

**A Comparative Study of the Efficacy of Group
versus Individual Cognitive Behavior Therapy
in the Treatment of Panic Disorder**



Inaugural-Dissertation
to obtain a Doctorate of Philosophy
Fachbereich G: Bergische Universität Wuppertal

PhD. Thesis
Author: Farangis Jamali Zadeh
Supervisor: Prof. Dr. Gudrun Sartory

Wuppertal 2014

Die Dissertation kann wie folgt zitiert werden:

urn:nbn:de:hbz:468-20140326-103426-5

[<http://nbn-resolving.de/urn/resolver.pl?urn=urn%3Anbn%3Ade%3Ahbz%3A468-20140326-103426-5>]

Acknowledgement

This undertaking would not have been possible without the generous support of many people.

First and foremost, I would like to express my gratitude to my supervising Prof. Dr. Gudrun Sartory. Without her outstanding support, mentorship and guidance this work would not exist.

I am also greatly indebted to my co-supervisor, Prof. Dr. Reinhard Pietrowsky for his support and in particular for his critical reading of this work. His guidance greatly improved the quality of this work.

I am also enormously grateful to Prof Dr. Alexandra Martin and PD Dr. Karin Elsesser for offering their valuable time to serve as my dissertation committee members.

I am grateful to individuals who enrolled in the protocol. Without their commitment this work could not have been undertaken and completed.

I would like to pay special tribute to my best friend Mara McClain who has been the driving force behind me and I can never thank her enough for all the support. She has provided me throughout the years.

TABLE OF CONTENTS

List of Abbrevations.....	V
List of Tables.....	VII
List of Figures.....	IX
Introduction.....	1
Chapter I - Theoretical Background.....	3
1.1 Historical Background.....	3
1.2 Panic Disorder with or without Agoraphobia.....	5
1.2.1 Definition of Panic Disorder.....	5
1.2.2 Diagnostic Criteria for Agoraphobia.....	5
1.2.3 Panic Disorder and Comorbidity.....	8
1.2.4 Epidemiology.....	12
1.2.4.1 Epidemiology of panic disorder.....	12
1.2.4.2 Epidemiological survey of panic disorders in Iran.....	14
1.2.4.3 Epidemiology of psychiatric disorders in the Hormozgan province.....	15
1.2.5 Etiology.....	16
1.2.5.1 Heredity.....	16
1.2.5.2 Neurobiological Models.....	18
1.2.5.3 Carbon dioxide sensitivity.....	20
1.2.5.4 False Alarm theory.....	22
1.2.5.5 Cognitive model.....	25
1.2.5.6 Anxiety sensitivity.....	28
1.3 Treatment of panic disorder.....	30
1.3.1 Pharmacological interventions.....	30
1.3.2 Psychological interventions.....	34
1.3.2.1 Habituation Training.....	35
1.3.2.2 Anxiety Management Training (AMT).....	44
Relaxation Therapy.....	44
Breathing retraining and Respiratory Control.....	50
1.3.2.3 Cognitive interventions.....	60
Panic Education.....	60
Cognitive Restructuring.....	62
1.3.2.4 Combination Treatments.....	69
1.4 Group Therapy for panic Disorder: An Overview.....	76
1.4.1 Benefits of the Group CBT Format.....	79
1.4.2 Previous Research on effect of Group CBT in Panic Disorder.....	85
1.4.3 Individual Therapy versus Group Therapy.....	89
1.4.4 Previous Research on Individual Therapy versus Group Therapy in Panic Disorder.....	93
1.5 Aim of the Study.....	96
1.6 Hypotheses and Research questions.....	98
1.6.1 Hypotheses.....	98
1.6.2 Research Questions.....	99
Chapter II - Methodology.....	100

2.1 Design and procedure	100
2.1.1 Participants	100
2.1.2 Study Design and Procedure.....	103
2.1.3 Treatment Protocol	105
2.2 Measures.....	110
2.3 Statistical Data Analyses	115
Chapter III - Results.....	116
3.1 Introduction	116
3.2 Group comparison pre-treatment.....	117
3.2.1 Demographic data.....	117
3.2.2 Pre-treatment comparison of questionnaire data	119
3.3 Effect of treatments pre-post and pre-post-follow-up	123
3.3.1 Beck Anxiety Inventory (BAI)	123
3.3.1.1 Treatment (ICBT/GCBT/WL) by time (pre/posttest)	123
3.3.1.2 Treatment (ICBT/GCBT) by time (pre/post/four-month follow-up)	125
3.3.2 Beck Depression Inventory (BDI)	127
3.3.2.1 Treatment (ICBT/GCBT, WL) by time (pre/posttest).....	127
3.3.2.2 Treatment (ICBT/GCBT) by time (pre/post/four-month follow-up)	129
3.3.3 Panic Disorder Severity Scale (PDSS)	130
3.3.3.1 Treatment (ICBT/GCBT, WL) by time (pre/posttest).....	131
3.3.3.2 Treatment (ICBT/GCBT) by time (pre/post/four-month follow-up)	133
3.3.4 Agoraphobic Cognition (ACQ)	135
3.3.4.1 Treatment (ICBT/GCBT, WL) by time (pre/posttest).....	135
3.3.4.2 Treatment (ICBT/GCBT) by time (pre/post/four-month follow-up)	137
3.3.5 Anxiety Sensitivity Severity (ASI)	139
3.3.5.1 Treatment (ICBT/GCBT, WL) by time (pre/posttest).....	139
3.3.5.2 Treatment (ICBT/GCBT) by time (pre/post/four-month follow-up)	141
3.3.6 Agoraphobic Avoidance Severity (FQ-AG).....	143
3.3.6.1 Treatment (ICBT/GCBT, WL) by time (pre/posttest).....	143
3.3.6.2 Treatment (ICBT/GCBT) by time (pre/post/four-month follow-up)	145
3.4 Correlations among pretest measures.....	147
Chapter IV - Discussion.....	158
4.1 Severity of PD	159
4.2 Effectiveness of treatment (pretest to posttest)	164
4.3 Effectiveness of treatment (Pretest-Posttest-Follow-up).....	172
4.4 Conclusions	178
4.5 Limitations of the Present Study	181
4.6 Future Directions of Research.....	182
Summary	183
Reference	184
Appendix A	225
Appendix B	226
Appendix C	227

List of Abbreviations

ACQ	Agoraphobic Cognitions Questionnaire
ALP	Alprazolam
AMT	Anxiety Management Treatment
ANOVA	Analysis of Variance
AR	Applied Relaxation
ASI	Anxiety Sensitivity Index
AS	Anxiety Trait
BAI	Beck Anxiety Inventory
BCBT	Brief Cognitive Behavior Therapy
BDI	Beck Depression Inventory
BR	Breathing Retraining
BT	Breathing Training
CBT	Cognitive Behavior Therapy
CGI	Clinical Global Impressions
CM	Cognitive Modification
CO2	Carbon Dioxide
CR	Cognitive Restructuring
CT	Cognitive Therapy
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders
EA	Episodic Anxiety
EXP	Exposure
EEXP	External Exposure
FQ	Fear Questionnaire
FQ-AG	Fear Questionnaire Agoraphobia
FU	Follow-Up
GCBT	Group Cognitive Behavior Therapy
HBET	Habituation Based Exposure Therapy
HAMA	Hamilton Anxiety Scale
HAMD	Hamilton Depression Scale
ICBT	Individual Cognitive Behavior Therapy
IEXP	Introceptive Exposure
IMI	Imipramine Therapy
MADRS	Montgomery-Asberg Depression Scale
MCC	Minimal-Contact Control
MIA	Mobility Inventory for Agoraphobia
NAC	Non Anxiety Controls
NCS-R	National Comorbidity Survey Replication
NCS	National Comorbidity Survey

NESARC	National Epidemiological Survey on Alcohol and Related Conditions
NIMH	National Institute Mental Health
NCS	National Comorbidity Survey
NFCT	Non Focal Cognitive Therapy
PBI	Panic Believe Inventory
PCO2	Partial Pressure of Arterial Blood Carbon Dioxide
PCT	Panic Control Treatment
PD	Panic Disordered
PDA	Panic Disorder with Agoraphobia
PDSS	Panic Disorder Severity Scale
PDWA	Panic Disorder with Agoraphobia
PHMT	Pharmachotherapy
PLC	Placebo
PMR	Progressive Muscle Relaxation
Parox	Paraoxetine therapy
QoL	Quality of Life
REL	Relaxation
SCID	Structured Clinical Interview for DSM-IV
SCT	Standard Cognitive Therapy
SH	Self Help bibliotherapy
SIB	Self-Information Booklet
SNS	Sympathetic Nervous System
SPSS	Statistical Package for the Social Sciences
SRT	Symptom Rating Test
SSRI	Selective Serotonin Reuptake Inhibitor
STAI-T	State-Trait Anxiety Inventory-Trait version
TAU	Treatment as Usual
VI	Vagal Innervation
vivo EXP	vivo Exposure
WL	Waiting List

List of Tables

Table 1.1: Comorbid disorder with panic disorder	11
Table 1.2: Family, twin studies of panic disorder	18
Table 1.3: Overview of exposure treatment studies in panic disorder	41
Table 1.4: Overview of Relaxation treatment studies in panic disorder.....	48
Table 1.5: Overview of Breathing Retraining studies panic disorder	57
Table 1.6: Overview of cognitive therapy versus other treatment modalities.....	67
Table 1.7: Overview of Panic Control Treatment (PCT) studies in Panic Disorder (PD).....	73
Table 1.8: Overview group psychotherapy format studies in panic disorder	87
Table 1.9: Overview of group versus individual psychotherapy format in panic disorder	94
Table 3.1: Descriptive Statistics and ANOVA results for Age	117
Table 3.2: Chi-Square Test of Demographic Variables by group.....	117
Table 3.3: Means and SDs of variables (BAI, BDI, PDSS, ACQ, ASI, and FQ-AG) in pre-treatment.....	119
Table 3.4: Levene's Test of Equality of Variance for all variables at pretest	120
Table 3.5: One-way ANOVA for all variables in pre-test	120
Table 3.6: Mean and SDs of BAI in Pre-treatment and Post-treatment.....	123
Table 3.7: Results of the ANOVA of Group, Time and Time by Group of BAI from Pre-treatment to Post-treatment	123
Table 3.8: Pairwise comparisons among Three Groups for BAI Scores.....	124
Table 3.9: Mean and SDs of BAI in Pre-treatment, Post-treatment and Follow-up in ICBT and GCBT	125
Table 3.10: Results of the ANOVA of Group, Time and Time by Group of BAI from Pre-treatment, Post-treatment to Follow-up.....	125
Table 3.11: Mean and SDs of BDI in Pre-treatment and Post-treatment.....	127
Table 3.12: Results of the ANOVA of Group, Time and Time by Group of BDI from Pre-treatment to Post-treatment	127
Table 3.13: Pairwise comparisons among Three Groups for BDI Severity Scores	128
Table 3.14: Mean and SDs of BDI in Pre-treatment, Post-treatment and Follow-up in ICBT and GCBT	129
Table 3.15: Results of the ANOVA of Group, Time and Time by Group of BDI from Pre-treatment, Post-treatment to follow-up.....	129
Table 3.16: Mean and SDs of PDSS in Pre-treatment and Post-treatment.....	131
Table 3.17: Results of the ANOVA of Group, Time and Time by Group of PDSS from Pre-treatment to Post-treatment	131
Table 3.18: Pairwise comparisons among Three Groups for PDSS Scores.....	132
Table 3.19: Mean and SDs of PDSS in Pre-treatment, Post-treatment and Follow-up in ICBT and GCBT	133

Table 3.20: Results of the ANOVA of Group, Time and Time by Group of PDSS from Pre-treatment, Post-treatment to Follow-up.....	133
Table 3.21: Mean and SDs of ACQ in Pre-treatment and Post-treatment	135
Table 3.22: Results of the ANOVA of Group, Time and Time by Group of ACQ from Pre-treatment to Post-treatment.....	135
Table 3.23: Pairwise comparisons among Three Groups for ACQ Scores.....	136
Table 3.24: Mean and SDs of ACQ in Pre-treatment, Post-treatment and Follow-up in ICBT and GCBT	137
Table 3.25: Results of the ANOVA of Group, Time and Time by Group of ACQ from Pre-treatment, Post-treatment to Follow-up.....	137
Table 3.26: Mean and SDs of ASI in Pre-treatment and Post-treatment.....	139
Table 3.27: Results of the ANOVA of Group, Time and Time by Group of ASI from Pre-treatment to Post-treatment.....	139
Table 3.28: Pairwise comparisons among Three Groups for ASI Scores.....	140
Table 3.29: Mean and SDs of ASI in Pre-treatment, Post-treatment and Follow-up.....	141
Table 3.30: Results of the ANOVA of Group, Time and Time by Group of ASI from Pre-treatment, Post-treatment to Follow-up.....	141
Table 3.31: Mean and SDs of FQ-AG in Pre-treatment and Post-treatment.....	143
Table 3.32: Results of the ANOVA of Group, Time and Time by Group of FQ-AG from Pre-treatment to Post-treatment.....	143
Table 3.33: Pairwise comparisons among Three Groups for FQ-AG Scores.....	144
Table 3.34: Mean and SDs of FQ-AG in Pre-treatment, Post-treatment, Follow-up in ICBT and GCBT	145
Table 3.35: Results of the ANOVA of Group, Time and Time by Group of FQ-AG from Pre-treatment, Post-treatment to Follow-up.....	145
Table 3.36: Pearson product-moment correlation between dependent variables at pretest N = 45.....	147

List of Figures

Figure 1.1: A model of the causes of panic disorder with or without agoraphobia (White & Barlow, 2002).....	24
Figure 1.2: The vicious circle of panic proposed by Clark (1986)	26
Figure 2.1: Flowchart of study participants, point of random assignment and dropouts	102
Figure 3.1: Means and standard errors for the Beck Anxiety Inventory (BAI) of groups at pre and post-test.....	124
Figure 3.2: Means and standard errors for the Beck Anxiety Inventory (BAI) of treatment groups at pretest, posttest and follow-up	126
Figure 3.3: Means and standard errors for the Beck Depression Inventory (BDI) of groups at pretest, posttest.....	128
Figure 3.4: Means and standard errors for the Beck Depression Inventory (BDI) of treatment groups at pretest, posttest and follow-up	130
Figure 3.5: Means and standard errors for the Panic Disorder Severity Scale (PDSS) of groups at pretest, posttest.....	132
Figure 3.6: Means and standard errors for the Panic Disorder Severity Scale (PDSS) of treatment group at pretest, posttest, and follow-up	134
Figure 3.7: Means and standard errors for the Agoraphobic Cognition (ACQ) of groups at pretest, posttest.....	136
Figure 3.8: Means and standard errors for the Agoraphobic Cognition (ACQ) of treatment groups at pretest, posttest, and follow-up.....	138
Figure 3.9: Means and standard errors for the Anxiety Sensitivity (ASI) of groups at pretest and posttest	140
Figure 3.10: Means and standard errors for the Anxiety Sensitivity (ASI) of treatment groups at pretest, posttest, and follow-up	142
Figure 3.11: Means and standard errors for the agoraphobic avoidance (FQ-AG) of groups at pretest and posttest	144
Figure 3.12: Means and standard errors for the Agoraphobic avoidance (FQ-AG) of treatment groups at pretest, posttest, and follow-up.....	146
Figure 3.13: Scatterplot between BAI and BDI.....	148
Figure 3.14: Scatterplot between BAI and PDSS	148
Figure 3.15: Scatterplot between BAI and ACQ.....	149
Figure 3.16: Scatterplot between BAI and ASI	150
Figure 3.17: Scatterplot between BAI and FQ-AG	150
Figure 3.18: Scatterplot between BDI and PDSS	151
Figure 3.19: Scatterplot between BDI and ACQ.....	152
Figure 3.20: Scatterplot between BDI and ASI	152
Figure 3.21: Scatterplot between BDI and FQ-AG	153
Figure 3.22: Scatterplot between PDSS and ACQ.....	154

Figure 3.23: Scatterplot between PDSS and ASI.....	154
Figure 3.24: Scatterplot between PDSS and FQ-AG	155
Figure 3.25: Scatterplot between ACQ and ASI.....	156
Figure 3.26: Scatterplot between ACQ and FQ-AG.....	156
Figure 3.27: Scatterplot between ASI and FQ-AG	157
Figure C1: Beck Anxiety means scores of ICBT, GCBT and WL in pretest, posttest (bars represent standard errors).....	227
Figure C2: Beck Anxiety means scores of ICBT, GCBT (bars represent standard errors) in Pretest, Posttest, Follow-up	227
Figure C3: Beck Depression means scores of ICBT, GCBT and WL in Pretest, Posttest (bars represent standard errors).....	228
Figure C4: Beck Depression means scores of ICBT, GCBT in Pretest, Posttest and Follow-up (bars represent standard errors).....	228
Figure C5: Panic Disorder Severity means scores of ICBT, GCBT and WL (bars represent standard errors) in Pretest, Posttest.....	229
Figure C6: Panic Disorder Severity means scores of ICBT, GCBT (bars represent standard errors) in Pretest, Posttest, and Follow-up	229
Figure C7: Agoraphobic Cognition (ACQ) means scores of ICBT, GCBT, WL (bars represent standard errors) in Pretest, Posttest.....	230
Figure C8: Agoraphobic Cognition (ACQ) means scores of ICBT, GCBT (bars represent standard errors) in Pretest, Posttest, and Follow-up.....	230
Figure C9: Anxiety Sensitivity mean scores of ICBT, GCBT and WL (bars represent standard errors) in Pretest, Posttest	231
Figure C10: Anxiety Sensitivity means scores of ICBT, GCBT (bars represent standard errors) in Pretest, Posttest, and Follow-up	231
Figure C11: Fear-Agoraphobia means scores of ICBT, GCBT, WL (bars represent standard errors) in Pretest, Posttest	232
Figure C12: Fear-Agoraphobia means scores of ICBT, GCBT (bars represent standard errors) in Pretest, Posttest, and Follow-up	232

Introduction

Panic disorder (PD) and panic disorder with agoraphobia (PDA) are common experiences today and are largely identified in primary and emergency care. A delayed diagnosis is often made due to the inexplicable somatic complaints of patients. This delay results in high costs, not to mention inadequate treatment, since several investigations as to a physical source of the complaints have been carried out prior to the diagnosis of PD or PDA (Roy-Byrne et al., 2005a).

Panic disorder carries a current prevalence rate of 3.7 percent in the population and may exist with or without agoraphobia (Kessler et al., 2006).

Patients often report extreme anxiety and physical symptoms that seemingly come out of nowhere (American Psychiatric Association, 2000) thus generating a sense of confusion or fear. They do not realize that emotional, not physical, triggers are causing these reactions.

As patients identify certain situations as causing panic, they begin to limit or avoid these events thus negatively impacting their personal or even occupational environments. Agoraphobic avoidance increases thus creating a need for even more intensive clinical treatments, not to mention costs.

Historically, pharmacotherapy has been the first line treatment for panic disorder (American Psychiatric Association, 2007). This has fallen out of mode however due to the high relapse rates once the medication is reduced, the side effects that outweigh any benefit felt, and the high rate of patients that simply refuse to medicate their symptoms (Pollack, Lepöla & Koponen, et al., 2006; Barlow, et al., 2000; Hofmann et al., 1998).

Cognitive behavioral therapy (CBT) has the best documented efficacy for the treatment of panic disorder in current psychiatric literature (American Psychiatric Association, 2007; Lydiard, Otto, & Milrod, 2001; Barlow & Craske., 2007; Öst et al., 2004; Kenardy et al., 2003). Unfortunately, barely any empirical research has been done regarding the effectiveness of different CBTs on panic disorder specifically. Each CBT program has varying factors that affect how treatment is provided, as well as what role the therapist plays, how the client is encouraged to share and discuss their problems, the interaction between therapist and client, as well as the types of

patients accepted into the program. One way to increase the efficiency of a CBT is to provide group treatment (Sharp, Power & Swanson, 2004).

To date, most investigations have employed nonstandard controls such as self help or bibliotherapy (Lidren, Watkins, Gould, et al., 1994) or no treatment controls (Otto, Pollack, Penava & Zucker, 1999) and are thus not clinically informative. Schwartz & Lellouch (1967), recommend using a widely available standard treatment in a comparison group to yield useful treatment outcome study designs. In relation to group CBT for panic disorder and agoraphobia, the clear comparison group choice would be individual CBT (Sharp, Power & Swanson, 2004).

The goal of this study is to analyze the efficacy of individual cognitive behavioral treatment and group cognitive behavioral treatment strategies for panic disorder.

Due to the change in policy in recent years regarding panic disorder treatments this study also aims to provide a prototype intervention for future policy direction.

Not only does this study aim to provide a model for future group treatment interventions in panic disorder, but other anxiety disorders as well, by evaluating the effectiveness of Group Cognitive Behavior and Individual Cognitive Behavior Therapy in panic disorder. This group treatment format should generate cost savings which may then be applied towards other pressing health concerns.

The present study investigates the relative efficacy of a group treatment CBT and an individual treatment CBT in comparison with a waiting list control group in the treatment of panic disorder with or without agoraphobia.

Chapter I - Theoretical Background

1.1 Historical Background

The word “panic” stems from Greek mythology. The god, Pan oversaw nature but often fell asleep near country roads. When awakened by travelers he would scream to such an extent that the traveler’s hair would stand on end or death could even occur (Barlow & Cerny 1988).

