed no improvement over time, a second treatment condition was employed. The choice of applied relaxation (AR; Öst, 1987) was made because it, at least in some studies, is equally as effective as CBT (Öst & Westling, 1995b). Furthermore, the delivery of this treatment is less demanding on the therapist and previous studies have shown that it can be delivered via the Internet (e.g., Andersson et al., 2002; Ström et al., 2000).

Method

Participants were recruited from a waiting-list of people who had expressed an interest in taking part of the Internet-administered self-help program for panic disorder. Originally they were recruited by means of newspaper articles in national and regional papers and notices in health magazines.

Participants were selected by an in-person Structured clinical interview for DSM-IV interview (SCID; First et al., 1997). The same inclusion criteria

and dependent measures as in Study III were used. Demographic data on the 22 participants included[6] in the study are presented in Table 2.

After randomization, five people dropped out during the course of the study. There were three dropouts from the CBT group and two from the AR group. Lack of time was given as the main reason for discontinuing.

In the statistical analysis, preassessment data for applicants who were allocated to one of the two study groupings but who did not complete the treatment were brought forward and used as postassessment data ($n = 5$). This was done on the basis of an intention-to-treat evaluation of the results, which is a more conservative approach compared to only including those who completed the treatment (Newell, 1992). Hence, it was assumed that the condition of the participants who dropped out neither improved nor deteriorated during the course of treatment.

The main treatment component in the CBT group was the same self-help material used in study III. It consisted of 197 pages of text and exercises divided into 6 modules: psychoeducation, breathing retraining, cognitive restructuring, interoceptive exposure, exposure in vivo, relapse prevention, and assertiveness training (for details see Study III).

In the AR group Öst's Applied Relaxation book (Öst, 1987) was adapted for self-help use via the WWW. A compact disc (CD) with three relaxation instructions was also sent to the participants. The treatment was divided into 9 modules: (1) psychoeducation, (2) rational, (3) progressive muscle relaxation: long version, (4) progressive muscle relaxation: short version, (5) conditioned relaxation, (6) differential relaxation, (7) quick relaxation, (8) applied relaxation, and (9) relapse prevention. Participants with a cellular phone ($n = 5$) were sent short message service (SMS) reminders to relax about twice every weekday.

Each module ended with five to eight questions. Participants were asked to explain, in their own words, the most important sections of the module they had just completed. The questions were intended to encourage learning and to enable the research supervisors to assess whether the participants had assimilated the material, and finished their homework. Standardized feedback was given within 7 days of the participants sending their answers via e-mail. On the basis of these e-mails, an assessment was made of whether the participant was ready to continue; if so, the password to the next module was sent. If not, the participant received instructions on what needed to be completed before proceeding to the next step.

The mean total time spent by the therapist on each participant was approximately 30 minutes, including administration, and responding to the e-

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[6] In the original paper reasons for exclusion was only given for 21 out of the 31 excluded participants. The remaining 10 were excluded because the PD was subclinical and/or due to suicidal ideation.

mails. Most answers were fully standardized. Often only the participant's name was altered in the greeting phrase of the e-mails.

Participants accessed to the first treatment module at the end of May 2001. They were expected to read the material and do the exercises described in the modules. No time limit was set for completing each module. An e-mail message to inquire how work with the current module was progressing was sent out once in September 2001. Post-treatment assessment was conducted in December 2001.

Results

The two groups did not differ significantly on any of the measurements at pre-treatment.

Two-way repeated measures ANOVAs of the self-report inventories showed that there were no significant interactions (Time X Treatment group) or main effects on the group variable, except for the subscale MI when accompanied. However, significant main effects on time were found for all scales, except for QOLI, where a trend was identified.

Two-way repeated measures ANOVAs on the panic diary recordings showed that there were no significant interactions (Time X Treatment group) or main effects on the group variable. However, significant main effects of time were found for the frequency of both limited and full-blown panic attacks, as well as on the fear barometer. There were no time effects on the daily anxiety or duration and intensity of the attacks. Six participants (55%) in the AR group and 4 (37%) in the CBT group were panic free the two weeks following treatment.

The effect size (pooled within *sd*) differed greatly across the different measurements. Highest value was found on BAI for the AR group (Cohen's $d = 1.40$) and on the Fear Barometer for the CBT group ($d = 1.40$). The lowest value was found for the duration of the limited symptom attacks for the CBT group ($d = -0.24$).

The overall effect size was $d = 0.42$ for the CBT group and $d = 0.71$ for the AR group. An independent samples *t*-test showed that the difference did not reach statistical significance ($t_{29} = -1.98$; $p = .057$)[7], but was in the direction of superior performance in the AR group.

Participants considered the self-help program and the included advisory service to be moderately personal. A number of participants reported feeling alone in cyberspace (cf. Lambert, Senior, Phillips, & David, 2000), and thought that they would have benefited more if a forum was included where

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[7] In the original paper the degrees of freedom was reported to be 23, but the correct number is 29. However, the originally reported *t* and *p*-values are still correct.

they could discuss difficult steps in the treatment program and give emotional support to each other. Such a forum, it was reported, would have motivated the participants to log in more frequently, and possibly work harder on the treatment modules. Almost all participants mentioned the advantage of being able to receive the treatment in the comfort of their own homes and at times that suited them. However, they felt that without prompts and deadlines it was difficult not to procrastinate.

Discussion

The results from the present study suggest that Internet-administered self-help plus minimal therapist contact via e-mail has an overall medium to large effect. Although not statistically significant, the AR condition has a better overall effect compared to the CBT program ($d = .71$ and $d = .42$ respectively). However, as no time-effect condition was included in the study the equivalence of the two treatments could indicate similar effectiveness or similar ineffectiveness. Although unlikely, all improvement could have been due to psychological "placebo" or produced by a time-effect. While it is true that there was no waiting-list group control for the mere passage of time, earlier studies (e.g., Richards, Klein et al., 2003) have shown that there is only a negligible change in results from pre- to posttest (Cohen's $d = .05$). The result cannot fully be explained by a placebo effect either. According to Rapaport and coworkers, patients who respond to a placebo in panic disorder treatment studies may show symptom relief but may not experience improvement in quality of life (Rapaport et al., 2000). Due to low power this study showed only a trend towards better quality of life, suggesting that the results were valid.

Reasons for why the AR group achieved better overall effect-sizes compared to the CBT condition could be that the AR participants received a CD with relaxation instructions, or that the treatment modules were shorter. Shorter modules were completed more quickly, which led to more frequent rewards (sense of accomplishment). Also, the frequent SMS-messages could have acted as prompts or reminders that increased motivation. Another plausible reason might be that cognitive therapy components of the CBT program might necessitate more interaction than the fairly straightforward AR components. This however is contradicted by previous results on CBT self-help for depression (Smith, Floyd, Scogin, & Jamison, 1997). Why was the CBT program in the present study less effective than the same program when tested earlier (effect size $d = 0.94$ vs. 0.42)? Apart from sampling issues (e.g., small sample size, rather heavy assessment procedure), reasons could be that less therapist involvement, leading to the use of standardized e-mails, in combination with the longer answer time (7 vs. 1 day) might have

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demoralized the participants. Furthermore, the fact that there was no time limit for the completion of each module also seems to play a pivotal role (cf time-effect). A suggestion for future treatments is to test if strict deadlines and setting up a treatment outline before commencing self-help treatment improves the results.

This study's largest shortcoming is probably the fact that only 56% of the treatment material was completed. In the earlier study comparing the same CBT treatment modules on the Internet with a waiting list, more than 90% of the participants completed all modules. Reasons for this relatively low module usage could in part be explained by the unfortunate timing of the start of the study (end of May). Another reason, expressed by some participants, was that the e-mails sent by the therapist were too impersonal. This was not the case in the earlier study that relied only on standardized comments in parts of the e-mails. Furthermore, there was significantly lower treatment credibility in this study (32.6 and 34.9 vs. 42.6 in Study III) compared to the earlier Internet study for both the AR and CBT groups (Tukey HSD; $p<.05$).