Over the years, panic has been defined by several elements such as sudden onset and uncontrollable fear. Panic can be overt, escaping the perceived danger or covert, a confused, disorganized state of mind which leads to an inability to take action (Ley, 1987).

The psychiatric roots of panic disorder stem from Sigmund Freud’s 1849 paper, “On the Grounds Detaching” a particular syndrome from Neurasthenia under the Description of “Anxiety Neurosis” which proposed a diagnostic category of anxiety neurosis (Weiner, 2008). Key to this diagnosis was a state of excitation and irritability, often displayed as irregular heart beat and respiration rates, coupled with dizziness. This condition was termed anxiety attack until Klein’s work in the early 1960’s (Barker, 1989).

As explained by Nardi (2006), Klein distinguished panic as a separate disorder from generalized anxiety. Using a pharmacologic approach, Klein distinguished three types of anxiety: panic, phobic and anticipatory (Nardi, 2006; McNally, 1990). Klein (1984) proposed that panic disorder actually occurred as a result of a lowered threshold of separation anxiety. Agoraphobia was considered a complication of panic disorder (Barker, 1989).

Panic disorder became an entry in the Diagnostic and Statistical Manual of Mental Disorders (DSM) III twenty-five years ago but accounts of this syndrome can be found in early publications such as Da Costa’s soldier’s heart, Wheeler’s neurocirculatory asthenia and Lewis’s effort syndrome (Nixon, 1993) which all reported aroused nervous systems and catastrophic thoughts. The defining difference in these early accounts is the symptom of extreme fatigue, which is not a current DSM diagnostic criteria. These reports were based on military experiences

which involved stress and trauma and thereby crossed over to post-traumatic stress disorder, which is another anxiety illness listing panic attacks as a diagnostic criteria. Of all the anxiety-related syndromes, panic disorder has been the most intensely researched anxiety illness during the past 25 years. Studies have contributed to a greater understanding of the psychology and neurobiology of anxiety, and have helped dispel the notion that anxiety is a trivial problem that does not require treatment (Roy-Byrne, Craske & Stein 2006).

1.2 Panic Disorder with or without Agoraphobia

1.2.1 Definition of Panic Disorder

According to the American Psychiatric Association (APA) Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR, 2000), panic attacks are a key feature of panic disorder (PD). A panic attack is defined as the sudden, unexpected onset of fear that is accompanied by the presence of four or more physical and emotional symptoms such as palpitations, shortness of breath or smothering sensations, chest pain or discomfort, sweating, trembling or shaking, dizziness, nausea or abdominal distress, choking, flushes and a fear of dying or losing control. Panic attacks typically peak within ten minutes of onset (see Appendix A for DSM-IV-TR criteria for Panic Attack).

A diagnosis of panic disorder is given when a patient suffers from recurrent unexpected panic attacks and evidences one of the following symptoms: persistent anxiety about the possibility of having more attacks, worry about the ramification of the attacks, or a modification of lifestyle in order to avoid having more attacks. These symptoms must be present for at least one month to meet criteria for panic disorder.

An important issue associated with panic disorder is agoraphobia. There are two subtypes of panic disorder: panic disorder with agoraphobia (PDA) and panic disorder without agoraphobia (PDWA). Agoraphobia is severe fear or anxiety related to a place or situation from which escape may be difficult. Often this anxiety is so severe that sufferers will rarely leave the house in an effort to avoid a panic attack. This avoidance can be seen as a coping mechanism to help deal with their anxiety. Because so many individuals with panic disorder (PD) also have agoraphobia, the American Psychiatric Association has given panic disorder with agoraphobia (PDA) a diagnostic code separate from panic disorder without agoraphobia (DSM-IV-TR, 2000).

1.2.2 Diagnostic Criteria for Agoraphobia

A) Anxiety about being in places or situations from which escape might be difficult (or embarrassing) or in which help may not be available in the event of having

an unexpected or situationally predisposed panic attack or panic-like symptoms. Agoraphobic fears typically involve characteristic clusters of situations that include being outside the home alone; being in a crowd or standing in a line; being on a bridge; and traveling in a bus, train, or automobile.

- B) The situations are avoided (e.g., travel is restricted) or else are endured with marked distress or with anxiety about having a panic attack or panic-like symptoms, or require the presence of a companion.
- C) The anxiety or phobic avoidance is not better accounted for by another mental disorder, such as Social Phobia, Specific Phobia, Obsessive-Compulsive Disorder, Post Traumatic Stress Disorder, or Separation Anxiety Disorder (DSM-IV-TR, 2000).

In addition, to meet the criteria for panic disorder (PD) at least some of these attacks must occur spontaneously or "out of the blue" when the patient is not exposed to a fear-inducing stimulus or in a situation in which the person is the focal point of other people's attention (DSM-IV-TR, 2000). At least four of these anxiety attacks must occur within a four week period, or one of the attacks must be followed by a period of at least a month of persistent fear of having another attack.

According to Bennett, (2004) the development of Panic Disorder has been defined into three phases:

Stage One: Initial acute panic attack or series of multiple attacks. The first attack is often an extremely frightening experience since it often occurs unexpectedly while the person is carrying out their normal everyday tasks, (in other words they are not in a high stress trigger situation) thus leading them to believe that there is something physically wrong with them. This sudden onset along with one or more of the somatic sensations listed above often lead the person to seek medical care immediately. Unfortunately their fear is further exacerbated when no medical diagnosis can be found. The diagnosis of panic disorder differentiates itself from panic attacks a person may experience in reaction to a stressful event in that patients experience these attacks on a more frequent, even regular basis (Holrander, Liebowitz & Gorman, 1988).

Stage Two: Patients who have already suffered attacks may then also begin to

anticipate anxiety about future attacks, causing a continuous vicious cycle (Holrander, Liebowitz & Gorman, 1988). In this stage, attacks begin to increase in frequency and phobias, as well as avoidance behavior, begin to develop. The patient begins to identify which situations serve as triggers for the attacks and then begins to avoid said situations. For example, someone who identifies riding on the subway as a trigger will first become anxious about future trips thinking that they might have another attack (anticipatory anxiety). This anticipation may trigger somatic symptoms thus generating a full panic attack. Later the person may avoid the subway completely thus leading to a subway phobia. A study by Katon, (1986) found that PD patients reported an average of 4.8 phobias compared to 1.2 phobias reported by the control group who did not report experiencing panic. When PD is not diagnosed early enough, the phobias tend to multiply to the point that the patient becomes more hindered in carrying out daily activities in order to avoid trigger situations. In this stage, the PD patient begins aggressively seeking medical attention in the hopes of receiving a medical diagnosis for their somatic complaints (Bennett, 2004; Katon, 1994). They begin to become hypochondriacs as they obsess over every physical sensation their body experiences. When told that the pains may stem from anxiety, patients argue that any anxiety is a result of the physical pain (Katerndahl, 1988).

Stage Three: At this point the PD patient has developed avoidant behavior to the point of agoraphobia. Agoraphobia stems from Greek and literally means “fear of the marketplace”. DSM-IV (2000) uses the term to mean fear of being in places or situations from which escape may be difficult or embarrassing, or where help might be unavailable in the event of a panic attack. Once agoraphobia develops the person may become homebound or at least extremely limited in his/her ability to function in the outside world. The patient often relies on the company of a significant other for any outing (Shoenberger & Hazlett-Stevens, 2007; Katon, 1994; Franklin & Andrews, 1989) which can then lead to interpersonal problems since now another is indirectly affected by the condition.

1.2.3 Panic Disorder and Comorbidity

PD has been associated with increased comorbidity with other mental disorders and can occur in conjunction with other anxiety disorders such as posttraumatic stress disorder, social phobias, agoraphobia, obsessive disorder as well as depression, personality disorders, substance abuse disorder (Bernstein et al., 2006), alcohol abuse (Kessler, et al., 2006; Kinley, et al., 2009), suicidal ideation (Goodwin et al., 2006; Kinley et al., 2009), negative life events such as illness, bereavement and legal problems (Cramer, Torgersen & Kringlen, 2005).

PD has also been shown to be associated with decreased quality of life (QoL), reduced contact with friends and family and reduced social support (Rufer et al., 2010; Cramer et al., 2005; Rubin et al., 2000). Rubin et al., (2000) in one investigation found that patients with panic disorder lost on average 39 quality adjusted days for each year that they lived with the disorder based on the Quality of Well-Being Scale (QWB) that can be described in terms of quality adjusted life-years.

Persons with panic attacks also have higher rates of disability and unemployment (Kessler et al., 2006; Marshall et al., 2008), lower education (Katon et al., 1995), lower income (Katerndahl & Realini, 1997) and increased financial dependency (Klerman, et al., 1991).

Agoraphobia disorder is strongly linked with PD; Klerman et al (1991) found about 33% of 254 subjects with PD have comorbid agoraphobia. Another study found that about one third to one half of those with panic disorder developed agoraphobia avoidance (Kessler, et al., 2006). Agoraphobia leads to avoidance of situations from which escape might be difficult or help unavailable in the event of a panic attack. Typical agoraphobic situations include driving, crowded restaurants, shopping malls, being far away from home or being alone (Craske, Miller, Rotunda & Barlow, 1990).

Among anxiety disorders comorbid with PD, social phobia may occur in up to one-third of patients with PD, because one major fear of patients with PD is of having a panic attack in social situations. According to DSMIV TR (2000) the most common comorbid PD with anxiety disorders are: social phobia and generalized anxiety

disorder (15% to 30%) specific phobia (2% to 20%), obsessive compulsive disorder (10%) and post-traumatic stress disorder (2% to 10%).

A study by Barlow, Brown & Antony (1995) examined diagnostic comorbidity in panic disorder in 126 patients with PD. Their results showed that of the 64 patients with comorbidity the most frequent additional diagnoses were: generalized anxiety (32.5%) social phobia (13.5%) and depression (12.7%).

Major depression is the most frequent comorbid diagnosis (Merikangas et al., 1996) and approximately 30-60% of PD patients suffer from a depressive disorder (Weissman et al., 1997; Roy-Byrne, Stang, & Wittchen, et al., 2000).

Kessler et al., (2006) reported that about 50% of patients with PD and 73.3% of patients with PDA have a comorbid mood disorder and another report found a lifetime prevalence of depression in PD patients of 55.6%.

Some studies have shown substantially elevated risks of suicide for patients with PD who present with comorbid depressive disorders, borderline personality disorder and/or substance use disorders (Barlow, 2002; Goodwin & Roy-Birne, 2006; Kinley et al., 2009). Weissman and her colleagues (1990) found that panic attacks and PD are strongly associated with suicidal ideation and actual suicide attempts. They reported a history of suicide attempts in 20 percent of the persons who met criteria for PD, as opposed to 12 percent among persons who experience panic attacks, but who did not meet all the criteria for panic disorder. After further calculation of their data, the research concluded that persons with PD were 5.4 times more likely to attempt suicide than persons who have never qualified for a psychiatric diagnosis. Also Özkan & Altindag (2005) in a study found that the rates of suicidal ideation and suicide attempts in subjects with panic disorder were 34.8% and 9.8%, consecutively. In particular, impaired social, marital functioning and comorbid lifetime with major depression, alcohol or substance abuse and brief depressive symptoms can increase the risk of possible suicide attempts in patients with PD (Kinley et al., 2009; Pollack, Rapaport & Clary, 2000; Uhlenhuth, et al., 2002).

PD is also associated with negative coping behaviors, including alcohol or substance abuse and dependence, particularly alcohol and psychoactive medication (Kinley, et al., 2009) and smoking (Cosci, Knuts, et al., 2010). These are about twice as common

among those with PD compared to those without (Ramage-Morin, 2004).

Epidemiological studies indicate that the prevalence of smoking in patients with PD is higher than that of the general population. McCabe et al., (2004) reported that smoking prevalence in PD is 40.4%.

The result of the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) showed that PDA or PDWA presented a nearly 8-fold risk for drug dependence (Compton et al., 2007). The National Institute of Mental Health (NIMH) (2007) reported that about 30% of people with PD use alcohol and 17% use other psychoactive drugs such as cocaine and marijuana. Mavissakalian & Guo's study (2002) showed a lifetime prevalence of alcohol abuse in 51 of 306 participants (16.7%) with PD.

As Barlow points out, studies show that there is no consistent pattern concerning the onset of alcoholism relative to major depression, dysthymia, or panic disorder-mental disorders which often co-occur. PD can occur "either as a consequence of alcoholism, or subsequent to attempts to self-medicate panic and anxiety" (Barlow, 2002).

Physical health problems such as hay fever (Goodwin, 2002), asthma (Goodwin, Pine & Hoven, 2003) and the presence of any medical condition (Kinley et al., 2009) occur more frequently in people with panic attacks and these individuals have lower perceived physical functioning and health (Marshall et al., 2008). The research evidence shows that there is a high level of comorbidity between panic disorder and somatization (Battaglia et al., 1995) and hypochondriasis (Furer et al., 1997; Hiller et al., 2005). One study showed that 48% of somatization disorder patients had also been diagnosed with PD (Katon, Lin et al., 1991). Another study provided evidence that 90% of people with PD have somatization disorder (Sheehan & Sheehan, 1982). Also Hiller et al., (2005) in a study showed that 57.1% patients with PD have hypochondriasis and 33.3% comorbid with somatization. The reason for the high comorbidity rate between these two disorders is open to speculation, but it is likely that the relationship is associated with the overlap of somatic symptoms which occur with both diagnoses. In order to receive a diagnosis for both disorders, the patient must exhibit somatic symptoms in the absence of a panic attack (American

Psychiatric Association, 2000).

Rates of migraine headache are increased in panic disorder (Jette et al., 2008).

Yamada et al., (2011) investigated the comorbidity rate of migraine and headache with PD in 54 patients with PD. They found forty-three (79.6%) patients were diagnosed as having some type of headache; 61.1% migraine, 32 tension-type headache. Breslau & Davis (1993) and Stewart, Breslau & Keck (1994) found a lower incidence rate of people with both migraine headaches and PD, but they still reported that 10.9% of people with migraine headaches have PD. The differences in the incidence rates between the studies could be accounted for by the fact that Breslau and Davis only used subjects between the ages of 21 to 30.

Hocaglu et al., (2008) in a study evaluated the comorbidity rate in patients with chest pain but without any detectable cardiac etiology. The result showed that PD was diagnosed in 47% of the non-cardiac chest pain group.

PD is therefore disruptive to many people as it occurs not only as a disorder by itself, but often overlaps with many other disorders. In people who exhibit comorbid disorders, it is difficult to determine if the disorders are reactive to one another or exist independently of one another. However, some studies have shown that the treatment of one disorder may reduce the symptoms of the other existing disorder (Brown et al., 1995).

The Comorbid disorders with panic disorder are shown below (Table 1.1).

Table 1.1: Comorbid disorders with panic disorder

Comorbidity	Author	Prevalence
Anxiety disorders		
• Agoraphobia	Klermann et al., (1991)	33%
	Eaton et al., (1994)	29.5% to 58.2%
• Generalized anxiety	Barlow, Brown, Anotony (1995)	32%
• Social phobia		13.5%
• Post-traumatic Stress Disorder	DSM IV TR (2000)	2% to 10%
• Obsessive Compulsive Disorder		10%
Mood Disorder		
• Depression	Kessler et al., (1998)	55.6%

	Hiller, Leibbrand, Rief, Fichter (2005)	71.1%
Suicidal:		
•Ideation	Özkan & Altindag (2005)	34.8%
•Attempts		9.8%
Substance abuse		
• Alcohol abuse	Mavissakalian & Guo (2002)	16.7%
	National Institute of Mental Health (NIMH) (2007)	30%
•Psychoactive drug (Cocaine and Marijuana)	National Institute of Mental Health (NIMH) (2007)	17%
•Smoking	McCabe et al., (2004)	40.4%
Somatization Disorder		
•Somatization	Sheehan & Sheehan, (1982)	90%
	Battaglia et al., (1995)	48%
	Hiller, Leibbrand, Rief, Fichter, (2005)	33.3%
•Hypochondria	Furer, Walker, Chartier, Stein (1997)	48%
	Hiller, Leibbrand, Rief, Fichter, (2005)	57.1%
•Headaches	Breslau & Davis (1993)	10.9%
	Yamada et al., (2011)	79.6%.
•Chest pain	Hocaglu et al., (2008)	47%

1.2.4 Epidemiology

1.2.4.1 Epidemiology of panic disorder

PD occurs frequently in the general population, but there are no certain figures to document the prevalence. This is partially due to significant misdiagnosis and the failure of many persons with PD to seek treatment.

The American National Comorbidity Survey Replication (NCS-R), an epidemiological study of prevalent psychiatric disorders, reported a life-time prevalence of 4.7% for Panic Disorder with or without agoraphobia (Kessler, et al., 2005a).

In a study by Kessler, et al., (2006) the life time prevalence for Panic Disorder without agoraphobia (PDWA) was 3.7% as opposed to 1.1% for Panic Disorder with agoraphobia (PDA).

Another large epidemiological study by Grant, et al., (2006) reported the following

lifetime prevalence: 5.1% for PD (with or without agoraphobia), 4.0% for PD without agoraphobia (PDWA) and 1.1% for Panic Disorder with Agoraphobia (PDA). The rate of lifetime agoraphobia was substantially lower, at 0.17%.

For a 12-month prevalence, the NCS-R (Kessler, et al., 2005b) reported a rate of 2.7% for PD (with or without agoraphobia), and for agoraphobia (without panic) 0.8%. Nevertheless, many studies have reported higher rates for the prevalence of panic attacks. For example, Norton, Harrison, Hauch & Rhodes (1985) found that one-third of university students experienced a panic attack in a one year period.

Telch, et al., (1989b) sampled 2,375 college students and found that 12% of the sample had at least one unexpected panic attack. However, Brown and Cash (1989) raised concerns about whether estimates of panickers may be inflated due to the use of the paper and pencil measure, such as the Panic Attack Questionnaire (PAQ). This measure provides participants with a two-sentence description of a panic attack, and participants are labeled as panickers based solely on their responses to the panic frequency items. Although the reliability of the reported percentage was questioned, it was evident that more people experience occasional panic attacks than panic disorder.

Warren et al., (1988) found that 32% of a high school sample (ages 12-19) reported having at least one panic attack. In addition, 4.7% of the sample met the criteria for PD. Despite the early onset of PD, the mean age of initial treatment was 34 years of age (Breier et al., 1986).

According to the National Comorbidity Survey (NCS), women are over two times more likely to be affected with PD than men (Sheikh, Leskin & Klein, 2002). Other studies have shown that up to 71% of panic disorder with agoraphobia patients are women (Yonkers et al., 1998).

Marital status is a significant risk factor for panic disorder, the highest lifetime prevalence rates are found in widowed, separated or divorced subjects (Yates, 2009; Wittchen & Essau, 1993). Additionally, panic disorder is associated with low education and many studies have reported higher rates of low education in patients with PD. For example, Tilli et al., (2012) in a study found that the panic disorder patients had significantly less education, so that only about one-third of panic

disorder patients had finished high school. Furthermore, 40% of patients with PD and over half of patients with PDA had no professional education, and were significantly less likely to be employed than controls.

1.2.4.2 Epidemiological survey of panic disorders in Iran

The nationwide epidemiological survey of lifetime prevalence of psychiatric disorders is not adequately known in Iran. Burden of psychiatric disorders in developed countries has been identified by screening questionnaires and standard clinical interviews at a high level, but the epidemiological studies of psychiatric disorders in Iran are brief and their numbers are few (Yasamy & Shahmohammadi et al., 2002).

Nevertheless the prevalence of lifetime psychiatric disorders was estimated in the year 2005 among the population aged 18 and stratified for gender, age group, educational level, occupational status, marital status and residential area. The subjects were 25,180 individuals selected through a clustered random sampling method. The psychiatric disorders were diagnosed on the bases of DSM_IV criteria. It was the first study in Iran to have administered a structured psychiatric interview to a representative sample, in this case an Iranian population aged 18 and over. The prevalence of psychiatric disorders was 10.81%. It was more common among females than males (14.34% vs. 7.34%, $P < 0.001$). The prevalence of anxiety and mood disorders was 8.35% and 4.29% respectively. Among mood disorders, major depressive disorder (2.98%) and among anxiety disorders, phobic disorder (2.05%) and PD (1.51%) had the highest prevalence. An increased prevalence of psychiatric disorders was found among divorced and separated 22.31%; residents of urban areas 11.77%; illiterates 13.80%; householders 15.48% and the unemployed 12.33% (Mohammadi, Davidian et al., 2005).

Ahmadvand et al., (2012) reported the prevalence of mental disorders in Iran during 2008-2009. They reported anxiety disorders were the most prevalent mental disorder (26%) and among anxiety disorder group, GAD and PDA had the highest range. the range of PD was 3.5%.

The result of a study about the prevalence of panic attacks among 347 university

students of Iran in 2003, showed 38% percent of participants reported panic attacks in the past year, and 21.4% reported panic attacks in the past four weeks, when prompted by a broad definition of panic. Men and those with unexpected panic reported greater panic severity, whereas women with panic attacks reported greater situational fear and avoidance (Nazemi, et al., 2003a).