In conclusion, the results from this experiment generally provide evidence to support continued use and development of Internet-based self-help programs for PD. However, more therapist involvement is probably needed.

Study V: *Treatment of Panic Disorder: Live Therapy vs. Self-Help via Internet*

Aims

The results from Studies III and IV generally provide evidence to support the continued use and development of self-help programs for panic disorder distributed via the Internet. However, there has never been a direct comparison between an Internet-delivered self-help program and traditional CBT. The aim of this study was to compare the two formats of panic treatment. Given that both treatments have been evaluated in separate controlled trials with untreated waiting list controls without any improvement in the waiting list group, it was decided not to include a no-treatment control group.

Method

Participants were recruited from a waiting-list of people who had expressed an interest in taking part of an Internet-administered self-help program for

panic disorder, after having heard about previous Internet studies on panic disorder (e.g., Study III). Mean time on the waiting list was 7 months (range: 0-24 months).

The inclusion criteria were the same as in Study III and IV. The selection of participants was achieved by a computerized screening interview consisting of MADRS (Svanborg & Åsberg, 1994) and 53 additional questions derived from the PD sections of Composite International Diagnostic Interview (CIDI 2.1; World Health Organization, 1997), the ADIS-IV (Di Nardo et al., 1994), and the PD and social phobia section from SCID-I (First et al., 1997).

All participants who fulfilled the inclusion criteria according to the computerized interview were called to an in-person SCID interview (First et al., 1997) to confirm the diagnosis.

Dependent variables in the study were the BSQ, ACQ, MI, BAI, BDI, MADRS, and the QOLI. As the validity of internet-administered questionnaires is not yet clear, all outcome measures were administered in paper-and-pencil form (c.f. Andersson, Kaldo-Sandström, Ström, & Strömgren, 2003; Buchanan, 2003). To investigate if a subject's opinion of the treatment's credibility could predict treatment outcome, participants were given a five-item, 10-point scale adapted from Borkovec and Nau (Borkovec & Nau, 1972). To determine the clinical significance of the treatment a clinical re-interview (SCID) was administered by an independent psychologist blind to treatment condition. This was done one month after the treatment ended, and at a one year follow-up. To ensure the validity of the diagnosis made, 10% of the tapes were randomly selected and reassessed by an independent psychiatrist with extensive SCID training. The agreement was excellent (Cohen's Kappa = .80).

Out of the 427 people who completed the computerized interview 363 (85%) were excluded. The most common reasons for exclusion were that; the panic attacks were better accounted for by social phobia, the panic attack frequency was too low, three or fewer symptoms, recent commencement of medication, recently commenced or intensified another unrelated psychotherapy, or that the depression point total was too high. Another reason for exclusion was if the person lived too far from the study site and did not agree to come to Uppsala for treatment if he/she was randomized to treatment in person.

Sixty-four people were called to an in-person SCID interview, but five failed to show up. Of the 59 people interviewed 10 were excluded because the panic attacks were better accounted for by social phobia ($n = 4$), post traumatic stress disorder ($n = 1$), dysthymia ($n = 1$), generalized anxiety disorder ($n = 2$), anxiety not otherwise specified ($n = 1$), and Asperger

syndrome ($n = 1$). Demographic data on the 49 participants included in the study are presented in Table 2.

The SCID-II screening questionnaire was used to estimate frequencies of personality disorders. Using the SCID-manual's suggested cut-off scores 82% had a possible ongoing Axis-II disorder; Obsessive-Compulsive (32.7%), Antisocial (26.5%), Dependent (24.5%), Avoidant (24.5%), Depressive (22.4%), Passive-Aggressive (10.2%), Schizoid (10.2%), Paranoid (6.1%), Borderline (6.1%), Histrionic (4.1%), Narcissistic (2.0%), and Schizotypal (0.0%).