1.2.4.3 Epidemiology of psychiatric disorders in the Hormozgan province

The results of a study of the epidemiology of psychiatric disorders in the Hormozgan province in 2001 showed a prevalence of 24.31 percent in women and 8.95 percent in men. The anxiety and mood disorders with 14.68 and 4.99 percent respectively, had the highest prevalence in the province. The prevalence of psychotic disorders in this study was 1.94 percent in men. The frequency of psychotic disorders in this study was 1.49 percent, neuro-cognitive disorders 2.22 percent and dissociative disorders 0.78 percent. In the group of mood disorders, major depression with 3.60 percent and in the group of anxiety disorders, panic disorder with 5.82 percent had the highest frequency (Mohammadi & Rahgozar, et al., 2001).

1.2.5 Etiology

Many different theories have been developed to explain why panic disorder occurs and how it is maintained. Five major etiological models of panic are examined here, including genetics effects, neurobiological models, carbon dioxide sensitivity, false alarm theory, cognitive model, and anxiety sensitivity model.

1.2.5.1 Heredity

Genetics and heritable effects are likely to play an important role in the cause of anxiety disorders. An at risk group for developing PD is the relatives of PD patients (Li, Sundquist & Sundquist, 2011; Gratacòs, et al., 2007).

A molecular genetic study by Maron, Hetteema, & Shlik, (2010) on PD suggests involvement of genetic factors in the familial transmission of PD with an estimate of nearly 40% heritability.

Crowe et al., (1983) in a family study of panic disorder found a genetic risk for PD of 24.7% among first-degree relatives of PD patients, compared with only 2.3% among normal controls. They also concluded the risk of PD in female subjects was twice that in male subjects. In another study, Crowe (1985) found that 17.3% of PD patient relatives met the criteria for PD, with an additional 7.4% reporting infrequent attacks. Goldstein et al., (1997) in a study of 152 probands with PD, concluded an early age at onset of PD has been associated with increased familial risk. They found that relatives of probands who developed panic disorder before age 20 had a 17-fold higher risk whereas only a 6-fold risk increase for PD was observed in first-degree relatives of probands when the onset age exceeded 20 year.

Li et al., (2011) examined sibling risk of any type of anxiety disorder in Sweden over a 40-year period. The results showed that among a total of 42,602 persons hospitalized for anxiety disorders, 2,093 affected siblings were identified. In this study, standardized incidence ratios (SIR) were calculated by comparing risk in siblings of persons hospitalized for anxiety disorders with risk in persons whose siblings had no hospital diagnosis of anxiety disorders. The result showed that, the sibling risk was 2.26. Analysis of risk by subtype showed that having a sibling

diagnosed with any anxiety disorder resulted in increased risks of a number of disorders.

In another study, Turner et al., (1987) found a significant difference on measures of fear and anxiety between offspring of anxious parents and the offspring of non-anxious parents. In addition, forty-four percent of the anxiety offspring met criteria for an anxiety disorder, whereas only 9% of the offspring of non-anxious parents had a diagnosable disorder.

Although these findings suggest a strong heritable component to PD a challenge with family studies is that the cause of the association could be either genetic, learned, or some combination of the two.

One step to exploring these issues is to use twin studies. More studies of twins separated at birth need to be done to gain more data on whether genetic and environmental influences contribute to a disposition for panic issues (McNally, 1990). One twin study estimated the heritability of panic disorder to range between 37% and 43% (Jang, 2005; Nauert, 2011).

Torgersen (1983) examined 299 sets of monozygotic or dizygotic adult twins for anxiety disorders. Concordance rates for panic disorder with or without agoraphobia for monozygotic twins were significantly higher than for dizygotic twins.

Differences between monozygotic and dizygotic twins in frequency of co-occurring panic disorder appear to be due to heredity. In addition, first-degree probands of persons with panic disorder are more likely to have panic disorder than probands of persons without panic disorder.

The results of family and twin studies of panic disorder are shown below (Table 1.2)

Table 1.2: Family, twin studies of panic disorder

Family Studies	First-Degree Relatives		Morbidity Risk in First-Degree Relatives	
	(Cases)	(Controls)	Cases	Controls
Crowe et al. (1983)	278	262	17.3%	1.8%
Noyes et al. (1986)	241	113	17.3%	4.2%
Hopper et al. (1987)	519	-	11.6%	-
Maier et al. (1993)	174	309	7.9%	2.3%
Weissman (1993)	141	255	10.6%	0.7%
Goldstein et al. (1994)	141	225	16.4%	1.8%
Fyer et al. (1996)	236	380	10%	3%
Twin Studies	n (MZ pairs)	n (DZ pairs)	MZ concordance	DZ concordance
Torgersen (1983)	13	16	31%	0%
Skre et al. (1993)	12	18	42%	17%
Perna et al. (1997)	26	34	73%	0,00%

1.2.5.2 Neurobiological Models

The biological model defines panic attacks as stemming from an extreme autonomic system arousal, hypothesized to be caused by a neurochemical imbalance, most likely a dysfunctional noradrenergic neurotransmitter system (Bremner, 2004; Garakani et al. 2006; Antony, Brown, & Barlow, 1992; Ninan & Dunlop, 2005; Gorman, et al., 2000).

There are three major neurobiological models of panic disorder although no model is definitive or conclusive:

First is the suffocation alarm model which claims over-reactive fear circuits located in the limbic system lead to PD (Klein, 1993). This hyperarousal then stimulates the area of the brainstem responsible for respiration, leading to the physical symptoms associated with panic disorder (Klein, 1993; Gorman et al., 2000). In this way, neurobiological reactivity in emotion centers of the brain perpetuates panic disorder. The second model emphasizes the role of the pre-frontal cortex, the brain region responsible for the modulation of the fear circuit. In this model, the amygdala (the emotion center of the brain), the hippocampus (the memory center of the brain), and the pre-frontal cortex (executive functioning), interact in a feedback circuit that either

inhibits or escalates the anxiety response. The pre-frontal cortex is responsible for inhibiting the amygdala. Interestingly, if the amygdala is over-active, the pre-frontal cortex is actually less able to exert control over the amygdala, creating a vicious circle (Ninan & Dunlop, 2005; Rauch, Shin, & Wright, 2003).

The neurobiological diathesis that maintains panic disorder is hypothesized as follows:

If the baseline activity of the amygdala is high (for example, high anticipatory anxiety or temperament) the likelihood that another stimulus will trigger a panic attack increases. If the hippocampally mediated explicit memory is constantly triggered by conscious associations to the panic attack (recounting the details of the attack in an effort to “forget” the experience), it also increases the likelihood of another panic attack. If there is a history of behavioral inhibition in childhood, there may be a temperamental skewing toward avoidance (Ninan & Dunlop, 2005). In this way, a synergy is created in which pathways are laid down that become strengthened by each experience of anxiety.

The third model maintains that in patients with panic, anxiety states stimulate the activation of the limbic system. However, higher order centers of the brain are not recruited to modulate the anxiety reaction. Thus the anxious thought that triggered the attack remains outside of conscious awareness (Rauch, Shin, & Wright, 2003; Whalen et al., 1998). The third model offers a rationale for panic being experienced as “out of the blue.”

These different models of the pathophysiology of panic disorder suggest that the regions responsible for emotion/fear responses are over-reactive, and the regions responsible for executive functioning and emotion regulation are under-active.

Psychotropic medications are thought to remediate the over-reactivity of the limbic system by dampening and modulating the responsiveness of this region (Gorman et al., 2000).

As emotional reactivity becomes less intense, patients are able to experience greater control over their affective experience, and they are less likely to become overwhelmed.

1.2.5.3 Carbon dioxide sensitivity

Some studies have shown that hyperventilation (which releases excess carbon dioxide) may lead to panic. When carbon dioxide is inhaled (causing an excess) this can cause peripheral acidosis which is an "excess retention of carbon dioxide in the body" (W.B. Saunders Company-Dorland's pocket medical dictionary, 2001). This in turn leads to increased respiration (hyperventilation) and respiratory alkalosis which leads to physical panic symptoms such as dizziness and heart racing (Wilhelm, Gevirtz, & Roth, 2001). The body then experiences blood vessel constriction which reduces the amount of blood supplied to the brain, heart, and skin is reduced as result of blood (Jacob & Rapport, 1984).

Alkin, Tural et al., (2007) and Gibbs (1992) found that panic disorder patients, when compared to controls, had a significant reduction in basal artery flow as a result of hyperventilation.

There have been many studies on patients diagnosed with panic disorder where the inhalation of carbon dioxide has been used to induce panic attacks in patients diagnosed with panic disorder (Coryell et al., 2006; Perna, et al. 2004; van Beek & Griez, 2000; Griez, et al., 1990a & 1990b; Perna et al., 1995).

Results of induced hyperventilation have not always led to panic (Gorman et al., 1984) leading some to believe that acute hyperventilation is not sufficient to trigger panic. Stronger evidence indicates a patient's sensitivity to bodily symptoms along with respiratory alkalosis results in the physiological symptoms of panic (Kenardy, Oei & Evans, 1990).

Many of the studies have shown that carbon dioxide inhalation provokes panic in panic disorder patients but not in controls (Caldirola et al, 2004; Alkin, Tural et al, 2007; Fyer, et al., 1987; Lousberg, Griez & van den Hout, 1988; Gorman, Martinez, Browne, Coplan & Papp 2001). It has been hypothesized that the patients who panic as a result of carbon dioxide inhalation may have a hypersensitivity to carbon dioxide (Gorman et al. 1984; Fyer et al., 1987; Nardi et al., 1999). For example, in a study of healthy individuals who received sodium lactate and placebo on two different days, only those who received the lactate infusion and anxious instruction experienced a significant increase in anxiety (van der Molen et al., 1986).

Berzak et al., (2004) found that sensitivity to carbon dioxide (CO₂) is lower in healthy volunteers than in panic disorder patients. In their study participants with a single lifetime panic attack and participants with panic disorder received an inhalation of 35% CO₂. The result showed none of the 14 subjects with a single lifetime panic attack, compared to 7 of 17 subjects with panic disorder (P=.009), had an attack.

Nardi et al., (2003) in a study examined the responses to a breath-holding challenge test in patients with anxiety disorders. The patients in this study were 29 panic disorder (PD) patients, 27 social anxiety disorder (SAD) patients, 21 generalized anxiety disorder (GAD) patients. They were induced to hold their breath as long as possible four times with two-minute intervals. The result showed panic disorder patients were more sensitive than other anxiety disorder patients. 44.8% PD patients, 14.8% SAD patients, 9.5% GAD patients had a panic attack after the test.

Gorman et al., (1984) suggested that carbon dioxide triggers locus ceruleus firing in sensitive individuals, which results in spontaneous panic. However, Gorman et al., (1988) found in tests in which patients hyperventilated room air (versus carbon dioxide enriched air), did not cause panic in panic patients. Therefore the conclusion was that respiratory alkalosis is not a sufficient cause of panic in patients with panic disorder, and some psychological mechanism is also needed.

Salkovskis and Clark (1990) examined the association between acute hyperventilation and panic attacks. In their study the patients underwent two minutes of hyperventilation (60 respiratory cycles / min). This resulted in about 60% of them experiencing panic attacks similar to a symptomatological actual attack. The subjects were less successful at distinguishing between the fear response and the bodily sensations as opposed to the control.

Griez et al., (1990b) in a study revealed that PD patients who had rated at least 50 on both the Zung self-rated Anxiety Scale (SAS) and the State-Trait Anxiety Inventory (STAI) and other anxiety patients who had rated at least 50 on both the Zung self-rated Anxiety Scale and the State-Trait Anxiety Inventory but without no history of panic attacks, do not significantly differ from each other in initial reporting of high

arousal state. However, they do suggest that the carbon dioxide differences between PD patients and the non-panic patients may be due to initial physiological differences of high arousal that may not be captured through a self-report measure.

Lousberg et al., (1988) suggest that the increased panic response to carbon dioxide is a psychological fear of the somatic sensations, which produces the panic, rather than the physiological symptoms themselves being the cause of panic.

Salkovskis and Clark (1990) and Papp, Klein, Gorman (1993) argued that panic disorder may be due to an inherently unstable autonomic nervous system or result of a hypersensitive carbon dioxide chemoreceptor system. When this hypersensitive system is challenged slightly hyperventilation is the result.

Papp et al., (1989) found a significant difference in carbon dioxide sensitivity between PD patients and normal controls. PD patients demonstrated greater sensitivity than the healthy subjects as measured by increased carbon dioxide levels in minute volume arterial blood samples for blood gases.

Woods et al., (1986) in a study demonstrated that the increased carbon dioxide sensitivity of panic disorder patients is not an outcome of having carbon dioxide chemoreceptor irregularity, but also is due to an increased firing rate of neurons in the locus coeruleus-noradrenergic system as an outcome of carbon dioxide.

It is still not clear what triggers panic in some patients. Is it solely that some are more hypersensitive to the physiological effects of carbon dioxide, thus leading them to hyperventilation? (Gorman et al., 1994) Or do panic prone individuals simply misinterpret the symptoms thus escalating the physiological effect? (Salkovski & Clark, 1990; Papp et al., 1993) This uncertainty as to the actual source impedes finding an effective treatment for the disease.

1.2.5.4 False Alarm theory

Alarm theory (Barlow, 1988, 2002, Bouton, Mineka & Barlow, 2001; Cartner & Barlow, 1995; Forsyth & Eifert, 1996) came about in order to distinguish between

panic and anxiety. Often unexpected panic attacks occur in the population at large (e.g., Norton, Cox, & Malan, 1992; Telch, et al., 1989a; Wittchen & Essau, 1991), but seldom result in PD and are referred to as "nonclinical" attacks. This population shows little or no concern of experiencing attacks in the future and understands them as being an isolated event. Other evidence proposes that panic attacks as a nonspecific response to stress, similar to hypertension or headaches that run in families (Barlow, et al., 1996).

In contrast PD patients anticipate the next apprehensively and view it as uncontrollable and unpredictable. They are extremely aware of somatic symptoms since they consider these a signal of an impending attack (Bouton, Mineka, Barlow, 2001).

The false alarm theory defines a panic attack as unconditional fear occurring at wrong time. These "false" alarm occur when there is no real danger making the panic an even greater surprise to the patients (Bouton, Mineka, Barlow, 2001).

It has been widely recognized that it is adaptive to learn to associate emotional responses very quickly with both discrete and contextual cues. When these alarms, true or false, are associated with, or conditioned to, external or internal cues, they become "learned alarms".

In a specific phobia, the fear or anxiety is clearly conditioned to an object or situation. In contrast, the source of fear in a PD patient cannot be easily distinguished. Thus following Goldstein and Chambless (1978), Barlow proposed that false alarms could be conditioned to internal physiological stimuli thus creating interoceptive conditioning (Razran, 1961).

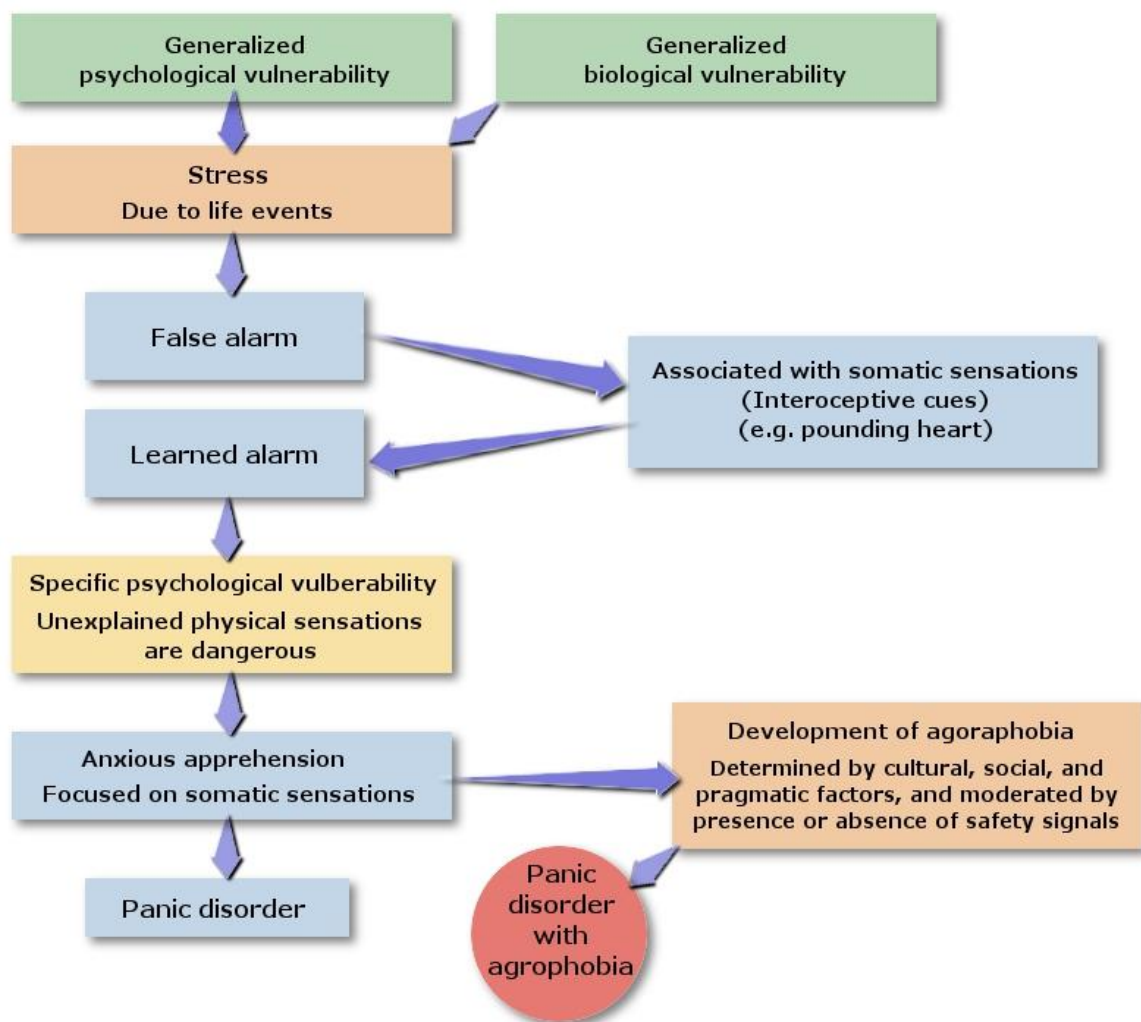


Figure 1.1: A model of the causes of panic disorder with or without agoraphobia (White & Barlow, 2002)

The occurrence of false alarms and subsequent learned alarms need not be pathological if the alarms are infrequent and anxiety towards future alarms does not develop. It is anxiety that stimulates vigilance for somatic sensations, increased somatic cues, tension and arousal which spirals into anxiety and panic. Anxiety focused on a possible future panic attack is now part of the defining DSM-IV criteria for PD (American Psychiatric Association, 2000).

Craske et al., (1990) with interview data from 162 subjects with panic disorder with or without agoraphobia found that, extensive avoiders tended subsequently to develop additional anxiety disorders more than minimal avoiders. Moreover, most individual with panic disorder with or without agoraphobia (approximately 72%) report identifiable stressors around the time of their first panic attack. The most

frequently reported stressors were somatic in nature. Almost half of the patients reported having experienced panicky feelings at some time prior their first full panic attack. There were no differences between minimal and extensive avoiders in terms of the presence of others, behavioral response, or location of the first panic attack. Moreover the groups did not differ with respect to the presence of other anxiety disorders prior to the first panic. However, high avoiders were more likely to develop anxiety disorders than low avoiders.

In support of this model, Öst & Hugdahl, (1983) found that 81% of their agoraphobic sample could identify a specific conditioning experience to account for their fear. They investigated the ways in which 73 phobic patients had acquired their phobia by asking subjects to answer a questionnaire concerning: (a) the origin of the phobia, items associated with conditioning experiences, vicarious experiences and experiences of negative information/instruction; (b) physiological reactions; (c) anticipatory anxiety; and (d) catastrophic thoughts while in the phobic situation. The reported anxiety reaction was conceptualized in terms of the 3-systems model of anxiety (i.e., anxiety as composed of a physiological, cognitive and behavioral component). The Results of study indicated that 61% of the participants attributed their phobias to a conditional stressor; while 18% recalled vicarious learning 7% instruction/information and 14% could not recall any specific onset circumstances at all.

1.2.5.5 Cognitive model

The cognitive behavioral conceptualization of panic is based on Clark's model (1986, 1988 & 1996), Beck (1985) and Casey et al., (2004a).

Clark's theory: This model holds that individuals who have panic attacks make catastrophic interpretations about their physical sensations symptoms. This focus on internal bodily sensations (whether produced by anxiety or not) leads to catastrophic thoughts (e.g., "I am going to have a heart attack"). Such catastrophic thoughts, which are anxiety-producing themselves, lead to further bodily sensations, which incites more catastrophic thoughts, leading to a vicious cycle that culminates in a panic

attack. This vicious cycle is shown in Figure 1.2.