Participants were divided into two groups, live therapy (Live) or Internet-based (IT) by a true random-number-service (http://www.random.org). After randomization, six people dropped out during the course of the study. There were three dropouts from the live therapy group and three from the IT group. Lack of time was given as the main reason for discontinuing. However, in accordance with the intention to treat paradigm (e.g. Nich & Carroll, 2002; Newell, 1992) post-treatment data was collected from all drop-outs. Six participants did not return their follow-up questionnaires, and their post-treatment scores were carried forward to the follow-up assessment point. Hence, all 49 participants that were randomized to one of the two conditions are included in the statistical analysis.

The treatment was manualized and divided into 10 modules; (1-2) psychoeducation and socialization, (3) breathing retraining and hyperventilation test, (4-5) cognitive restructuring, (6-7) interoceptive exposure, (8-9) exposure in vivo, and finally (10) relapse prevention and assertiveness training. Each module consisted of approximately 25 pages, and was in large part similar to the previously tested self-help material in Study III.

The therapists were four clinical licensed psychologists with research and/or clinical experience with anxiety disorders, three advanced graduate students with a master's degree in clinical psychology, and one person with 4.5 years of psychologist training (i.e. the last semester of the master's degree program). During 8 of the 10 treatment weeks the therapists received a total of 16 hours of group supervision by a person licensed as psychologist, CBT-therapist, and CBT-supervisor, with extensive experience of working with panic disorder treatments.

In the IT group each module was converted into web pages and was accessible via the WWW. Each module included information and exercises, and ended with three to eight essay questions. Participants were asked to explain, in their own words, the most important sections of the module they had just completed, provide thought records and describe their experience with and results of their exposure exercises. The questions were intended to promote learning and to enable the research supervisors to assess whether

the participants had assimilated the material, and completed their homework. Also, each module ended with a multiple-choice quiz that the participants needed to get 100% correct in order to proceed. Finally, in every module the participants were required to post a message in a discussion forum about a specific topic.

Feedback on the homework was usually given within 36 hours after sending their answers via e-mail. On the basis of these e-mails, an assessment was made of whether the participant was ready to continue; if so, the password to the next module was sent. If not, the participant received instructions on what needed to be completed before proceeding to the next module.

Participants in the live therapy condition received 10 weekly individual sessions lasting 45-60 minutes. Between each session the participant was expected to do homework, which included reading a module handout identical to the text in the IT condition. Furthermore, each session was tape recorded and the participant was instructed to listen to it after the sessions to consolidate learning (Clark, 1989). The tapes were later used for adherence checks and supervision.

Results

The two groups did not differ significantly on any of the measures at pre-treatment. Repeated measures ANOVA revealed no significant interactions (smallest $p = 0.19$). However, as evident from Table 2 all self-report measures showed significant improvements both at pre-treatment vs. post-treatment and at pre-treatment vs. follow-up (all p's $<.025$ with one-tailed paired samples t-test). There were no differences between post-treatment and follow-up.

The within-group effect size (pooled SD) differed greatly across the different measures. Highest value was found on BSQ (Cohen's $d = 2.14$ for the live group and 1.45 for the IT-group). Lowest value was found for QOLI ($d = 0.48$ and 0.37 respectively). There were no significant differences between the two conditions, but in 31 of the 32 effect size calculations the live group scored higher. The overall effect size was 0.99 for the live group and 0.78 for the IT group at post-treatment, and 0.93 and 0.80 respectively at follow-up.

Using a clinical re-interview (SCID) to determine the clinical significance of the treatment revealed no difference between the two groups in the proportion of participants no longer meeting criteria for PD. One month after the treatment ended, 80% in the IT group and 67% in the Live group no longer met criteria for PD (ns). At the one year follow up the figure was 92% in the IT group and 88% in the Live group (ns). However, 20% in each

group of those participants not meeting the criteria for PD still had some residual problems.

The treatment credibility scale did not predict outcome except in two cases. For the IT-group the treatment credibility for the IT-condition correlated significantly with the change scores on BSQ ($r = .46$; $p = .02$). Parallel, for the live group the treatment credibility for the live-condition correlated significantly with the change scores on BSQ ($r = .44$; $p = .03$).

Table 2. Mean (SD), Cohen's pooled within-group effect size for the questionnaires used at pre- and post-treatment, and follow-up for the two treatment groups respectively. *=All p's <.025 with t-test pre vs. posttreatment or follow-up.

Measure	Group	Pre	Post	Follow up	Within-Group Effect Size (Cohen's d)	
					Pre-Post	Pre-F-U
BSQ	LIVE	52.6 (10.8)	31.3 (9.1)	31.9 (10.7)	2.14 *	1.92 *
	IT	48.7 (11.7)	31.8 (11.6)	32.1 (11.5)	1.45 *	1.43 *
ACQ	LIVE	34.6 (9.3)	23.6 (7.2)	23,1 (8,6)	1.33 *	1.29 *
	IT	34.5 (8.6)	23.8 (9.0)	23.0 (9.6)	1.22 *	1.27 *
MI -Alone	LIVE	2.7 (0.9)	1.9 (0.8)	2.0 (0.9)	0.85 *	0.76 *
	IT	2.2 (0.9)	1.7 (0.7)	1.6 (0.7)	0.64 *	0.68 *
MI -Accomp	LIVE	2.1 (0.8)	1.5 (0.6)	1.5 (0.6)	0.84 *	0.81 *
	IT	1.8 (0.5)	1.4 (0.4)	1.5 (0.5)	0.71 *	0.63 *
BAI	LIVE	24.5 (10.4)	12.3 (7.7)	12.3 (10.1)	1.35 *	1.18 *
	IT	18.7 (10.3)	10.9 (7.1)	10.7 (7.9)	0.90 *	0.88 *
BDI	LIVE	15.9 (9.0)	10.2 (7.0)	8.8 (6.7)	0.71 *	0.91 *
	IT	11.8 (7.8)	6.6 (5.5)	6.2 (5.4)	0.78 *	0.83 *
MADRS	LIVE	16.0 (4.3)	10.4 (5.6)	10.1 (6.9)	1.15 *	1.05 *
	IT	13.4 (5.3)	8.6 (5.7)	8.1 (5.7)	0.87 *	0.97 *
QOLI	LIVE	0.9 (1.6)	1.7 (1.5)	1.7 (1.3)	-0.48 *	-0.50 *
	IT	1.4 (1.7)	2.0 (1.4)	1.9 (1.4)	-0.37 *	-0.31 *
Free from Panic Disorder	LIVE	0%	67%	88%		
	IT	0%	80%	92%		

Discussion

The results suggest that Internet-administered self-help plus minimal therapist contact via e-mail can be equally effective as 10 sessions of manualized individual cognitive behavior therapy. Both treatments showed large effect sizes both at posttreatment and at follow-up. Specifically, bodily sensations associated with the arousal accompanying anxiety were reduced, as well as anticipatory and catastrophic thoughts, agoraphobic avoidance, severity of anxiety symptoms, and depression. Finally, overall life satisfaction was increased and a large proportion did not meet diagnostic criteria for PD after treatment.

While the efficacy was equivalent, there were substantial differences between the groups in the proportion of treatment modules finished in time. Perhaps contact purely via e-mail is not powerful enough to stimulate the maintenance of the treatment pace. However, one of the advantages of internet-based self-help is that the treatment can be done at a time that fits the client's individual agenda. It is possible that the pace of one module per week is too rapid. Perhaps the first five modules should be administered once a week and the following every fortnight. That would give patients more time for in vivo exposures. On the other hand, having extended time limits or no deadlines at all seem to have disadvantages (cf. Study IV).

There is a need to investigate the optimal level of therapist involvement. In the present study approximately 150 minutes was used in total for each participant in the self-help condition. Maybe short weekly complementary telephone calls could have an additive effect. A step in that direction has been taken by Richards and Alvarenga (2002), who contacted the participants by telephone to monitor progress and answer any questions which may have arisen. Although more costly in the short term, the results might outweigh the disadvantages in the long run. However, in a recent randomized trial on treatment of headache no differences were found between participants who received weekly telephone calls and those who did not in addition to the Internet based self-help treatment (Andersson, Lundström, & Ström, 2003).