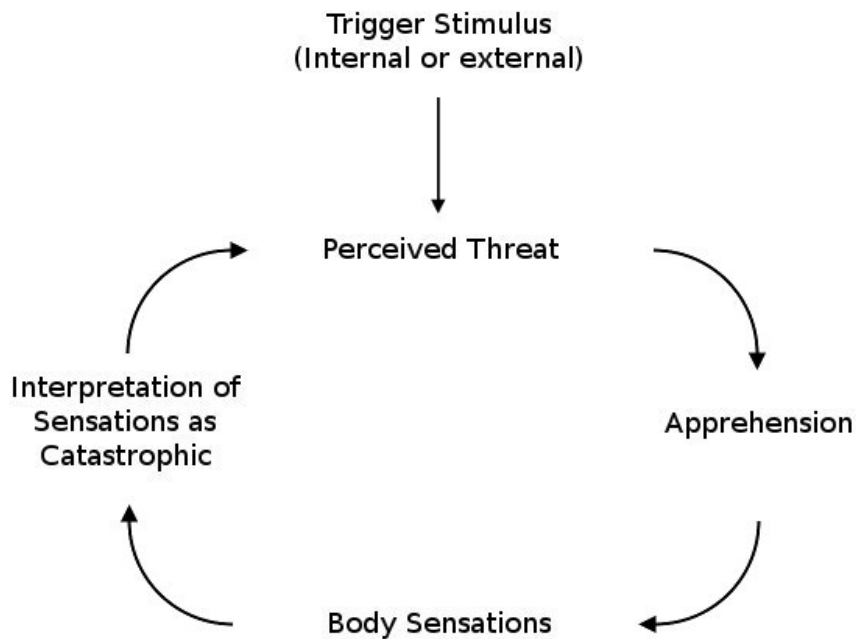


Figure 1.2: The vicious circle of panic proposed by Clark (1986)

According to Craske (1999) initial panic attacks often occur due to a fear of adverse consequences. For example, someone might avoid driving due to a fear of being injured; air travel might be avoided due to a fear of entrapment; social events are avoided due to a fear of negative social evaluation. Physiological events such as illness, occupational stress, medications/drugs (allergic reactions/side effects) or environmental conditions (heat, snow) can also trigger fears and are thus avoided. Panic disorder distinguishes itself from a panic attack in that the bodily sensations are misinterpreted (Barlow) and the person cannot find an explanation for their anxiety, thus leading them to believe there must be an internal reason (e.g., they are dying, losing control or going crazy). This creates a “fear of fear” (Razran) where the physical symptoms lead to uncontrollable frightening thoughts which then snowball into increased fear, exacerbate negative physical feelings and lead to panic behaviors (avoidance). The fear of something unpredictable and inescapable creates a high anxiety about when it will happen again and how to deal with it when it does recur (Barlow, 2002).

There is strong empirical support for the catastrophic misinterpretation hypothesis (Austin & Richards, 2001; Khawaja & Oei, 1998; Casey et al., 2004b). Misinterpreting

physical or mental sensations as signifying an imminent threat has been consistently found in self-report, clinical, and experimental studies and its presence influences the intensity of panic symptoms. Although a number of studies have supported the catastrophic misinterpretation hypothesis of bodily sensations, most found that the interpretation bias is not specific to internal sensations alone and that anxiety interpretations (i.e., an expectation of becoming more anxious) are much more common than truly harm-related catastrophes (i.e., appraisals of dying from suffocation or a heart attack).

A few studies have investigated the presence of catastrophic misinterpretation in panic disorder samples that have been exposed to fear situations. Occurrence of a panic attack leads to greater expectation of subsequent fear or a heightening of anticipatory anxiety, which increase the likelihood that individuals will consider their anxious symptoms highly threatening (i.e., Rachman & Levitt, 1985). Moreover, when panic occurs during exposure to a feared situation, panic disorder individuals experience more bodily sensations and catastrophic cognitions, although 27% of the panic episodes were not associated with any fearful cognition (Rachman, Lopatka, & Levitt, 1988). In a further analysis of these data, Rachman et al., (1987) reported that patients with PD are four times more likely to have a panic attack when the physiological sensation is accompanied by catastrophic misinterpretations.

Westling and Öst (1993) examined the relation catastrophic cognitions and symptoms experienced during panic attacks. In this study, 36 participants were asked to record the types of cognitions experienced during panic attacks over a two-week period. Out of 285 panic attacks, over 90% contained catastrophic cognitions and specific panic symptoms. Catastrophic cognitions were associated with more severe panic attacks and an increased number of reported symptoms.

Kenardy & Taylor (1999) investigate the factors related to prediction of panic attacks. In their study, ten women with panic disorder used a computer diary to self-monitor onset of panic attacks over a 7-day period. This allowed them to prospective assessment of expected versus unexpected panic attacks. Analysis revealed that individuals with expected versus unexpected panic attacks do not differ in the

experience of the actual attack (in 70% of cases the expectation of an attack never materialized). Moreover, sense of helplessness, catastrophic cognitions and somatic symptoms were more frequent before expected but not unexpected panic attacks, indicating that catastrophic thoughts were associated with prediction or expectation of a panic attack rather than its actual occurrence.

Finally, a small pilot study found that 3.25 hours of belief disconfirmation exposure resulted in significantly greater reduction in frequency and belief of agoraphobic cognitions as well as symptom measures than the group who received habituation exposure training only (Salkovskis et al., 2006). This suggests that reducing catastrophic interpretations leads to an improvement in anxious and panic symptoms.

1.2.5.6 Anxiety sensitivity

Anxiety Sensitivity (AS) has been considered as a cognitive risk factor for the development of panic attacks (Kashdan, Zvolensky & McLeish, 2008; McNally, 2002; Schmidt, Zvolensky, & Maner, 2006). AS refers to fear of anxiety-related sensations and is measured by the Anxiety Sensitivity Index (ASI).

Some studies (McNally & Foa, 1996; Struzik et al., 2004; Sturges et al., 1998) found that Anxiety Sensitivity is a dispositional variable which is especially elevated in people with panic disorder. The most important finding was that ASI scores predict panic symptoms in response to biological challenges (e.g., carbon dioxide inhalation) that provoke feared bodily sensations.

Ehlers (1993) revealed that individuals with panic attacks and panic disorder, in comparison to normal controls and patients with other anxiety disorders reported that as children their families experienced more severe illnesses and physical symptoms typical of anxiety such as dizziness, shortness of breath, palpitations or nausea. Ehlers supposed that childhood and adolescent learning experiences may contribute to how panic disorder patients misappraise physical sensations.

Although misappraisal of physical sensations has been proposed as a factor leading to panic disorder, the debate continues regarding the distinction between AS and

Trait Anxiety. Trait Anxiety has been defined as a tendency to respond anxiously to stress and threat. AS on the other hand has been identified by some researchers as an aspect of Trait Anxiety, where bodily sensations are viewed with severe negative consequences. Thus Trait Anxiety can be considered a first-order tendency of anxiety in general, whereas AS can be considered a second-order tendency for the development of panic. According to Lilienfeld (1997) AS is not distinct from Trait Anxiety. Taylor (1999) on the other hand, claims that AS is independent and distinct from other fears and from trait anxiety, even if the two may be hierarchical. Regardless of the debate, there is sufficient evidence that AS is a predictor of panic attacks and panic disorder in non-clinical and clinical samples. In his review of AS literature, Taylor (1999) reported that people with elevated AS, as measured by the Anxiety Sensitivity Index (ASI; Reiss, Peterson, Gursky & McNally, 1986) are more likely to have histories of panic attacks than people with low AS. Likewise, people with panic disorder are more likely to have higher AS scores than people without panic disorder. There is evidence that AS is a predictor of panic attacks and panic disorder in non-clinical and clinical samples.

Ehlers (1995) found in one-year prospective naturalistic study that participants with simple phobias or no anxiety disorders, who experienced their first panic attack, had higher AS than participants who did not have panic attacks. Furthermore, AS showed incremental validity in predicting of panic disorder beyond other factors such as the frequency of baseline panic attacks as, patients with simple phobias or normal controls who experienced their first panic attack during follow-up had shown higher anxiety sensitivity at baseline than nonpanickers.

Norton, Cox, & Malan (1992) in their review of research on non-clinical panickers, concluded that non-clinical panickers (i.e., people who have panic attacks but do not have panic disorder) had lower anxiety sensitivity than individuals with panic disorder, but higher anxiety sensitivity than those who did not experience panic attacks.

Schmidt, Lerew & Jackson, (1997) indicated that Major stressors, such as military

basic training, is a risk factor in the development of anxiety conditions and panic attacks. Their study, found that approximately 20% of the participants scoring in the upper decile on the ASI, experienced a panic attack during a period of five weeks following military training (i.e., a major stressor) in comparison to 6% in the lower decile of the sample.

Anxiety Sensitivity has also been studied in a sample of nonclinical adolescence aged 14 to 18 years. Lau, Calamari & Waraczynski (1996) found that anxiety sensitivity scores were positively associated with the frequency and severity of panic symptomatology among 77 high school students.

Maller & Reiss (1992) examined AS and the relation to panic symptoms in a sample of 151 college students. Results indicated that students who reported high AS had a greater chance of developing panic attacks over three years compared to those who reported low AS.

Kashdan, Zvolensky & McLeish (2008) found that high AS is more associated with panic disorder than any other anxiety disorder. Other researchers have also found that panic patients report higher AS than people with other anxiety disorders (e.g., Taylor, Koch, & McNally, 1992; Zeitlin & McNally, 1993; Apfeldorf et al., 1994). All together, there is evidence of a relationship between Anxiety Sensitivity and panic.

1.3 Treatment of panic disorder

1.3.1 Pharmacological interventions

Treatments for panic disorder vary depending on the presumed etiological cause of the disorder. Psychiatrists and other medical researchers who accept the primacy of the biological factors associated with panic disorder will most likely endorse psychopharmacological treatments.

Currently, there are five major groups of medications that are used to treat panic disorder directly: tricyclic antidepressants, monoamine oxidase inhibitors, minor tranquilizers, high-potency benzodiazepines, and beta-blockers (Baldwin, Anderson,

Nutt, et al., 2005).

Although researchers have discovered that antidepressants such as imipramine (Tofranil) and amitriptyline (Elavil) are quite effective at relieving anxiety symptoms of Panic Attack when accompanied by exposure-based treatments (Barlow, 1988), contrary evidence has also been found. In one well-controlled study by Marks et al., (1983) groups of agoraphobics were treated with imipramine and therapist-assisted exposure both separately and in combination. All groups received a manual on structured self-exposure homework assignments. The results immediately following treatment, as well as at one and two year follow-ups, revealed no differences among the four treatments and all groups demonstrated substantial improvement. Thus, adding imipramine to exposure provided no advantage over placebo with exposure, even after treatment (Marks et al., 1983).

Mavissakalian and Michelson (1986) also studied the effect of adding imipramine to exposure in four groups of agoraphobics receiving systematic instruction on self-directed exposure between sessions. As in the Marks et al., (1983) study, all four groups demonstrated substantial improvement but, in this study the researchers found imipramine to be effective on several outcome measures immediately after treatment termination. However, one month later, the advantage of imipramine with exposure disappeared. Although imipramine may initially potentiate *in vivo* exposure, there is weak evidence that imipramine directly and differently reduces panic and avoidance behavior (Barlow, 1988).

Although imipramine received the most attention among drugs, a number of other antidepressant drugs such as Desipramine and Clomipramine proved effective (Loughlin & Generali, 2006 & Barlow, 1988). There was a 63% effectiveness of experienced symptom relief from antidepressants, which is defined as at least a 50% decrease in the frequency of panic disorder (Clum, 1989).

A disadvantage of tricyclics is that, it usually takes between three and four weeks to experience therapeutic effects. Furthermore, antidepressants produce several anticholinergic side effects such as blurred vision, rapid heart rate, constipation, and jitteriness which patients may view as symptoms of a panic attack and therefore discontinue the drug before experiencing any benefits (Marcus, Gorman, & Shear, et

al., 2007; Hollander, Liebowits & Gorman, 1988). More than 30% of panic sufferers who stop taking these medications experience a relapse that requires additional treatment. Clum (1989) believed this estimate to be rather low considering most of these individuals were also receiving some form of psychotherapy.

Results from studies with monoamine oxidase inhibitors (MAOIs), appear to be much like the results with imipramine in the sense that phenelzine (Nardil) seems to potentiate self-initiated exposure (Sheehan, Ballenger, & Jacobson, 1980). The expected effectiveness of phenelzine is approximately 58% and again, this estimate is derived from individuals who were simultaneously involved in some form of psychotherapy or supportive therapy (Clum, 1989). Complications from this drug include extreme dietary restrictions, dangerously high blood pressure, dry mouth, difficulty sleeping, and difficulty with orgasmic functioning. There is a high drop-out rate (40%) even when a supportive type of therapy is concurrently provided.

Furthermore, the relapse rate for phenelzine is approximately 55% which is one of the highest rates among all medications used for panic sufferers (Clum, 1990).

Benzodiazepines such as diazepam (Valium) and chlordiazepoxide (Librium) have been extensively used in the treatment of anxiety disorders, but the most results indicate that they are only effective in preventing panic attacks when administered in high dosages and potency (Hollander & Simeon 2010; Argyropoulos, Sandford, Nutt, 2000; Hollander, Liebowitz & Gorman, 1988). Alprazolam (Xanax) is the major representative of the high potency benzodiazepine category (Pollack, 2005) and appears to have the highest success rate (60%) of all anti-panic medications (Clum, 1989).

Low potency benzodiazepines are less effective for treating the primary symptoms of panic attacks and anticipatory anxiety (Chouinard, 2004; Barlow, 1988).

Benzodiazepines under certain conditions tend to hinder rather than facilitate exposure-based anxiety reduction procedures in both animals and humans. It is assumed that exposure to interoceptive symptoms characteristic of anxiety is a necessary condition for the process of long-term anxiety reduction (Barlow, 1988).

The effectiveness of benzodiazepine has a 45% averages. A reliable estimate of the relapse rate after treatment does not exist, but there is presently at least a 20% drop-

out rate from treatment due to lack of drug effectiveness and side effects such as physical and psychological addictiveness (Clum, 1989; 1990).

Unfortunately, psychological and physiological addictions and other concomitant effects with alcohol and medications are often associated with alprazolam. Other side effects such as drowsiness, unsteady gait, headaches, and cognitive and motor impairment are associated with this drug. Furthermore, relapse rates in current studies appear to be extremely high (up to 80%) but the average rate across all studies is approximately 40% (Clum, 1989). In addition studies show that chronic use of benzodiazepines causes a decrease in overall effectiveness, increase in tolerance, and ultimately an increase in psychological and physical dependencies (Stevens & Pollack, 2005).

Beta-blockers such as propranolol (Inderal) target symptoms such as rapid heart rate, respiratory distress, sweating, and general tension (Stein, Steckler et al., 2010). However the results with beta-blockers are disappointing. Hafner and Milton (1977) reported that adding propranolol to an in vivo exposure treatment produced significantly worse results than exposure with placebo. Noyes et al., (1984) also reported that only 7 out of 21 panic or agoraphobic patients receiving propranolol showed even moderate improvement. Propranolol's overall expected effectiveness of symptom relief is only approximately 30% for both avoidance and non-avoidance behaviors (Clum, 1989). The drop-out rate from propranolol is approximately 20% which reflects the minimal side effects of this drug. However, it is contraindicated for those individuals who suffer from lung disease, diabetes, or severe depression (Sadock & Sadock, 2008). The relapse rate has not been thoroughly studied for this medication class.

Although drug treatments will not solve underlying panic issues, they may provide relief of symptoms that could enable an individual to cope more effectively or facilitate a psychotherapeutic intervention such as in vivo exposure (Choy, 2008; Barlow, 1988). Additionally, drug treatments may help in situations where avoidance behaviors are prominent, since they reduce the severity and intensity of anxiety and panic attacks. However, a common consequence is that patients may attribute

therapeutic gains to medication rather than to their own personal efforts. Thus, when drugs are withdrawn the patient may expect therapeutic gains to disappear (Seddon, & Nutt, 2007; Barlow, 1988). Although psychopharmacological treatments treat the physical symptoms and manifestations of panic attacks, they do not address the other elements of the disorder, namely, the cognitive fear, avoidant behavior, and phobias. As Baldwin, Anderson, Nutt, et al., (2005) also point out, all psychopharmacological treatments have side effects and since a person with panic disorder is already hypersensitive and hypervigilant about bodily symptoms, such medications may be subject to abuse and overuse leading to dependence with prolonged use. These disadvantages coupled with the high cost, lack of long term treatment response, and high relapse rates necessitate other forms of treatment (Barlow, 1988) that help the client develop coping skills to handle the various aspects of panic disorder (Williams, Kinney, & Falbo, 1989).

1.3.2 Psychological interventions

Psychotherapy is the principal alternative to pharmacological interventions to treat PD. Although different therapy modalities may be used to treat panic disorder, CBT demonstrates the greatest effectiveness in empirical studies (e.g. Barlow & Craske, 2007; Olatunji, Cisler, Deacon, 2010; Hofmann, Smits, 2008; Stewart & Chambless, 2009; Mitte, 2005; Westen & Morrison, 2001; Barlow, Craske, Cerny, & Klosko, 1989). Treatment is generally conducted individually or in groups, and the length of treatment ranges from ten to twenty, one and a half hour weekly sessions (Craske, 1999; Hazlett-Stevens & Craske, 2004). In addition to this time commitment, clients are asked to complete homework assignments that assist them in the therapy process.

Forms of CBT vary according to emphasis on the "cognitive" side or the "behavioral" side of treatment (Barlow & Craske, 2007). A truly comprehensive cognitive-behavioral therapy is an amalgam of both approaches which addresses the entire scope of panic disorders:

- 1) The panic attacks themselves with the cognitive, affective, and somatic symptoms
- 2) The anticipatory anxiety (the so-called fear of fear)

- 3) The avoidant behavior that develops subsequent to a panic attack
- 4) The low self-esteem and sense of hopelessness that frequently accompanies the disorder.

Barlow & Craske (2007) suggest that the specific components of such a treatment approach include: psychoeducation about the nature and course of panic attacks and panic disorder, cognitive restructuring, anxiety management skills, breathing retraining, relaxation training and in vivo exposure/desensitization to phobic stimuli.

Most forms of panic-focused CBT employ the following treatment components:

- 1) Habituation training or exposure to feared bodily sensations (i.e., interoceptive exposure) and external fear cues (i.e., agoraphobic situations).
- 2) Anxiety management or coping skills for managing bodily symptoms (i.e., relaxation and rebreathing training).
- 3) Cognitive interaction, cognitive restructuring and education about the nature and physiology of anxiety and panic, or cognitive techniques designed to modify the tendency to misinterpret catastrophically bodily sensations.

1.3.2.1 Habituation Training

Exposure plays an important role in preventing PD based on learning theory and the extinction model (Pérez-Ara et al 2010). Exposure therapies were originally derived from a behavior therapy technique called flooding which may expose the individual to the fear-evoking stimulus, either in real life (*in vivo*), in fantasy (imaginal), or in some structured artificial situation (*in vitro*) such as a clinical laboratory (Abramowitz et al., 2011). The basic goal of exposure treatment is to decrease a person's anxious and fearful reactions (emotions, thoughts, or physical sensations) and changes the participant's faulty cognitions regarding their symptoms through repeated exposures to anxiety-producing material (Abramowitz et al., 2011; Salkovkis et al., 1991).

This reduction of the patient's anxiety response association with prolonged confrontation of fearful stimuli is known as habituation (Rubenstein, 2003).

The concept of habituation posits that the body is not able to maintain an acute fear

state for an indefinite amount of time. In a sense, the body is thought to “tire” of producing substantial amounts of sympathetic activity, resulting in a reduced state of arousal over time (Ronen, Freeman, 2007). Another related purpose of exposure treatment is to eliminate the anxious or fearful response altogether so that the patient can face the feared situation repeatedly without experiencing anxiety or fear. This elimination of the anxiety response is known as extinction (Wolpe, 1958).

Interoceptive exposure involves a series of exercises designed to induce the feared bodily sensations associated with panic attacks such as dizziness, nausea, sweating, or heart palpitations through various exercises designed in order to reduce the fear associated with these physical sensations through habituation (Eifert & Forsyth, 2005; Forsyth, Acheson & Fuse 2009). With exposure, patients apply new learned coping methods by changing the psychophysiological responses during a panic attack (Sanderson & Wetzler, 1995) and learn to tolerate fear without the need to avoid, escape, or escalate into a panic attack (Cabill & Foa, 2003).

Studies have reported that patients who are able to discern and control internal somatic symptoms of anxiety that trigger panic attacks are successful in reducing panic (Beamish et al., 1996). Physical sensations are capable of increasing arousal and catastrophizing cognitions and exposure to somatic sensations are able to quench anxiety related with bodily symptoms of panic attack (Cabill & Foa, 2003; McCarter, 1996).

Interoceptive exposure combines techniques that attempt to gradually expose the individual to internal physiological cues and confront the physical sensations of panic (Barlow, 1994; Agras, 1993; Sanchez-Meca et al., 2010) by identifying a hierarchy of exercises that evoke the most anxiety and result in sensations similar to those which the client experiences during a natural panic attack. The patient practices each identified exercise, working towards the most difficult on the hierarchy. Through repeated exposure to the feared bodily sensations, clients will become less fearful of the sensations they associate with panic attacks and thereby decrease their vulnerability to the attacks themselves (Tompking, 2002).

Barlow, Craske, Cerny & Klosko (1989) compared Bernstein and Borkovec's (1973) relaxation to cognitive therapy with exposure therapy, and a combined condition of

cognitive therapy, relaxation, and exposure. All three techniques were shown to be superior to a waitlist control in the reduction of panic attacks. But the combined condition and the cognitive therapy plus exposure, were both superior to relaxation therapy, in eliminating panic attacks in 85% or more of patients who were panic free at post treatment. However, relaxation therapy positively affected the score on the psychosomatic checklist more than the other treatments.

The same group of patients was assessed 6 months and 24 months following treatment completion (Craske, Brown, Barlow, 1991). They found that 81% of clients in the exposure plus cognitive therapy group maintained their status over the 2 year follow up.

Arntz, (2002) evaluated treatment effects of Cognitive Therapy (CT) and interoceptive exposure (IE) as treatments of panic disorder without agoraphobia. The sample of 69 patients was randomly allocated to conditions. There were no significant differences between treatments in reducing panic frequency, daily anxiety levels and a composite questionnaire score at post-test after the 12-session treatment, and at both follow-ups (4 weeks, 6 months). In both conditions, high percentages of patients were panic free at post and follow-up tests (range 75-92%). Although the reduction in idiosyncratic beliefs about the catastrophic nature of bodily sensations was equally strong in both conditions, post-treatment beliefs correlated strongly with symptoms at post and follow-up tests in the CT condition, but not in the IE condition. Reduction of beliefs may be essential in CT, but not in IE. This suggests that the two treatments utilize different change mechanisms.

Most, if not all, PD patients exhibit some degree of agoraphobia. Indeed the most profound consequences of PD may arise from the professional and personal limitations caused by attempts to avoid or escape panic. For this reason, situational exposure is an important component in the treatment of anxiety and panic (Tompking, 2002; Fava et al. 2001).

Situational exposure involves the repeated approach (rather than avoidance) to the feared object or situation. Simply put, the fearful situation is broken down into small manageable steps which the patient works through one at a time until the most difficult level is mastered (Nutt, & Ballenger, 2003; Barlow, 1988). Typical situations

feared by panickers include crowded places (malls, theaters, public transportation), performance situations (public speaking, business meetings), driving situations (freeways, tunnels, bridges, overpasses), or any situation from which escape might be difficult in case of a panic attack. Situational exposure treatment takes three forms. During *in vivo* exposure the client approaches the fear-evoking stimulus in real life, such as driving on a specified stretch of freeway.

During *imaginal* exposure the client approaches the fear evoking stimulus by imagining interacting with the stimulus such as sitting in a business meeting when a colleague notices that he is blushing and laughs at him.

During *in vitro* exposure the client approaches the fear evoking-stimulus in a structured, controlled, and artificial setting such as the therapist's office (Tompking, 2002).

By repeatedly engaging in a structured process of incremental exposure and retreat from phobic stimuli the patient learns to tolerate the initial anxiety and develop appropriate coping mechanisms (Nutt, & Ballenger, 2003).

Some investigators have demonstrated very clearly that direct *in vivo* exposure is the central ingredient in the behavioral treatment of agoraphobia, and that this procedure is more effective (60%-70%) than any number of credible alternative psychotherapeutic procedures (Lazarus, 2006; Botella, et al., 2007; McNally, 1990). Follow-up studies reveal that these effects have been maintained, on the average, for periods of four years or more (Burns, Thorpe & Cavallaro, 1986; Jansson, Jerrem-alm & Öst, 1986).

Swinson, Soulios et al., (1992) examined the effectiveness exposure therapy in treatment for 33 patients with panic attacks who were seen in the emergency room. The patients were randomly assigned to groups receiving reassurance (N = 16) or exposure instruction (N = 17). The results showed that the subjects who received exposure instruction significantly improved over the 6-month period on depression, avoidance, and panic frequency. The reassurance subjects did not improve on any measure and eventually reported more agoraphobic avoidance.

Beck et al. (1994) in a study indicated the importance of exposure in treatment of PD.

They compared a treatment package consisting of (a) relaxation training (b) cognitive therapy and exposure therapy for the treatment of PD. In this study 64 subjects with PD were assigned randomly to one of two treatment conditions or to a minimal contact control condition. The results showed both treatments to be equally effective, and they were unable to note any differences in the specific mechanism (i.e., cognitive or physiological) that these treatments may affect. The significant percentage of patients after treatments were CT (82%) and REL (68%), compared with the control group (36%). Moreover the participants in cognitive therapy showed better outcomes in agoraphobic fear measure, than relaxation group. These results indicated the importance of exposure in its treatment.

Kiliç, Noshirvani, Başoğlu & Marks (1997), examined 69 patients with PD with agoraphobia who had been in an 8-week controlled study of alprazolam and/or exposure. 31 were followed up at a mean of 3.5 years later (4 years after trial entry). These follow-up patients had more cases of relapse at week 43 than did the group which did not attend the 3.5-year follow-up. The results further showed as a group, followed-up cases maintained their gains over the 3.5 years. Ex-alprazolam and ex-exposure patients did not differ significantly on any variable at the 3.5-year follow-up.

Ito, de Araujo et al., (2001) in a study compared the effectiveness of self-exposure therapy for PD with agoraphobia. In their study eighty PD patients were randomized to a control group or to one of three forms of self-exposure treatment (external, interoceptive, or combined). Each treatment included seven sessions over 10 weeks and daily self-exposure homework. Assessments were at pre- and post-treatment and up to 1 year post-entry. Assessors remained blind during treatment. The results showed that the three methods of self-exposure were equally effective in reducing panic and agoraphobic symptoms in the short- and long-term. Rates of improvement on main outcome measures averaged 60% at post-treatment and 77% at follow-up.

Craske et al., (2003) studied efficacy of CBT for panic control alone versus this treatment containing an additional in vivo exposure component. The sample in this

study was 68 individuals with diagnosis of PD with agoraphobia. Participants were randomly assigned to one of two 16-week treatment conditions, panic control only and panic control with in vivo exposure. Assessments were repeated at baseline, mid-treatment, post-treatment, and a 6-month follow-up using diagnostic and behavioral measures. Results indicated that the two treatment conditions were equally efficacious for both PD and agoraphobia.

Öst, Thulin & Ramnerö (2004) investigated cognitive behavior therapy vs exposure *in vivo* in the treatment of panic disorder with agoraphobia. Seventy-three psychiatric patients with DSM-IV diagnosis of PD with agoraphobia were assessed with a battery of independent assessor, self-observation, self-report and behavioral measures before and after therapy, and at a 1-year follow-up. They were randomly assigned to exposure, CBT, or a wait-list control and received 12-16 individual therapy sessions, once a week. The treatments yielded significant improvements, both on panic/agoraphobia measures and on measures of general anxiety, depression, social adjustment and quality of life, which were maintained at follow-up. The result showed cognitive therapy did not yield significantly better results than exposure. The three criteria of clinically significant improvement were achieved by 67% of the Exposure-patients and 79% of the CBT-patients at post-treatment, and 74% and 76%, respectively, at follow-up.

Uhle (2006) examined the effectiveness up to 7 years post-treatment of exposure for PD with agoraphobia. The participants in her study were 379 inpatients with PD plus agoraphobia that received a 3-4 week long treatment program with "high density" cognitive behavioral *in vivo* exposure that was symptom-focused. Each patient is treated with one therapist, up to 8 hours a day. The results at the 6 week, 1 year and 7 year follow-up showed a high significant reduction in anxiety cognition, anxiety sensation, agoraphobia avoidance and depressive symptoms.

Marchand, et al., (2008) compared four psychosocial treatments: cognitive and graded in vivo exposure treatments, graded in vivo exposure, cognitive treatment, and supportive therapy, to evaluate the benefits of combining cognitive therapy with

exposure in vivo. These treatments were combined with imipramine or placebo for a total of eight experimental conditions. Participants presented moderate to severe agoraphobia. The method involved a randomized, double-blind, placebo-controlled trial with 137 participants who completed a 14-session protocol involving the treatments just mentioned. Measures were taken at baseline and post-treatment and at 3-, 6-, and 12-month follow-ups. The study found that all treatment modalities proved statistically and clinically effective in reducing panic and agoraphobia symptoms over the 1-year follow-up period.

Peter et al., (2008) in a study compared treatment outcome of female agoraphobics 3–9 years after exposure in vivo with healthy controls. The results showed a stable treatment outcome among two thirds of the patients during follow-up. A total of 17 (40%) of the patients had no further agoraphobic symptoms at all. A total of 15 (36%) patients still had mild-to-moderate agoraphobic symptoms at follow-up. A total of 10 (24%) were non-responders and suffered from severe agoraphobia at follow up.

An extensive review on exposure treatment in panic disorder is presented below (Table 1.3).

Table 1.3: Overview of exposure treatment studies in panic disorder

Barlow, Craske, Cerny, Klosko (1989)	Participants	Fifty-six patients with PD or PDA.
	Condition	A long term clinical outcome study testing variations of behavioral treatments for PD. Patients were randomly assigned to (a) relaxation (REL), b) exposure+cognitive restructuring (EXP + CR), (c) combined relaxation with exposure and cognitive restructuring (REL+EXP+CR) and (d) waiting list (WL).
	F/Up	3 months, 6 months, 12 months and 24 months
	Outcome	(REL)+(EXP+CR), (REL+CR+EXP) > WL (EXP+CR), (REL+CR+EXP)>(REL)
Craske, Barlow, Brown (1991)	Participants	Forty-one patients with PD or PDA
	Condition	A long-term study for efficacy of behavioral treatment in PD. Participants were randomly assigned one of three CBT conditions: (a) relaxation (REL) (b) exposure plus cognitive restructuring (EXP+CR), (c) combination of relaxation and exposure plus cognitive restructuring (REL+EXP+CR).
	F/Up	Six months, Two years
	Outcome	(EXP+ CR)>(REL+CR+EXP), (REL)

Swinson, Soulios, Cox, Kuch, (1992)	Participants	Thirty-three patients with PD and panic attack
	Condition	A pre-post design to examine the efficacy of exposure instruction in PD. The subjects were randomly assigned one of two conditions: (a) exposure instruction (b) receiving reassurance
	F/Up	3 months, and 6 months.
	Outcome	EXP > reassurance group
Marks, Swinson, Başoğlu, Kuch, Noshirvani, et al., (1993)	Participants	One hundred fifty-seven PDA patients
	Condition	A pre-post design to examine the efficacy of Alprazolam and exposure alone and combined in PDA. The patients were randomly assigned to one of three groups (a) alprazolam plus exposure, (b) alprazolam plus relaxation, (c) placebo plus exposure, and (d) placebo plus relaxation. Patients had eight weeks treatment.
	F/Up	Six months
	Outcome	(ALP+EXP)=(ALP+REL)=(PLC +EXP)=(PLC+REL)
Beck et al. (1994)	Participants	Sixty-four PD patients
	Condition	A pre-post test design comparing cognitive therapy and relaxation training for PD. Patients were assigned randomly to one of groups (a) relaxation training (RT) (b) cognitive therapy and exposure-based components (CT+EXP) and (c) a minimal-contact control (MCC) condition. The patients received 10 sessions once a week.
	F/Up	6 months
	Outcome	RT=CT+ EXP CT> RT+ EXP in reduction of agoraphobic avoidance
Kiliç, Noshirvani, Başoğlu, Mark (1997)	Participants	Sixty-nine PDA patients
	Condition	A long-term study of PDA patients after alprazolam and/or exposure. 8-week controlled study.
	F/Up	3.5-years
	Outcome	EXP=Alprazolam
Craske, Rowe Lewin, Noriega- Dimitri (1997)	Participants	Thirty-eight PDA patients
	Condition	A pre-post design to examine Interoceptive exposure vs breathing retraining within CBT for PDA: The patients were randomly assigned to (a) cognitive restructuring + interoceptive exposure and in vivo exposure or (b) cognitive restructuring + breathing retraining and in vivo exposure to agoraphobic situations.
	F/Up	Six months
	Outcome	IEXP+ vivo EXP+CR > vivo EXP+BR+CR
Ito, de Araujo, Tess, de Barros- Asbahr, Marks (2001)	Participants	Eighty PDA patients
	Condition	A pre-post design to examine self-exposure therapy for PDA. Randomized controlled study of external vs. interoceptive self-exposure. Patients were divided to a (a) external exposure (b) interoceptive exposure (c) combined exposure (d) control group. Each group included seven sessions over 10 weeks and daily self-exposure homework.

	F/Up	One year
	Outcome	EXP > Control group IEXP=EEXP=Combined EX (Introceptive+External)
Arntz (2002)	Participants	Sixty-nine patients with PD
	Condition	A pre-post design to examine cognitive therapy versus interoceptive exposure. Patients randomly allocated to two treatment conditions. A 12-session treatment in each group.
	F/Up	Six months
	Outcome	CT=IEXP
Öst,Thulin, Ramnerö (2004)	Participants	Seventy-three PDA patients
	Condition	A pre-post design to examine CBT vs exposure in vivo in the treatment of PDA. The patients were randomly assigned to three groups (a) Exposure, (b) CBT or (c) WL control and received 12-16 individual therapy sessions, once a week.
	F/Up	One year
	Outcome	EXP=CBT
Uhle (2006)	Participants	Three hundred seventy-nine inpatients with PDA
	Condition	To examine the short and long term effectiveness of vivo exposure for PDA in an inpatient setting: A 7 year follow-up. The patients received an individual treatment program with "high density" cognitive behavioral in vivo exposure (HDE) averaging 3-4 weeks, 8 hours total.
	F/Up	Six weeks, one year, seven years.
	Outcome	High significant reduction in anxiety cognition, anxiety sensation, agoraphobia avoidance and depressive symptoms.
Marchand Coutu, Dupuis, Fleet, Borgeat, Todorov, Mainguy (2008)	Participants	One hundred thirty-seven PDA patients
	Condition	A randomized double-blind, placebo-controlled trial for treatment of PDA in four psychosocial treatments: (a) cognitive and graded in vivo exposure treatments, (b) graded in vivo exposure, cognitive treatment, and supportive therapy. These treatments were combined with imipramine or placebo. All patients completed a 14-session protocol.
	F/Up	3-, 6-, and 12-months
	Outcome	(EXP+CT+IMI)=(EXP+CT+ PLC)
Peter, Bruckner, Hand, Rohr, Rufer (2008)	Participants	Forty-two female participants with PD/PDA
	Condition	A pre-post design to examine treatment outcome of female agoraphobics 3-9 years after exposure in vivo: In comparison with 42 healthy controls that were matched according to gender, age, marital and occupational status. All patients received exposure in vivo either in group or individual therapy.
	F/Up	3-9 years
	Outcome	40% of the patients had no further agoraphobic symptoms at all. 36% patients still had mild-to-moderate agoraphobic symptoms 24% were non-responders and suffered from severe goraphobia.

Note*: ALP: Alprazolam; BR: Breathing Retraining; CBT: Cognitive Behavior Therapy; CR: Cognitive Restructuring; CT: Cognitive Therapy; EXP: Exposure; EEXP: External Exposure; IEXP: Introceptive Exposure; vivo EXP: vivo Exposure; IMI: Imipramine; PLC: Placebo; REL: Relaxation Therapy; WL: Waiting List; FU: Follow-Up.

In summary, all these studies indicated Exposure therapy was effective in reducing anxiety cognition, anxiety sensation, agoraphobia avoidance and depressive symptoms compared to the control group and relaxation treatment immediately after treatment and follow-up, but not compared to Cognitive Behavior Therapy.

1.3.2.2 Anxiety Management Training (AMT)

Panic Management Training is a general approach to treating panic attacks and involves teaching the client how to control severity of panic attacks and maladaptive responses in panic situations by using some specific behavioral skills such as Progressive Muscle Relaxation (PMR), Diaphragmatic Breathing training (BT) as means to reduce anxiety responses or eliminate agoraphobia.

Relaxation Therapy

Relaxation training as a form of anxiety management strategies is characterized by its focus on self-regulation strategies for reducing physiological arousal and anxiety, particularly the central nervous system-mediated symptoms most often associated with panic disorder (Barlow & Craske 2007).

In stressful situations or panic attacks, there is increased activity of the sympathetic nervous system (SNS) which leads to physiological arousal or the "fight or flight" response (Conrad & Roth, 2007; Klerman et al., 1993). The most remarkable physical change that occurs during the fight-or-flight response is the increased heart rate, blood pressure, rate of breathing, dilation of the pupils, blood supply to the muscles and increased muscle tension experienced in the large muscles of the arms, legs, back, shoulders, neck and jaw (Conrad & Roth, 2007). Hence, in contrast to the stress response, relaxation is characterized by reduced sympathetic nervous system tone and increased parasympathetic activity. This may include decreased metabolism, blood pressure, oxygen consumption, and heart rate, as well as a feeling of calmness

(Wilson, 2009). On the other hand when the body is in a relaxed state there is little muscle tension, leading to decreased anxious feelings (Jacobson, 1938). According to Jacobson if one's body is relaxed, one's mind cannot be in a state of fear.

Relaxation as an anxiety management technique can have various forms. A form of relaxation known as applied relaxation has shown good result as a treatment for panic attack. This technique induces relaxation in order to diminish the physiological symptoms of panic (Ruhmland & Margraf, 2001).

Applied relaxation entails training patients in progressive muscle relaxation (PMR) until they are skilled in cue control relaxation, at which point relaxation is used as a coping skill for practicing exposure to items from a hierarchy of anxiety-provoking tasks (Öst, 1987; Manzoni, et al. 2008; Craske, Maidenberg & Bystritsky, 1995; Salkovskis, Clark & Hackmann, 1991).

Progressive or active muscle relaxation is a systematic technique for achieving a deep state of relaxation and was described by Edmund Jacobson in the 1920s. Jacobson noted that because anxiety accompanies muscle tension one can reduce anxiety by learning to relax the muscular tension. According to Jacobson, induction of a deep state of relaxation does in fact attenuate various reflexive responses as well as improve mental activities and reduce emotional reactions, including reactions to sudden pain (Calloway, 2007). Later studies have proved Jacobson's early work and have shown that patients who display chronic anxiety and/or other forms of anxiety disorders have higher levels of resting baseline muscle tension and autonomic activity than do non patient controls (Barlow 1988, p. 96).

Progressive Muscle Relaxation (PMR) involves the active tensing and relaxing of sixteen different muscle groups of the body, focusing attention on the sensation of tension and relaxation.

A theoretical basis for relaxation as a treatment for panic attacks has not been elaborated beyond the provision of a somatic counter response to the muscular tension that is likely to occur during anxiety and panic (Barlow, 2008, p. 25).

However evidence does not lend support to this theory (Rupert, Dobbins & Mathew, 1981). As found in breathing retraining, fear and anxiety are reduced to the extent that the relaxation provides a sense of control (Barlow, 2008). Therapeutic gains are

more difficult to identify in instances of applied forms of relaxation which involve exposure based procedures as anxiety- provoking situations are faced.

Öst (1987) developed an applied relaxation (AR) technique which was used as the relaxation treatment. His technique includes: explaining the rationale for the treatment specific to each patient, increasing the patient's awareness to their anxiety reactions, progressive relaxation, breathing until the patient feels physically relaxed, generalizing the relaxation techniques outside of the therapist's office, and learning to rapidly reach the relaxation state. Although Öst's technique includes a breathing component, it does not teach the patient to breathe diaphragmatically. Instead, the participant is instructed to focus on inhaling and relaxing as they exhale.

Öst (1988) investigated the efficacy of applied relaxation (AR) vs. Progressive Muscle Relaxation (PMR) in treatments of PD. Eighteen PD outpatients were randomly assigned to AR and PMR. The patients were treated individually for 14 weekly sessions and were followed up 6-29 months later. The results showed that both treatments yielded very large improvements, which were maintained or furthered at follow-up (approximately 19 months after treatment completion). All members of the AR group were significantly better than those in PMR at follow-up. The proportion of clinically improved patients (according to stringent criteria) was 38% for PMR and 75% for AR at post-treatment, and 25% vs 100% at follow-up.

Öst, Westling & Hellström (1993) evaluated the effects of three different behavioral methods: Applied Relaxation (AR), exposure *in vivo* and cognitive methods in the treatment of PD with agoraphobia (PDA). Forty-five PDA patients were assessed with a battery of self-report, behavioral and cognitive measures before and after therapy, and at a 1-year follow-up. They were randomly assigned to Applied Relaxation (AR), Exposure *in vivo* or Cognitive Treatment (CT) and received 12 individual therapy sessions, once a week. All patients also had self-exposure instructions. The three treatments yielded significant improvements that were maintained at follow-up. One criterion of clinically significant improvement was fulfilled by 87% of the AR group, 80% of the exposure group and 60% of the CT-

patients at the end of treatment, and 85, 79 and 67%, respectively, at follow-up. Between-group differences were observed on two measures only, both showing better results for AR than for CT.

Öst & Westling (1995) investigated the efficacy of a coping technique, Applied Relaxation (AR) and cognitive therapy, in the treatment of PD. The PD patients were randomly divided PD patients into applied relaxation and cognitive therapy treatment groups. In post-treatment, there were no significant differences between panic patients and normal controls when interpreting internal events. Therefore, both cognitive therapy and applied relaxation therapy were equally successful in normalizing cognitions, and there were no significant differences between the treatment groups. Thus they concluded that the two different treatments, one aimed at generating cognitive changes, and one aimed at creating physiological changes, both produced the same results.

Clark, Salkovskis et al., (1994) also used a modified version of Öst's Applied Relaxation technique and compared its effects to those of cognitive therapy and imipramine in the treatment of PD. The study group consisted of 64 PD patients who were treated over 12 sessions once a week. They found the three treatments were effective, with cognitive therapy being initially more effective than either pharmacotherapy or AR as measured by a panic/anxiety composite score comprised of 17 panic/anxiety measures. Comparisons between treatments showed that at 3 months cognitive therapy was superior to both AR and imipramine on most measures. At 6 months cognitive therapy did not differ from imipramine and both were superior to AR on several measures. At 15 months cognitive therapy was again superior to both AR and imipramine but on fewer measures than at 3 months.