Even though the treatment credibility was lower for internet-based self-help, and the treatment dosage was lower in the self-help group, it did not seem to influence the level of recovery, since the proportion of participants reaching high end-state functioning was equal.

Apart from possible cost-effectiveness, one of the justifications of Internet based self-help therapy is the possibility of treating people who would not otherwise seek treatment. For example those with severe agoraphobia who may not seek therapy due to fear of leaving their houses or

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travelling certain distances (Newman et al., 2003). By asking participants to come to a selection interview in which the SCID interview was conducted, self-selection bias for the treatment applications via Internet may have been induced. This may be an important flaw in view of the high proportion of PD-patients not asking for professional help and may limit the generalizability to the intended population. Furthermore, the exclusion of participants if they were in immediate need of psychiatric treatment due to suicidality, may have resulted in low severity overrepresentation in the sample. However, the means on the pre-treatment measures are comparable to the norms of a PD population (Antony, 2001).

The study is of course afflicted with a few additional problems. First, the therapists had only minor to modest clinical experience of working with PD patients. This might have affected the outcome for the live group, whereas the Internet treatment (e.g., responding via e-mail) might be less susceptible to lack of extensive experience, given the time to check, and consult colleagues. However, all therapists were given regular supervision from a licensed CBT supervisor and 50% of the therapists had experience of working with panic disorder patients both in clinical and in research settings. Second, the study was conducted by a research group closely affiliated with Internet research, and as researcher allegiance is known to influence outcome in psychotherapy research (Luborsky et al., 1999), we cannot exclude this possibility. Independent replication would therefore be welcome. Third, low statistical power limited the possibility to secure differences between two treatments. Then again, the value of increasing power in order to establish an effect of small magnitude is of less practical interest. Overall, the data suggest that the differences between the two treatments were small.

There is a need for future studies to examine the effect of internet-based self-help with minimal therapist contact via e-mail in primary care, and also in relation to and in combination with best-practice psychotropic medication (e.g. SSRIs), although it is not obvious that combination treatments will yield superior outcomes (Barlow, Gorman, Shear, & Woods, 2000; Foa, Franklin, & Moser, 2002). Another interesting topic would be to transfer this research-based treatment into a clinical setting (Wade, Treat, & Stuart, 1998).

General discussion

The present thesis suggests that during the past 12 months 197,500 people in the Swedish general population have suffered from panic disorder with or without agoraphobia. However, as only 25% of the people suffering from PD seek any kind of treatment, and those that do are often undertreated (Roy Byrne et al., 2002), there is room for improvement.

The advent of Internet technology has given rise to new opportunities in treatment and prevention research and is a potentially powerful delivery method for psychological interventions. Newman and colleges (2003) have suggested that for agoraphobia the absence of physical therapist interaction may be better, as there is a documented tendency to form intense attachments and to exhibit heightened fears of abandonment. Hence, extended therapist contact may facilitate countertherapeutic dependency on the therapist, making relapse more likely. The three randomized treatment trails included in this thesis show that self-help via the Internet, plus minimal therapist contact via e-mail, is superior to a waiting-list, and can even be comparable to traditional face-to-face therapy.

However, as almost all subjects where self-recruited the transportability of the results to a community mental health center is unclear. In spite of this, the human suffering and the large costs when PD sufferers seek emergency treatment necessitate exploring new ways of identifying and treating these individuals.

Longitudinal studies suggest that it may be possible to identify people at high risk of developing PD and apply preventative treatments before full-blown PD develops (Ehlers, 1995; Kenardy, McCafferty, & Rosa, 2003; Schmidt, Lerew, & Jackson, 1997).

Haaga (2000) has suggested that not all patients need the same type and intensity of intervention. Some may be helped greatly by reading a self-help book, watching an instructional video, or using a computer program. Others could benefit from a brief psychoeducational group conducted by a paraprofessional, and still others may require long-term individual treatment from a highly trained professional therapist with specialized expertise.