Carlbring et al., (2002) examined the efficacy of CBT vs. Applied Relaxation (AR) for PD on the Internet. For this purpose participant were randomized to either AR or a multi-modal treatment package based on cognitive behavioral therapy (CBT). In the Öst's Applied Relaxation (AR) group was adapted for self-help with three relaxation instructions. The treatment was divided into: (1) psychoeducation, (2) rational, (3)

PMR: long version, (4) PMR: short version, (5) conditioned relaxation, (6) differential relaxation, (7) quick relaxation, (8) AR, and (9) relapse prevention. The results indicated that two groups did not have significant difference in any of the measurements at pre-treatment. Although not statistically significant, the AR condition had a better overall effect compared to the CBT program.

Arntz & van Hout (1996) compared cognitive therapy to Öst's (1987) applied relaxation (AR) protocol. Thirty-six outpatients with the DSM-III-R diagnosis of PD with no or mild agoraphobia were randomly assigned to cognitive therapy (CT) or applied relaxation (AR). Eighteen similar patients constituted a waiting list group. Treatment consisted of 12 weekly sessions. Patients self-monitored panic attacks during the whole treatment period, and the following 4 weeks, and during 1 week at a half-year follow-up. Results of this study indicated that cognitive therapy group was significantly superior to relaxation therapy in reducing panic frequency, and somewhat less strongly superior to relaxation therapy group in reducing the questionnaire scores. At the end of treatment 77.8-83.3% of the cognitive therapy patients were panic-free, compared to 50% of the patients who received relaxation therapy and 27.7% of the waiting-list patients.

An extensive review on relaxation treatment in panic disorder is presented below (Table 1.4).

Table 1.4: Overview of Relaxation treatment studies in panic disorder

Öst (1988)	Participants	Eighteen patients: 14 PD patients and 4 Generalized Anxiety Disorder (GAD)
	Condition	A pre-post test design comparing of Applied relaxation (AR) vs Progressive muscle relaxation (PMR) in treating PD, the patients were randomly assigned to into two treatments groups, AR and PMR. The patients treated individually for 14 weekly sessions.
	F/Up	6-29 months
	Outcome	AR >PMR
Öst, Westling, Hellström (1993)	Participants	Forty-five PDA patients
	Condition	A pre-post test design to examine applied relaxation (AR), exposure in vivo and cognitive methods in treating PDA. Patients received 12 individual therapy

		sessions, once a week.
	F/Up	One year
	Outcome	AR=CT=EXP
Clark, Salkovskis, Hackmann Middleton, Anastasiades, Gelder (1994)	Participants	Sixty-four PD patients
	Condition	A pre-post test design comparing cognitive therapy (CT), applied relaxation (AR) and imipramine (IMI) in the treatment of PD: patients were initially assigned to CT, AR, IMI or WL group. During treatment patients had up to 12 sessions in the first 3 months and up to three booster sessions in the next 3 months. CT and applied relaxation sessions lasted one hour.
	F/Up	3, 6, and 15 months.
	Outcome	At 3 months: CT > AR , IMI At 6 months: CT, IMI > AR At 15 months: CT > AR, IMI
Öst & Westling (1995)	Participants	Thirty-eight participants with PD
	Condition	A pre-post test design to examining the Applied Relaxation (AR) vs cognitive therapy (CT) in the treatment of PD, the patients randomly assigned into two treatment groups, AR and CT. The patients were treated individually for 12 weekly sessions.
	F/Up	One year
	Outcome	AR= CT
Arntz & Van Hout (1996)	Participants	Fifty-four patients with PD with or without agoraphobia
	Condition	A pre-post test design to examining cognitive therapy (CT) vs applied relaxation (AR) in PD. The patients were randomly assigned to CT or AR, and WL group. Treatment consisted of 12 weekly sessions. Patients self-monitored panic attacks during the whole treatment period.
	F/Up	a half-year
	Outcome	CT > AR > WL group
Carlbring, Ekseliusb, Anderssona, (2002)	Participants	Twenty-two PD /PDA
	Condition	A randomized trial of CBT vs. applied relaxation (AR). Participants were randomized to either (AR) or (CBT). CBT group had a self-help manual consisting of psychoeducation, BR, CR, exposure, relapse prevention and assertiveness training. In the AR group Ost's applied relaxation book was adapted for self help use with three relaxation instructions was sent to the participants. The treatment was divided into psychoeducation, rational, PMR long version, PMR short version, conditioned relaxation, differential relaxation, and quick relaxation, AR, and relapse prevention.
	F/Up	Not reported
	Outcome	AR=CBT

Note*: AR: Applied Relaxation; BR: Breathing Retraining; CBT: Cognitive Behavior Therapy;

CR: Cognitive Restructuring; CT: Cognitive Therapy; EXP: Exposure; IMI: Imipramine; MCC: Minimal-Contact Control; PMR: Progressive Muscle Relaxation; RT: Relaxation Training; WL: Waiting List; FU: Follow-Up.

In summary, each of these studies shows that relaxation training was effective in panic management and reduction of anxiety and physiological arousal symptoms in panic situations both immediately after treatment and follow-up. Relaxation therapy was effective compared to the control group but not compared to CBT alone or exposure treatment.

Breathing retraining and Respiratory Control

Breathing Training (BT) is a central component early on in the development of panic treatment and consists of diaphragmatic breathing techniques (Meuret, Ritz, Wilhelm & Roth, 2008). A high percentage of patients with PD tend to hyperventilate during a panic attack (Sullivan, Kent & Kleber, et al., 2004). As mentioned earlier, during panic attacks, the respiration rate often increases and patients experience uncomfortable physical symptoms that are similar to those produced by hyperventilation such as dizziness, tachycardia, palpitations, nausea and breathlessness. The patients who experience chronic hyperventilation often report being “short of breath” (Leahy, Holland & McGinn, 2011).

The general goal of BT is to decrease the patient's respiratory rate (Beamish et al., 2002), reduce the probability of hyperventilation, and make it less likely for patients to catastrophize physiological symptoms (Meuret, Ritz, Wilhelm & Roth, 2008). Breathing Training assists individuals in proper breathing, which regulates the balance of oxygen and CO₂ and increases the threshold for hyperventilation (Courtney, 2011; Meuret, Ritz, Wilhelm & Roth, 2008). BT shows the patient that many of the sensations they experience during a panic attack are the result of over breathing, rather than the actual manifestations of feared conditions (Taylor, 2001). Studies have shown that individuals who are able to identify and control internal somatic symptoms of anxiety that trigger panic attacks are successful in reducing panic (Meuret, Ritz, Wilhelm & Roth, 2008; Beamish, et al., 2002).

In this regard, diaphragmatic breathing exercises designed to “normalize” breathing,

are easily learned and can be quickly applied in anxious situations (Barlow & Craske 2007; Rapee & Barlow, 1991). Diaphragmatic breathing promotes slow, deep and rhythmic breathing with emphasis on the diaphragm muscle moving downward on inhalation and upward on exhalation (Hazlett-Stevens & Craske, 2009). The respiration rate is 5 to 8 respirations per minute and is associated with a return of a normal respiratory sinus arrhythmia. As the patient slows their respiration rate, the tidal volume tends to increase while the minute volume decreases. The tidal volume in diaphragmatic breathing ranges from 750 to 2000 ml of air per inhalation (Kajander & Peper, 1998). The exhalation phase is longer than the inhalation phase. While breathing diaphragmatically, people are encouraged to relax and give their breathing "passive attention." Therefore this breathing pattern promotes relaxation as well as other physical effects that are contrary to hyperventilation and autonomic nervous system arousal (Nezo, Lombardo & Netzo, 2004).

In addition to diaphragmatic or abdominal breathing, a relatively new technique, the Valsalva maneuver, is specific breathing training to lower fast heart beat (tachycardia) that can be taught to enable patients to avert attack.

As mentioned earlier, the onset of tachycardia is the most frequently reported symptom of panic attacks. Over 80% of those experiencing panic list a rapid or irregular heart rate as a symptom (DSM-IV, American Psychiatric Association, 2000). Margraf, Taylor, Ehlers, Roth and Agras (1987) reported that the incidence of heart palpitations during panic attacks was as high as 73%.

Vagal maneuvers are physical techniques that stimulate the vagus nerve to induce a slower heart rate. The two common vagal maneuvers are carotid massage and Valsalva maneuvers. In carotid massage, trained individuals apply external pressure to the carotid artery in the neck to stimulate the nerve, which raises blood pressure there and slows heart rate. The Valsalva maneuver can be performed by moderately forcing attempted exhalation against a closed airway, usually done by holding one's breath and bearing down as if having a bowel movement, or pinching one's nose shut while inhaling as if one were trying to block a sneeze (Luster, Baumgartner, Adams, Convertino, 1996; Lim et al., 1998). This will cause a quick spike in heart rate, followed by a slowing of the heart rate.

Sartory & Olajide (1988) examined the efficacy of vagal innervation techniques to terminate tachycardia in treatment of panic disorder patients. In their study nine participants were randomly assigned to either experimental or control groups. Patients in both groups were seen on four occasions, twice during the first week and then at weekly intervals. The patients in the experimental group were taught to slow their heart rates by vagal innervation, slower abdominal breathing, and relaxation techniques and the control group was trained in breathing and relaxation techniques. The result showed both groups had improved after four treatment sessions but patients in the experimental group experienced a 50% reduction in the number of symptoms occurring during panic attacks and also reported less generalized cognitive anxiety.

However, research indicates that BT is effective in treating panic disorder (Meuret et al., 2010a; Meuret, et al., 2008) but combining BT with cognitive intervention has better effect than BT alone (de Ruiter, Rijken, Garssen, & Kraaimaat, 1989). Some research shows that when BT is used alone, it is no more effective than a placebo treatment (Klosko, Barlow, Tassinari & Cerny, 1990; Garssen et al., 1992; Meuret et al., 2008).

Rapee (1985) examined the effectiveness of breathing training on panic attacks in a case study with panic disorder. In this study the patient received three sessions of diaphragmatic breathing training program, and reduction of her respiratory rate to seven breaths per minute. The result showed that a significant decrease in number of symptoms of panic and panic frequency from 22 to only 2 attacks at 3 weeks post-treatment.

Clark, Salkovskis, & Challey (1985) showed that brief respiratory control training alone would produce substantial reductions in panic attack frequency and anxiety symptoms. In their study, eighteen patients who experienced frequent panic attacks and responded positively to an initial hyperventilation challenge were taught to reattribute the cause of their panic attacks to stress-induced hyperventilation.

Therapy was conducted in the following sequence: (1) brief, voluntary hyperventilation to reproduce a mild panic attack (2) reattribution of the cause of the symptoms to hyperventilation: (3) training in a respiratory control technique by

spacing audiotape (12 breaths per minute). The results of study showed significant improvements in reduction of panic attack frequency and self-reported anxiety and depression. Further reductions in panic attack frequency were maintained at 6-month and 2-year follow-ups.

Salkovskis et al., (1986) replicated and extended the treatment introduced by Clark et al., (1985) by concurrent measurement of behavior and pCO₂ in nine patients who experienced phobic and/or non-phobic panic attacks. They tested whether patients suffering from panic attacks had lower resting pCO₂ levels before treatment and whether these levels increased during treatment. The results showed a significant reduction in panic attack frequency and questionnaire report of fear. Patients' resting pCO₂ was significantly lower than controls' and rose to normal levels during treatment. In fact, PCO₂ values at the end of treatment were similar to those found in non-patient samples.

Hibbert and Chan (1989) compared the effectiveness of five sessions of BT with a placebo treatment in PD and PDA patients. They divided forty PD patients into hyperventilators and non hyperventilators on the basis of a conventional provocation test. All patients were treated for two weeks with either training in controlled breathing or a placebo treatment. They found both treatments were effective; respiratory control did not differ significantly from placebo treatment on any of the self-report measures. The only difference that emerged was with regard to observer ratings of anxiety, which showed more improvement in the respiratory control group.

Bonn et al., (1984) investigated the effect of diaphragmatic breathing in combination with exposure in agoraphobic patients. Twelve agoraphobic patients received respiratory control plus exposure *in vivo* or exposure *in vivo* alone. At one month follow-up, the two groups of patients showed similar degrees of improvement in frequency of panic attacks and other psychophysiological scores. At a six month follow-up the patients treated with *in vivo* exposure alone were beginning to show a fall-off in relearned adaptive behavior (learning decrement), whereas those given

breathing retraining showed further improvement. This suggests that patients pretreated with BT are less likely to need further treatment.

Meuret, Wilhelm, & Roth (2001) developed a respiratory biofeedback-assisted therapy for panic disorder in 4 participants that were trained to raise their end-tidal pCO₂ by slow, diaphragmatic breathing. Results showed a lower basal pCO₂ before treatment and an increase to normal levels after BT, along with improvement in clinical measures such as panic attack frequency and severity, trait anxiety, anxiety sensitivity, and depression.

Franklin (1989) evaluated the effectiveness of BT compared to relaxation therapy, cognitive modification, and a placebo in treatment of PDA. Four of eight patients in this study were treated with four different sequences of these interventions, and 4 control patients were treated with the same sequences after a 4-week waiting period. The results showed the BT group yielded highly significant reductions in panic attack frequency and intensity, and it was the only component that produced significant improvements in the behavioral measures of agoraphobia. Relaxation produced significant reductions only in frequency of panic attacks. Cognitive modification reduced cognitive distress significantly, but it affected no other measure.

Wollburg (2007) studied the psychophysiological effects of respiratory challenges before and after BT in PD and patients with Episodic Anxiety (EA) attacks. This study included 45 PD patients and 39 EA patients who suffered from subclinical panic attacks, and 20 non-anxious controls (NAC). Patients were randomized to one of two versions of a 4-week therapy with BT, either lower or raise end tidal pCO₂, or a waiting list. Before and after treatment, participants underwent in randomized order a Voluntary Hypoventilation (VHO) test and a Voluntary Hyperventilation (VHT) test in which they were asked to either lower or raise their pCO₂ while psychophysiological measures were recorded. At pre-treatment, PD and EA patients were more anxious, distressed, tense, and worried than NAC, and reported more dizziness chest pain and nausea during the laboratory assessment.

After treatment, the results showed that both therapies improved the main outcome measure and BT was also equally effective for the lower and raise Breathing Training (BT). Furthermore, BT affected baseline $p\text{CO}_2$, resulting in lower levels in the hypocapnic groups and higher levels in the hypercapnic groups without affecting any other measures.

Berger (2001) conducted a comparative study between breathing training BT and CBT on the treatment PD. Ten people with PD were randomly assigned to CBT without BT and eleven were randomly assigned to a BT group. The BT group included six 30 to 60 minute sessions of breathing training. The CBT group followed a modified version of Craske, Barlow & Meadows' protocol (1994) which consisted of ten 45 to 90 minute sessions. Results showed that BT appears to be as effective as CBT in treating PD. There were no significant pre to post differences in the severity or frequency of panic attacks between the two groups.

Although there are not many studies that demonstrate the effectiveness of breathing retraining for panic disorder, there are some that demonstrate its effectiveness for hyperventilation (DeGuire et al. 1992; Tweeddale, Rowbottom, & McHardy, 1994). DeGuire et al. (1992) established that breathing retraining increased end-tidal CO_2 and decreased respiratory rate in participants with signs of hyperventilation syndrome and who complained of cardiac symptoms such as chest pain, heart palpitations, and shortness of breath. The physiological changes that occurred as a result of breathing retraining resulted in a decrease in the frequency of cardiac symptoms experienced by the participants. Because the somatic symptoms associated with PD are likely to result from hyperventilation, the results of the DeGuire, Gevirtz, Hawkinson & Dixon study, (1996) suggested that breathing retraining may therefore also be effective as a treatment for PD. They also investigated the long-term effects of paced diaphragmatic breathing on subjects who reported functional cardiac symptoms and who also demonstrated associated signs of hyperventilation syndrome. Participants were a representative sample composed of 10 out of the original 41 subjects who had participated three years previously in the study designed to evaluate the short-term effects of breathing retraining on

functional cardiac symptoms and respiratory parameters (respiratory rate and end-tidal carbon dioxide). The results of this follow-up study showed that breathing retraining had lasting effects on both respiratory parameters measured. Participants evidenced significantly higher end-tidal carbon dioxide levels and lower respiratory rates when compared to pre-treatment levels measured three years earlier. Subjects also continued to report a decrease in the frequency of functional cardiac symptoms when compared to pre-treatment levels.

De Ruiter, Rijken, Garsen & Kraaimaat (1989) compared (a) Breathing Retraining plus Cognitive Restructuring (BRCR), (b) in vivo graded self exposure, and a (c) combined BRCR plus exposure, in the treatment of PD. Outcome measures consisted of a battery of self-report measures of phobic anxiety and avoidance, panic, fear of somatic symptoms, general anxiety, somatic complaints, and depression. All measures were administered 4 weeks prior to treatment, immediately prior to treatment and post-treatment. They found that the three treatments produced improvement on all the self-report measures between pre and post-treatment, except frequency of panic/day. There were no significant differences between treatments. Craske et al., (1997) compared interoceptive exposure and breathing retraining in treatment of panic disorder. Thirty-eight participants with PD A were randomly assigned to (a) cognitive restructuring plus interoceptive exposure and in vivo exposure to agoraphobic situations; or (b) cognitive restructuring plus breathing retraining and in vivo exposure to agoraphobic situations. Assessments were conducted at pre intervention, post-treatment and six months later. They found that both post-treatment and 6-month follow-up, participants receiving interoceptive exposure reported fewer panic attacks and less overall severity, general anxiety, overall severity and functioning and distress than did those receiving breathing retraining.

An extensive review on Breathing Retraining in panic disorder is presented below (Table 1.5).

Table 1.5: Overview of Breathing Retraining studies panic disorder

Bonn, Readhead, Timmons (1984)	Participants	Twelve PD patients
	Condition	A pre-post test design to examine enhanced adaptive behavioral response in agoraphobic patients with BT. The patients were alternately allocated to two treatment groups: (a) breathing training and exposure therapy (BT+EXP) and (b) only exposure (EXP).
	F/Up	6 month
	Outcome	(BT+ EXP)=(EXP) at post-treatment, (BT + EXP) > (EXP) at FU
Clark, Salkovskis, Chalkley, (1985)	Participants	Eighteen PD patients
	Condition	Longitudinal pretest-posttest designs to assess respiratory control as a treatment for panic attacks. Treatment consisted of (a) brief, voluntary hyperventilation (b) explanation of the effects of overbreathing and reattribution of the cause of a patient's attacks to hyperventilation; (c) training in a respiratory control technique.
	F/Up	6-month and 2-year
	Outcome	Reduction in panic attack frequency, self-reported anxiety and depression.
Rapee (1985)	Participants	One PD patient
	Condition	3 breathing training sessions/4 weeks.
	F/Up	Not reported
	Outcome	Decrease in panic attack frequency and severity of symptoms and anxiety.
Salkovskis, Jones & Clark (1986)	Participants	Nine PD patients
	Condition	4 sessions/4 weeks, replication of respiratory control in the treatment of panic attacks by concurrent measurement of behavior and pCO ₂ based on the supposition that catastrophic interpretations of sensations produced by hyperventilation.
	F/Up	Not reported
	Outcome	Reduction in panic attack frequency, self-reported anxiety and depression; increase of pCO ₂ to normal levels.
Sartory & Olajide (1988)	Participants	Eight patients with generalized anxiety disorder with the distinct, spontaneous panic attacks and one patient with epileptic
	Condition	Examine the efficacy of Vagal Innervation techniques in the treatment of PD; the subjects allocated randomly to (a) Relaxation+ Vagal Innervation (REL+V. I) group and (b) Relaxation control group (REL). Patients were seen on four sessions individually treatment.
	F/Up	Not reported
	Outcome	REL+ V.I=REL But reducing of number of panic symptoms and anxiety: REL+V.I >REL
de Ruiter,	Participants	Forty-six PD patients

Garssen, Rijken, Kraaimaat (1989)	Condition	Examine hyperventilation syndrome in PDA and generalized anxiety disorder, the patients were randomly assigned to (a) BT plus Cognitive Restructuring (BT+CR) (b) in vivo exposure, (c) combined BT+CR plus exposure. Treatments consisted of 8 sessions.
	F/Up	Not reported
	Outcome	BT+CR=EXP=BT+CR+EXP
Hibbert & Chan (1989)	Participants	Forty PD patients with with or without avoidance
	Condition	Examine the efficacy of respiratory control in PD. All patients were divided into (a) BT or (b) a placebo treatment. The patients in each group were treated for two week and both groups received conventional anxiety treatments, most commonly, in vivo exposure.
	F/Up	Nor reported
	Outcome	BT+ EXP > Placebo +EXP on observer-rated anxiety BT+EX=Placebo+EX on self- report measures
Franklin (1989)	Participants	Eight patients with PD/A
	Condition	To evaluate the short-term effectiveness of BT compared to relaxation (REL) and cognitive modification (CM), and a placebo treatment (PLC), 4 patients were treated with four different sequences of these interventions 1 session/4 weeks and 4 patients were assigned to waiting list group.
	F/Up	Not reported
	Outcome	BT > REL, CM and PLC
Craske, Rowe, Lewin & Noriega- Dimitiri (1997)	Participants	Thirty-eight participants with PD/A
	Condition	To examine the short and long term effectiveness of BT and exposure for PDA, the patients were randomly assigned to (a) cognitive restructuring plus interoceptive exposure and in vivo exposure (CR+IEXP+in vivo EXP) or (b) cognitive restructuring plus BT and in vivo EXP (CR+BT+in vivo EXP).
	F/Up	6 months
	Outcome	(CR+IEXP+in vivo EXP) > (CR+BT+in vivo EXP)
Schmidt, Woolaway- Bickel et al., (2000)	Participants	Seventy-seven PD/PDA patients
	Condition	Longitudinal pretest-posttest designs to assess BT in the context of CBT protocol. Patients were assigned to receive (a) two sessions/two weeks (CBT + BT), (b) twelve sessions only CBT (c) WL.
	F/Up	One year
	Outcome	CBT>CBT+BT
Meuret, Wilhelm, Roth (2001)	Participants	Four PD patients
	Condition	A pre-post test design to examine respiratory biofeedback assisted therapy in PD. Patients assigned to one of two conditions: (a) an immediate treatment group or (b) WL group. Patients assigned to the immediate treatment group received five individual treatments. Duration of treatment: 5 sessions/4 weeks.

	F/Up	8 weeks
	Outcome	Respiratory group: Reduction of PDSS, ASI, BDI, and STAI-T and increase of pCO ₂ to normal levels through FU.
Berger (2001)	Participants	Twenty-one PD/PDA patients
	Condition	A pre-post test design to compare BT and CBT on the treatment of PD. Patients randomly assigned to (a) CBT without BT and (b) BT group. The BT group included six sessions of BT. The CBT group consisted of ten sessions.
	F/Up	4 weeks
	Outcome	BT=CBT
Meuret, Wilhelm, Ritz, Roth (2006)	Participants	Thirty-seven PD patients with or without Agoraphobia
	Condition	A pre-post test and FU design to test capnometry-assisted BT as a therapeutic approach for PD. Patients randomly assigned to BT or a WL group. Patients underwent a four-week BT consisting of five-weekly/ 1 h treatment sessions.
	F/Up	2 and 12-month
	Outcome	BT > WL
Wollburg (2007)	Participants	Forty-five PD patients, 39 Episodic Anxiety (EA) patients who suffered from subclinical panic attacks and 20 non-anxious controls (NAC)
	Condition	Psychophysiological effects of respiratory challenges before and after BT in PD patients and patients with episodic anxiety attacks. Therapy consisted of five weekly sessions of biofeedback-assisted breathing training and practice of breathing exercises at home on a daily basis.
	F/Up	4 weeks
	Outcome	Hypercapnic (Raise-CO ₂) = Hypocapnic (Lower-CO ₂) breathing.
Meuret, Rosenfield Hofmann, Suvak Roth (2009)	Participants	Thirty-five PD/A
	Condition	A pre-post test design to examine whether changes in pCO ₂ mediate changes in fear of bodily sensation in a bio-behavioral treatment for PD that targets changes in end-tidal pCO ₂ . Patients underwent 4 weeks of capnometry-assisted breathing training targeting respiratory dysregulation.
	F/Up	2-month
	Outcome	BT targeting pCO ₂ reduced fear of bodily sensations.

Note*: BT: Breathing Training; BTCR: Breathing Training & Cognitive Restructuring; CBT: Cognitive Behavioral Therapy; CM: Cognitive Modification; CR: Cognitive Restructuring; EXP: Exposure; IEXP: interoceptive exposure; in vivo EXP: in vivo exposure; WL: Waiting List; FU: Follow-Up; REL: Relaxation; VI: Vagal Innervation; ASI: Anxiety Sensitivity Index; BDI: Beck Depression Inventory; PDSS: Panic Disorder Severity Scale; STAI-T: State-Trait Anxiety Inventory, trait version.

In summary, each of these studies found Breathing Training was effective in panic management and reduction of anxiety, physiological arousal symptoms and hyperventilation rate in panic situations both immediately after treatment and follow-up. Berathing Training was effective compared to the control group, relaxation therapy alone or exposure therapy alone, but not compared to CBT alone.

1.3.2.3 Cognitive interventions

The aim of cognitive interventions in PD is to change irrational or disturbing belief patterns such as catastrophic misinterpretation of bodily sensations or experiences by revealing to patients the way they evaluate upsetting situations. In cognitive therapy of PD, the person examines his feelings and teaches that fearing the way their body feels at a particular moment is not necessarily dangerous. In fact, the patients learn how to separate unrealistic thoughts from realistic ones and develop techniques to change the way they respond to panic situations (Clark & Beck, 2009; Sargent, 1990).

Panic Education

Psychoeducation is designed to provide patients with accurate information about panic attacks and panic disorder, particularly the symptomatology of panic attacks and some explanatory mechanism such as catastrophic misinterpretation of bodily signals.

Psychoeducation may also involve asking the client to register symptoms in line with a model such as the panic circle developed by Clark (1986).

It is thought that by the time a person with PD finally encounters a mental health professional she/he is often convinced that she/he has a life threatening physical condition that has eluded diagnosis.

A primary goal of the psychoeducational components is to allay these fears by explaining the physiology of a panic attack and also tailored information to help the patient understand maintaining factors (Anderson & Carlbring, 2010).

Panic education commonly occurs during the first few sessions and is based upon the postulate that patients need to know the relationship between cognitions and sensations and the development of panic attacks before they can participate in

specific therapeutic interventions. The purpose of panic education is to allay the fears experienced and introduce a new view on the panic experience. Thus, panic education is not planned as a stand-alone treatment, but as a supplement to other interventions.

Patients are informed about symptoms of PD. Some of the information includes an explanation of panic attacks, and the cause of the symptoms, common myths about the dangers of panic attacks, and a clear definition of the fight-or-flight response (Houghton, & Saxon, 2007; McNally, 1994). Commonly, it is explained that PD is a reaction to stress and anticipatory anxiety a way to ward off a repetition of a panic attack (Sanderson & Wetzler, 1995). Sometimes group sharing of personal experiences of panic attack is used to help the individual realize that they are not alone in the experience of panic disorder. Sometimes group sharing of personal experiences of panic attack is used to dispel the individual's perception that they are alone in the experience of panic disorder. Individuals are provided with success experiences about the treatment of panic attacks. Therefore, panic education presents information about PD, and provides support, and encouragement as the first stage in treat panic disorder (Anderson & Calbring, 2010).

Therapists may also examine with their patients some of the assumptions and beliefs about the meaning attributed to the panic experiences (McNally, 1994). This may provide a base for later changes in beliefs.

There may be initial effects of psychoeducation that facilitate further progress in treatment. For instance Shear et al., (1994) found that by starting treatment with psychoeducation the subsequent treatment, which was either based on CBT or a non-prescriptive supportive therapy, did not differ.

Hu, Choi & Park (2003) in a study examined which treatment component was most helpful in treatment group behavioral therapy for panic disorder. In their study 161 patients with panic disorder, after treatment, were asked to rank for five components of panic control treatment (PCT). The results showed that most helpful component of PCT was psychoeducation that was constructed to provide the corrective information for PD.

Dannon, Iancu & Grunhaus, (2002) examined the effects of a self-information booklet (SIB) program in decreasing frequency and severity of panic attacks in PD patients. In this study Eighty-four patients were randomly assigned to receive either paroxetine with self-information booklet (Group A) or paroxetine alone (Group B). Follow-up was done after 1, 3, and 12 weeks. After 3 weeks of therapy, the outcome of study showed that Group A had significantly greater improvement than patients in group B in reduction of anxiety and panic attack symptoms. After 12 weeks of treatment intervention, two groups were not statistically significantly different from each other. The authors concluded that administration of a psychoeducational brochure to PD patients at the initiation of therapy had beneficial effects during the first weeks of treatment.

Cognitive Restructuring

The cognitive restructuring is based on Beck's work on how dysfunctional information processing may underlie affective disturbances and the resulting dysfunctional behaviors (Beck & Emery, 1985; Sanderson & Wetzler, 1995). The goal of cognitive restructuring is to alter the relationship between physiological arousal and the meaning of the arousal (McCarter, 1996; Choy, 2008).

Cognitive models of PD suggest that change in catastrophic misinterpretations of bodily sensations will predict symptom reduction and is a central mechanism of change in cognitive therapy of PD (Teachman, Marker, Clerkin, 2010; Casey, et al., 2004b). Hence, the therapeutic effects of cognitive restructuring emphasized that targeting the catastrophic misinterpretation of bodily sensation is a central mechanism of change in cognitive therapy of PD (Casey, et al., 2004a).

Through therapy faulty cognitions and processes are identified, challenged through reality-testing and then restructured in more realistic form (Clark, 1986; Barlow, Craske, Cerny & Klosko 1989). It is important to note that in order for the therapy to be genuinely effective it is the patient who must ultimately conclude that certain cognitions or cognitive processes are distorted or incorrect.

Cognitive restructuring includes four components: (a) description of the cognitive model of panic and educating patients about exacerbating panic symptoms through

catastrophic thoughts (vicious cycle) (b) identifying negative and anxious thought cognitions associated with physical sensation triggers of recent panic attacks (Sanderson & Rego, 2002; Gabbard, 2004; McCarter, 1996), (c) practicing replacement of maladaptive cognitions with noncatastrophic explanations, and providing information about the individual panic sequence and the panic inducing and maintaining cognitions, (d) instructing patients in between session exercises. Patients were asked to describe examples of recent panic attacks and to identify maladaptive thoughts and consequences associated with them (Meuert et al., 2010b). Catastrophic misinterpretations of panic related to somatic cues are specially targeted (Wells, 1997; Clark, 1986). Interruption of catastrophic interpretations such as fear of having a heart attack, losing control or going insane are challenged and changed with more positive internal conversations, such as “This has happened before, but I can stand this. This is anxiety and this will go away” other common misinterpretations also may be targeted such as over-valuing the consequences of a panic attack, i.e., public humiliation, losing one's job or interpersonal rejection (Sanderson & Wetzler, 1995).

Sanderson & Wetzler (1995) employed logs which targeted certain areas with patients who had learned how to restructure their cognitions to facilitate the self-monitoring process. In the logs clients were asked to: (a) report the status in which the panic attacks happened; (b) determine the feelings at the time of the attack and rate their severity; (c) in three columns, log the negative automatic thoughts, the kind of cognitive distortion for example Catastrophizing, Overgeneralizations, All-or-nothing thinking, Jumping to conclusions, Disqualifying the positive), and a rational (i.e., realistic) response; and (d) describe the feeling after they completed the log. Often patients continued to keep these logs throughout the course of treatment. Cognitive restructuring, in combination with other techniques, has been used successfully to modify dysfunctional thoughts and catastrophic misinterpretation of bodily sensations. It is commonly combined with exposure especially when agoraphobic avoidance is prominent (Marchand et al, 2008; Ost, Thulin, Ramnero 2004; Arntz & Van Hout, 1996; Bouchard et al., 1996).

In this regard, Foa & Kozak, (1986) postulated that combining exposure with

cognitive restructuring provided the patient with corrective information about the dangerousness of feared situations.

The problem is that exercises called 'behavioral experiments' or 'hypothesis testing' play an important role in cognitive restructuring (Bouchard et al, 1996). They are used to test the validity of the subject's beliefs and to induce reappraisal of the threatening stimulus by allowing the client to confront the anxiety provoking stimulus. Without them, cognitive restructuring would not be clinically valid (Beck & Emery, 1985). This means that the patient is exposed to somatic and cognitive impulses related with panic attacks in order to learn to reattribute the misinterpretations (Beamish et al., 2002). In this regard, exposure usually focuses on interoceptive phobic stimuli and agoraphobic situations. In the case of exposure to interoceptive cues, hyperventilation, aerobic exercises or inhalation of CO₂ are generally used to elicit feared stimuli (Barlow, Craske, 2007; Watkins, Sturgis, & Clum, 1988; Nazemi, et al., 2003b). Within the context of experiencing bodily and cognitive symptoms similar to those experienced during a panic attack, the patient learns a series of cognitive restructuring procedures for dealing with these symptoms (Barlow, Craske, 2007; Bystritsky et al., 2000; Beamish et al., 2002). As already mentioned, exposure therapy is typically programmed to move more or less progressively from the least to the most fearful stimuli and, at each step, contact with the panicogenic stimulus is maintained until the anxiety has subsided. The amount of exposure in exposure therapy of course will always exceed what is found in cognitive restructuring and behavioral experiments.

However, Margraf and Schneider (1991), Salkovskis, Clark and Hackman (1991), Bouchard, et al., (1996), Clark et al. (1994), Williams and Falbo (1996), Ost, Thulin, & Ramnero (2004), Beck et al., (1992), Brown et al., (1998), Wenzel et al., (2006), Arntz (2002), Arntz & Van Hout (1996) have demonstrated that cognitive restructuring can be effective even in the absence of any exposure intervention, including behavioral experiments. However, outcome studies have also shown that it is not necessary to directly challenge dysfunctional beliefs with cognitive restructuring to obtain effects that are comparable to those of cognitive restructuring (Marchand et al., 2008; Beck et al., 1994; Margraf & Schneider, 1991; Ost, 1987; Ost, Westling & Hellström, 1993).

Margraf and Schneider (1991) in a study with eighty PDA patients found cognitive restructuring to be as successful as interoceptive exposure alone, or a combination of cognitive and interoceptive exposure. Up to 93% of their participants were panic-free at 3 month follow-up. The short interval of the follow-up may explain why no differences were found between experimental groups.

Margraf et al., (1993) reported in their meta-analysis of PD treatment that the cognitive component of assisting patients to reattribute their bodily sensations was found to be more important to recovery than simply habituating participants through exposure.

Salkovskis et al., (1991) proposed that cognitive restructuring therapy focusing on changing the misinterpretation of bodily sensations (focal therapy) would be more effective in reducing the frequency of panic attacks than cognitive therapy which did not focus on misinterpretations of bodily sensations (non-focal therapy). Five participants were in the first group and two in the second group. They found that treatment consisting of reattribution of the physical symptoms associated with panic, without implementing any breathing retraining or exposure techniques, was more effective at reducing the frequency of panic attacks in PD patients than non-focal therapy.

Brown, Beck, Newman, Beck, Tran (1998) examined the efficacy of focused cognitive therapy (FCT) and standard cognitive therapy (SCT) in PD patients. In their study, FCT focused specifically on the “catastrophic misinterpretation” of physical and psychological sensations experienced during panic attacks induced in the office or occurring spontaneously between sessions. SCT focused primarily on the cognitions and beliefs relevant to interpersonal concerns involved in generalized anxiety. The result showed that both groups had significant decreases in the severity of the clinical measures after treatment. Moreover, 89.5% of the SCT group and 84.2% of the FCT group were free of panic attacks at 1-year follow-up.

Bouchard, et al., (1996) compared cognitive restructuring versus exposure in the treatment of PDA. A total of 28 subjects with PDA were randomly assigned to either

of two treatment conditions: exposure therapy or cognitive restructuring. Both conditions comprised 15 therapy sessions lasting 90 min each. The exposure therapy (interoceptive and exteroceptive) was conducted according to a written treatment manual based on descriptions from Barlow and Cerny (1988) and Wolpe (1990). The cognitive restructuring group received at each weekly session. The results showed no significant difference among the groups and both treatment groups were statistically and clinically effective in reducing panic and agoraphobic symptoms.

Arntz & van Hout (1996) compared cognitive therapy versus applied relaxation in PD treatment in thirty- six patients. Each group received 12 treatment sessions. The results showed the cognitive therapy group achieved superior outcomes in reducing panic frequency compared to the relaxation therapy group at post treatments and follow-up.

Williams and Falbo (1996) investigated the effectiveness of cognitive therapy and exposure treatment on panic symptoms. They found that both treatments did not differ from one another in effectiveness. 94% of the low agoraphobia patients were free of panic after treatment and 52% of the high agoraphobia patients became panic free.

Wenzel et al., (2006) evaluated the effectiveness of cognitive therapy in dysfunctional beliefs in PD. The results indicated that patients who received cognitive therapy achieved significant reductions in level of panic belief or dysfunctional cognitions across treatment, with the largest decline occurring between intake and 4 weeks into treatment.

Clark et al., (1994) compared cognitive restructuring with drug therapy and relaxation in treatment of PD. They found that cognitive restructuring was more effective in reducing panic and panic-related conditions than applied relaxation or imipramine. At a 12 month follow-up, the same pattern of results emerged.

An extensive review on cognitive treatment in panic disorder is presented below (Table 1.6).

Table 1.6: Overview of cognitive therapy versus other treatment modalities

Margraf & Schneider (1991)	Participants	Eighty PDA patients
	Condition	Evaluated outcome and components of CBT for PD. The participants were randomly assigned to either of four conditions: (a) CT (b) Ex (c) CT+EX (d) WL.
	F/Up	One month
	Outcome	CT=EX=CT+EX
Salkovskis, Clark, Hackmann (1991)	Participants	Seven PD patients
	Condition	Assessment of Cognitive Restructuring alone in treating of PD. 5 patients allocated in focus cognitive therapy for changing the misinterpretation of bodily sensations (focal therapy) and 2 patients were allocated in non-focus on misinterpretations of bodily sensations (non-focal therapy).
	F/Up	Not reported
	Outcome	FCT>NFCT
Clark et al. (1994)	Participants	Sixty-four PD patients
	Condition	A comparison of cognitive therapy, applied relaxation and imipramine in the treatment of PD. Participants were assigned to (CT), (AR), (IM) or (WL).
	F/Up	3, 6, 15 months
	Outcome	At 3 months:CT>AR+IM At 6 months :CT=AR=IM At 15 months:CT>AR+IM
Williams and Falbo (1996)	Participants	Forty-eight PDA patients
	Condition	A comparison of the efficacy of cognitive therapy and performance-based exposure in panic attacks. Participants were assigned to (a) cognitive therapy, (b) exposure therapy, (c) combined cognitive/performance treatment and (d) WL. 8 weekly individual 1 hour treatment sessions.
	F/Up	6 weeks, 1-2 years
	Outcome	CT=EX=COM > WL
Bouchard, et al., (1996)	Participants	Twenty-eight PDA patients
	Condition	A comparison of the efficacy of cognitive restructuring vs exposure therapy. Patients were randomly assigned to (a) exposure therapy or (b) cognitive restructuring for 15 weekly sessions.
	F/Up	4 weeks, 6 months
	Outcome	CR=EX
Arntz & Van Hout (1996)	Participants	Fifty-four PD/PDA patients
	Condition	A pre-post test design to examine cognitive therapy vs applied relaxation in PD. The patients were randomly assigned to (a) cognitive therapy or (b) relaxation, (c) WL group. Treatment consisted of 12 weekly sessions.
	F/Up	Six months
	Outcome	CT > AR

Brown, Beck, Newman, Beck, Tran (1998)	Participants	Forty PD patients
	Condition	A comparison of efficacy of focus cognitive therapy and standard cognitive therapy for PD. The patients were randomly assigned to the (a) standard cognitive therapy (SCT) and (b) focused cognitive therapy (FCT) groups for 12 to 18 sessions of treatment.
	F/Up	One year
	Outcome	FCT=SCT
Dannon, Iancu, Grunhaus (2002)	Participants	Fifty-four PD/PDA patients
	Condition	A pre-post test design to examine effectiveness of Psychoeducation by a self-information booklet (SIB) in PD. The patients were randomly assigned to receive (a) paroxetine with brochure (b) paroxetine without a brochure. Treatment consisted of 12 weekly sessions. Patients self-monitored panic attacks during the whole treatment period.
	F/Up	1, 3, and 12 weeks
Arntz (2002)	Condition	A pre-post design to examine cognitive therapy vs interoceptive exposure. Patients randomly allocated to (a) cognitive therapy (b) interoceptive exposure group, 12-session treatments in each group.
	F/Up	Six months
	Outcome	CT=IEX
	Participants	Sixty-nine PD patients
Wenzel, Sharp, Brown, Greenber & Beck, (2006)	Condition	A longitudinal pre test-posttest design study to assess dysfunctional beliefs in PD. Patients received 8 weeks cognitive therapy.
	F/Up	3, 6, 12, and 24-months
	Outcome	CT produced a significant reduction in panic belief (PBI) at posttreatment and FU.
	Participants	197 PD patients

Note*: AR: Applied Relaxation; CR: Cognitive Restructuring; CT: Cognitive Therapy; COM: Combination of Cognitive and Behavioural Interventions; EX: Exposure; IEX= Introceptive Exposure BT: Breathing Training; Relaxation; FCT: Focused Cognitive Therapy; NFCT: Non Focal Cognitive Therapy; SCT: Standard Cognitive Therapy; SIB: Self-Information Booklet; IMI: Imipramine therapy; Parox: Paraoxetine therapy; WL: Waiting List; FU: Follow-Up; PBI: Panic Believe Inventory.

In summary, each of these studies showed cognitive restructuring and psychoeducation were effective in changing irrational or disturbing belief patterns such as catastrophic misinterpretation of bodily sensations. Cognitive therapy was effective compared to the waiting list control group, relaxation therapy alone and supportive therapy, immediately after treatment and follow-up but not compared to

exposure treatment.