There already exists a stepped-care model for depression inclusive of a self-administered treatment component (Scogin, Hanson, & Welsh, 2003). A similar model for PD, backed up by empirical findings, would be welcome

since psychiatric care has limited resources. A step in that direction has been taken by Baillie and Rapee (in press), who have developed a prognostic scale which can be used to guide the choice of psychoeducation, self-help, or face-to-face therapy as the first step in stepped care. Hence, one should provide all the time, expertise, and individual attention a patient needs, but not more (Haaga, 2000). Perhaps prognostic validity can be increased even more if attention is given to the individual's position in the *Stages-of-change* (c.f. McConnaughy, Prochaska, & Velicer, 1983; Prochaska & Norcross, 2001).

According to Prochaska and colleagues (Prochaska, DiClemente, & Norcross, 1992), patients go through several distinct stages-of-change; not considering any change (Precontemplation), serious consideration of change sometime in the future (Contemplation), initial behavioral steps toward change (Preparation), concrete activities that will lead to the desired change (Action), and active efforts to sustain the changes made (Maintenance).

Reid and colleges (1996) have shown that PD-patients with low predisposition to change changed more slowly than those in the Contemplation or Action stages of change. Consequently, a person in the action-stages of change might be more suited for self-help than for example precontemplators, or contemplators.

Apart from relatively small sample sizes in Studies I, II, and IV, the thesis of course requires a few additional caveats. In study III and IV data collection was done entirely on the Internet. Since then there have been reports that while the psychometric properties replicate over media, score distributions may differ across testing media, even when comparisons are made between equivalent samples (Buchanan, 2003; Buchanan & Smith, 1999). Hence, while the measures are reliable and valid it is recommended that if online tests are used for clinical purposes, this should currently be done in a manner that does not rely on normative data. Hence, the clinically significant change reported in Study III, which was based on normative data from a paper-and-pencil sample, should be interpreted with caution. On the other hand, there are also reports of lower social desirability when the Internet is used (e.g., Joinson, 1998, 1999). In any case, the treatment efficacy was replicated when using paper-and-pencil questionnaires in Study V.

Unfortunately, the results from Study II appear to confirm the negative findings of brief diagnostic screening tools for panic disorder (Lowe et al., 2003; Stein et al., 1999). In fact, there are reports that even telephone administrated structured clinical interviews have a poor agreement for current diagnoses (Cacciola, Alterman, Rutherford, McKay, & May, 1999). However, given that a large proportion of the screened participants in Studies III, IV and V were excluded because their panic attacks were better accounted for by social phobia, perhaps the CIDI-SF could prove valuable if

people with social phobia first were excluded by the Social phobia screening questionnaire (SPSQ; Furmark et al., 1999). The SPSQ has proven to have excellent specificity and sensitivity. More research on screening for panic disorder via the Internet is needed before it is dismissed.

Future research should also investigate the optimal level of therapist involvement and how rapid the e-mail turn-around should be. Additionally, as cost-effectiveness is a key factor in guided self-help, the impact of therapist experience should be evaluated. Perhaps the CBT-based self-help techniques are so powerful in themselves that the human-interaction can be handled by a trained layperson. This has been tested in binge eating, and Carter and Fairburn (1998) have found some evidence of this. However, it could be argued that the quality of the therapy might suffer. Schmidt and colleagues (2000) have suggested that the quality of the participant's work, relative to the quantity of the work, were relatively better predictors of outcome.

Finally, another important issue is the timing and pacing. Ten weeks might not be the optimal duration of the self-help program – what the most advantageous length is, and if the material should be paced (one module per week given that homework has been properly finished), remains to be explored in future studies.

In conclusion, the Swedish panic disorder prevalence is relatively consistent with findings in most other parts of the Western world. The agreement between CIDI-SF and SCID was generally low. However, if the panic disorder module from the long version of CIDI is used instead, the Kappa is fair with an agreement of 75%. The results from the randomized treatment trials provide evidence to support the continued use and development of Internet-distributed self-help programs.

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