1.3.2.4 Combination Treatments

Cognitive behavioral therapy in treating panic disorder focuses on targeting the fear of bodily sensations, apprehension of panic and agoraphobic avoidance through a combination of cognitive and behavioral techniques (Rayburn & Otto, 2003; Otte, 2011).

Recent evidence supports combining CBT techniques for PD treatment (Pincus et al., 2010; Gallo et al., 2012; Butler et al., 2006; Barlow, et al., 2000). There are a number of different multi-model treatment approaches to treating PD, each using some combination of the treatment strategies (Barlow, 1990; Carlbring et al., 2006; Sánchez-Meca et al., 2010). CBT approaches have been found to produce total cessation of panic attacks in over 80% of PD patients according to Beck et al., (1988a).

Across studies, there is some variation in the emphasis placed on cognitive and behavioral elements, and the extent to which all elements are included. Panic control treatment (PCT) includes all these elements, whereas Clark's cognitive therapy for panic largely focuses on cognitive restructuring (Roth & Fonagy, 2005).

Panic Control Therapy (PCT), or panic inoculation, is a well validated CBT approach (Barlow & Craske, 2007; Craske et al., 2003). The main goal of PCT is to better control anxiety and panic symptoms and promote a greater sense of mastery over panic attacks (Barlow & Craske 2007). PCT is a widely used form of CBT, with combination of behavioral and cognitive components for managing anxious sensations and breaking the association between these sensations and catastrophic interpretations in panic disorder (Barlow, Craske, 2007). PCT combines psychoeducation, cognitive restructuring, breathing retraining and progressive muscle relaxation, and exposure-based procedures designed to reduce fear of somatic sensations and agoraphobic situations (Barlow & Craske 2007). In fact PCT is an amalgam of techniques drawn from a variety of cognitive and behavioral methods and based largely on the interactions of three systems affecting the human experience in panic and anxiety: physiological (e.g., palpitation, sweating, dizziness, nausea), cognitive (fears of losing control or going crazy), and behavioral (avoidance, pacing) (Barlow & Craske 2007;

Hofmann & Spiegel, 1999). PCT techniques are thus directed towards each of these systems and based on a 12-to 15 session manualized treatment protocol (Barlow & Craske 2007).

PCT first uses psycho education focusing on the etiology, prevalence, and hypothesized maintenance of panic and cognitive restructuring to identify and monitor negative thoughts that contribute to panic.

Second, somatic control exercises, such as breathing retraining and progressive muscle relaxation, are included to reduce or eliminate physical symptoms that often trigger panic attacks and improve the patient's ability to lessen somatic arousal and to change misappraisals of somatic cues (Barlow, 1990).

Third, interoceptive exposure, which refers to gradually exposing the patient to the feared somatic sensations in a systematic manner, is added to increase tolerance to the sensations and to demonstrate that they are harmless. Finally, the patient is exposed to previously avoided situations in which panic attacks are likely to occur, thus decreasing future avoidance of these situations and feared catastrophes associated with them (Levitt & Karekla, 2005).

Numerous research studies have been conducted to investigate the efficacy of PCT including dismantling studies investigating the mechanisms of action of the overall treatment package and the efficacy of its component parts (e.g, Barlow, et al., 2000; Barlow et al.,1989; Craske, Brown, & Barlow, 1991; Gallo et al., 2012; Addis, Hatgis, et al.,2006). Studies evaluating the effectiveness and efficacy of PCT and its components have consistently shown that the overall PCT package results in significant reduction in frequency of severity of panic attacks in approximately 80% of individuals treated (Barlow, et al., 2000; Barlow, Craske, Cerny & Klosko, 1989; Hofmann and Spiegel, 1999).

Based on the results of follow-up studies of patients who receive PCT demonstrated that most of them remain better after at least 2 years (Craske & Barlow, 2008)

Barlow et al., (1989) randomly assigned patients with panic disorder to receive (a) PCT alone, (b) relaxation alone, (c) relaxation and PCT in combination, or (d) wait-list control group. They found that all three treatment groups were successful and superior to the wait list control, but PCT and PCT in combination with relaxation

were superior to relaxation alone in reducing panic frequency but not generalized anxiety. At post treatment, 87% of the PCT group and 85% of the PCT plus relaxation group, and 60% of the relaxation group were panic free, compared with only 6% of the control group; however, relaxation training led to a higher dropout rate, both when used alone and in combination.

PCT has also been delivered and tested in group formats. In a study, Craske et al., (2003) examined the effectiveness of group PCT delivered in decreasing panic attacks in PD patients. Patients were randomly assigned to receive 16 weekly, 90-min sessions PCT with/without the addition of in vivo exposure. The results of study showed that both treatment conditions were effective in the reduction of frequency and severity of panic attacks. At post-treatment, 79% of the sample reported no panic attacks. The majority of this sample was categorized as having moderate to severe agoraphobia at pre-treatment (82%), compared to 29% in the moderate to severe range at post-treatment.

Support for PCT also comes from a study by Klosko et al., (1990). They compared the efficacy of PCT and Alprozolam to a drug placebo condition and a wait list control condition. They found that 87% of the patients in the PCT condition had achieved panic free status compared with 50% of the patients in the Alprazolam condition, 36% of the patients in the placebo drug condition, and 33% of the patients in the wait list control condition. The PCT was found to be significantly more effective than the other three conditions.

Barlow, et al., (2000) in a study compared PCT to imipramine, a placebo, and combinations of PCT with imipramine or a placebo. Results indicated that after treatment all active treatments were equivalent and all were better than placebo. However at the 6 month follow-up, individuals who received PCT alone had significantly more durable effects and significantly less intent to treat. Analysis of the clinical Global Impression Scale were 31.9% for PCT alone vs 19.7% for imipramine alone and 26.3% for PCT combined with imipramine. Moreover, more than one-third of subjects refused participation in the study because they were unwilling to take

imipramine. Only, 1 out of 308 potential participants refused the study because of the possibility of receiving psychotherapy.

Addis et al., (2006) examined the effectiveness of CBT for panic disorder versus treatment as usual in a managed care setting with a 2-year follow up. Eighty outpatients with PD received either PCT or treatment as usual (TAU). The results showed no significant differences between the treatments across the follow-up period. However when treatment completer status was added as a moderator, those receiving PCT showed lower levels of panic severity and phobic avoidance and a greater likelihood of achieving and maintaining clinically significant change.

Pincus et al., (2010) evaluated the efficacy of PCT in thirteen adolescent case with PD. Participants were 26 adolescent subjects that were randomly assigned to receive either 12 weeks of PCT or a self-monitoring control group. The results showed that adolescents receiving PCT showed a significant reduction in clinician-rated severity of panic disorder and in self-reported anxiety, anxiety sensitivity, and depression, in comparison to control group participants. These treatment gains were maintained at 3- and 6-month follow-ups.

Öst, Thulin & Ramnero (2004) examined a combination of CBT packages for treatment of panic disorder. They used a range of cognitive and behavioral coping strategies to identify the misinterpretation of bodily sensations and generate an alternative, non-catastrophic interpretation of the sensations. The results showed 79% of the patients at post-treatment were panic free. They had significant improvements, both on panic/agoraphobia measures and on measures of general anxiety, depression, social adjustment and quality of life, which were maintained at a one year follow-up.

Combined CBT and pharmacological therapy in treatment PD is common in clinical practice and numerous studies using a variety of medications and CBT packages (McCabe & Gifford, 2009). This compares favorably with any of the pharmacological treatments in the acute phase of the treatment and may in fact be more effective in the long run.

The results of a comprehensive review of the literature on the efficacy of psychotherapy and pharmacotherapy in PD/PDA showed that of 124 studies included, CBT was more effective than a non-treatment control and a placebo control (Mitte, 2005).

Furukawa, Watanabe & Churchill (2006) examined 23 studies (involving 1,709 patients) comparing a combination of psychotherapy and pharmacotherapy vs treatment alone for patients with PDA. The results showed of twenty- three studies, twenty-two studies used CBT as the psychotherapy intervention. The author found that in the acute-phase treatment combined CBT and medication was superior to pharmacotherapy or psychotherapy, although at follow up (6 to 24 months) combined treatment was superior to medication but equivalent to CBT alone.

Roy-Byrne et al., (2005b) in a randomized controlled trial examined the effectiveness of a combined pharmacotherapy and cognitive-behavioral intervention on PD. The patients randomly received either treatment as usual or an intervention consisting of a combination of up to 6 sessions of CBT. They found combined cognitive-behavioral and pharmacotherapy resulted in sustained and gradually increased improvement relative to treatment as usual.

An extensive review on Panic Control Treatment (PCT) in panic disorder is presented below (Table 1.7).

Table 1.7: Overview of Panic Control Treatment (PCT) studies in Panic Disorder (PD)

Klosko, Barlow, Tassinari & Cerny (1990)	Participants	Forty-seven patients with PD
	Condition	Compared PCT vs Alprazolam. Subjects were randomly assigned to PCT or Alprazolam treatment. These conditions were compared with a medication placebo and a waiting-list control group.
	F/Up	Not reported
	Outcome	PCT > ALP
Telch, Lucas, Schmidt, et al.,(1993)	Participants	Sixty-seven patients with PD/PDA
	Condition	Comparative effectiveness of CBT for PD. Subjects was randomly assigned to treatment CBT or waiting list group. 12 PCT sessions over 8 weeks consisted of: (a) psychoeducation (b) cognitive therapy, (c) breathing training and (d) interoceptive exposure.

	F/Up	6 months
	Outcome	PCT > WL
Barlow, Gorman Shear & Woods (2000)	Participants	Three hundred twelve PD patients
	Condition	A randomized controlled trial to compare CBT, imipramine, or their combination for PD. Patients randomly assigned to receive: (a) CBT (b) Imipramine (c) CBT + imipramine (d) Placebo (e) CBT + placebo.
	F/Up	6 months
	Outcome	(CBT), (IMI) > PLC in reduction of PDSS (CBT), (IMI) =PLC in reduction of CGI. At FU: (IMI), (CBT) > PLC in reduction of PDSS, CGI (IMI+CBT) = (CBT+PLC) in reduction of PDSS (CBT+PLC) > (IMI+CBT) in reduction of CGI
Roy-Byrne et al., (2005)	Participants	Two hundred thirty two PD patients
	Condition	A pre-test, post-test, FU design to test the effectiveness of a combined pharmacotherapy + CBT versus TAU (typically pharmacotherapy) for PD. Subjects in combination group received 6 CBT sessions (across 12 weeks).
	F/Up	One year
	Outcome	CBT +PHMT>TAU
Addis, Hatgis Cardemil, et al., (2006)	Participants	eighteen patients with PD
	Condition	A long-term outcome study to compare PCT vs Treatment as Usual (TAU). Subjects randomly assigned to one of the two groups.
	F/Up	2 years
	Outcome	PCT=TAU
Furukawa, Watanabe & CHurchill (2006)	Participants	1,709 PD patients
	Condition	A Meta-analysis for Psychotherapy plus antidepressant for PD/A.
	F/Up	Not reported
	Outcome	In the acute-phase treatment: CBT+PHMT > PHMT After termination of the acute-phase treatment: CBT+PHMT=CBT
Marcus, Gorman, Shear, et al., (2007)	Participants	One hundred seventy two PD patients
	Condition	A Comparison of medication side effect reports by PD Patients With and Without Concomitant CBT. Subjects randomly assigned to one of three conditions (a) CBT plus imipramine, (b) imipramine and (c) placebo.
	F/Up	2 years
	Outcome	(CBT+IMI)>(IMI) and (PLC)
Pincus, May et al., (2010)	Participants	Twenty-six adolescents with PD
	Condition	A randomized controlled trial to evaluate the efficacy of PCT for PD. Subjects assigned to receive (a) CBT or (b) a self monitoring control group.
	F/Up	3- and 6-months
	Outcome	PCT> control group
Gallo,	Participants	Fifty-five adolescents with PD/PDA

Chan, Buzzella, Whitton & Pincus (2012)	Condition	Assessed the impact of an intensive CBT vs Wait-list group. The treatment entailed 8 days of 2 to 6 hours of treatment for a total of 20 hours of treatment.
	F/Up	Not reported
	Outcome	CBT> WL

Note*: ALP: Alprazolam therapy group; CR: Cognitive Restructuring; EXP: Exposure therapy; IMI: Imipramine; PCT: Panic Control Therapy; PHMT: Pharmacotherapy; PLC: Placebo; REL: Relaxation Therapy; TAU: Treatment As Usual; WL: Waiting List group; FU: Follow-Up; CGI: Clinical Global Impressions; PDSS: Panic Disorder Severity Scale.

In summary, each of these studies found that a combination of cognitive and behavioral techniques was effective in managing anxious sensations and breaking the association between these sensations and catastrophic interpretations in panic disorder. Panic Control Therapy (PCT) or combination of cognitive behavior therapy was effective compared to the control group or relaxation alone, pharmacotherapy alone and placebo.

1.4 Group Therapy for panic Disorder: An Overview

Cognitive behavioral therapy for panic disorder and agoraphobia may be conducted in individual or group formats (Barlow, 2008). Although psychotherapy has been demonstrated in a large body of research to be an effective treatment for anxiety disorders, the individual format has been the norm, both in CBT and other therapies. So that even when given choice, patients will likely choose individual treatment over group treatment. In one study, 95% of the sample chose individual treatment over group when asked for their preference (Sharp, Power & Swanson, 2004).

Group psychotherapy is a form of psychotherapy during which one or several therapists treat a group of clients usually between eight and twelve individuals (although it is possible to have more participants) together as a group (Andersson & Calbring, 2010). The length of every session can be from an hour and a half to three hours and can be conducted, once to twice a week (Rutan et al., 2007).

The most prominent theories on the influence of groups upon individuals came from Gustav LeBon in 1895, when he identified the phenomenon of the “group mind”.

LeBon hypothesized that when an individual is in a crowd, his level of human functioning declines, (Rutan et al., 2007). LeBon proposed that large groups by nature regress to a more uncivilized, even primitive level of behavior. He attributed this decline to three factors:

First, he linked the theory of strength in number, as impacting the individual to feel stronger, even invincible, when among the group, thus increasing their likelihood to behave differently.

Secondly, LeBon stated that the mind set of the group develops to the point of a hypnotic state, or as he termed it, a contagion, which overcomes and directs its members.

The last, but most important in LeBon’s opinion was that due to this contagion, the level of suggestibility increases, making it easier to influence an individual (Rutan et al., 2007).

Group psychotherapy was further developed by Moreno, Slavson, Spotnit, Yalom and Ormont (Yalom & Leszcz, 2005). Yalom's approach to group therapy has been very influential throughout the world (Corey, 2009).

Prior to the mid 1980s, groups were seldom focused on a homogeneous treatment population, but were usually comprised of clients suffering from various complaints. Conventional wisdom began to change with the increasing research evidence for the efficacy of psychotherapies such as CBT which at first specifically targeted depression (Niemeyer, 1985).

Luby (1995) noted that CBT could be easily adapted to diagnostically homogeneous group formats. Because of its established research efficacy, specific focus, and manualized treatments protocols, CBT is well suited to group applications.

GCBT may be defined as therapy that uses the dynamics of the group format, in addition to common CBT techniques, to change distorted, maladaptive, and dysfunctional beliefs, interpretations, behaviors, and attitudes (Bieling, McCabe & Antony, 2009; Petrocelli 2002; Van Dam-Baggen & Kraaimaat, 2000).

The format of GCBT could be psycho-educative in nature, being open-ended or manualized. The frequency and duration of session in CBT-groups can vary considerably, depending on the choice of format and other patient-dependent variables (Morrison, 2001).

White & Freeman (2000) suggested that clients' understanding of the cognitive model is fundamental to the CBT approach in both group and individual formats.

In early sessions, members learn the principles of cognitive behavioral theory. This learning does not require that the group therapist lecture to members while they remain passive. The term that characterizes the relationship between group therapist and members is collaborative empiricism (Brabender, Fallon & Smolar, 2004).

Group CBT is often practiced in more linear fashion however, with emphasis on the thought=>feeling=>behavior causal chain. In this regard, the GCBT therapist employs a clear understanding of the interaction between thoughts, feelings, and behaviors (White, 2000).

Member and therapist function as co-investigators joined in the effort to understand the interrelationships of each member's cognitions, affects, and behaviors (Bieling, McCabe, Antony, 2009). Establishing this type of relationship encourages

responsibility-taking rather than answer-seeking on the part of the member (White, 2000).

In the early phase of treatment, the therapist launches the collaboration using a Socratic method wherein a line of questioning enables the member to discover how systems of meaning influence feeling and behavior in the problems emerging in his or her life. The systematic exploration of members' experiences shows them that some reactions in situations are preceded by barely discernable and fleeting automatic thoughts that give rise to the painful feelings (Bieling, McCabe, Antony, 2009). For instance, heightened stress and arousal increase the flow of adrenaline, which may result in hyperventilation, shortness of breath, and dizziness. The patient misinterprets these sensations ("I'm dying; I'm going crazy"), thus creating a vicious cycle. To combat this the therapist explains the benign nature of the panic attack to group members and then offers instruction on how to induce a mild attack and then control it using proper breathing techniques and progressive muscular relaxation. Members become skilled through the use of thought records in analyzing their experience into thoughts, feelings, and behaviors. As a result, clients learn new skills to manage distressing feelings (Brabender, Fallon & Smolar, 2004). Clients also receive feedback from other group members regarding the evidence for and against their automatic thoughts. This corrective feedback within a peer group is an important component of the group process (Bieling, McCabe, Antony, 2009). A core principle that separates GCBT from individual CBT is the social force of cohesiveness (the degree to which group members find themselves personally interested in relating to each other) (Petrocelli, 2002). However group cohesiveness can only be arranged by the group, GCBT is like most cognitive-behavioral approaches in that it is task oriented and designed to seek problem resolution (Petrocelli, 2002, White, 2000).

It is thought that as people join together to form an effective therapy group, they also form a positive alliance whose purpose is to reduce the panic attacks of all team members. Although this positive working alliance is related to the working alliance and relationship that is essential to individual treatment (Horvath et al., 2011). There

appears to be a higher order of allegiance that develops in a successful group atmosphere.

Senge (1990) attributed these higher group goals to an atmosphere where “people continually expand their capacity to create the results they truly desire, where new and expansive patterns of thinking are nurtured, where collective aspiration is set free, and where people are continually learning to learn together” (p.3).

In CBT, learning is a central component. But learning for the benefit of the group is a unique characteristic of the group format (Yalom & Leszcz, 2005).

According to Stein, et al., (2009) in a group, clients can share their experience and problems and learn that they are not alone or 'different'. Furthermore, they will feel less isolated and begin to realize that they have a specific, understandable syndrome and not a unique bizarre condition.

According to, Zal, (2001) “in group therapy they can experience a decrease of anxiety and obtain relief of guilt feelings. They can also achieve an increase in self- esteem, as they are taken seriously, perhaps for the first time. Group therapy can foster self-expression and ventilation, as well as better interpersonal relationships and communication. A supportive group can do much too foster risk taking and assertiveness and encourage the growth and maturity of the personality. Initially, the more adventurous patients will take risks and be more active. They can serve as significant role models, encouraging others to follow. Groups can utilize each other for support for some of the exposure and behavioral exercises and continue to act as a support system to help maintain improvement” (p. 69).

1.4.1 Benefits of the Group CBT Format

In light of the market driven demands for cost-effectiveness, there has been an increased interest in the application of the cognitive therapy principle in group context (Segal & Shaw, 1996). From an economic standpoint the charge for 90 minutes of group psychotherapy is generally one-half to one - third the cost of 50 minutes of individual therapy (Vos, Corry, Haby, Carter, Andrews, 2005).

Some authors estimate that individual therapy is 64% more expensive than group therapy (McCrone et al., 2005). An additional advantage of CBT over pharmacotherapy appears to be greater cost-effectiveness. In a study examining the cost and outcomes of CBT and pharmacotherapy, Otto, Pollack, and Maki (2000) found that group CBT was a more cost-effective treatment than pharmacotherapy, with equivalent acute treatment efficacy and greater maintenance of treatment gain, without requiring ongoing treatment. In addition, group treatment was more cost-effective than individual treatment, with a total annual cost of \$523 per person for group treatment compared to \$1,357 per person for individual treatment. In contrast, the annual cost for pharmacotherapy was \$2,305 (Bieling, McCabe & Antony, 2009). In addition due to limited resources most treatment programs, especially those supported by public funds, are unable to make individual therapy routinely available to their patients. As compared to individual therapy, group therapy allows a larger number of patients to be treated by fewer clinicians on a given work day (Washton, 2011).

Aside from the obvious practical advantages of treating several patients at the same time, cost effectiveness and reducing waiting lists, there are some unique benefits to the group CBT format (Morrison, 2001). In comparison with individual cognitive behavioral therapy, cognitive behavioral groups have the opportunity to demonstrate the relationship between thoughts and feelings through the negative thoughts of the group members, and recognize the cognitive distortions of others, which could help the reattribution of their own cognitions (Bieling, McCabe & Antony, 2009).

According to Yalom and Leszcz (2005), the gathering together of people who share a common problem often creates a bond between them, stemming from a sense of mutual identification and an expectation of being intuitively understood. This is critically important in counteracting the intense feeling of isolation, alienation and shame that patients with panic disorder often experience.

More specific advantages of group treatment include reassurance by learning that others have similar problems, vicarious learning, learning through helping others, observing others' success thus reinforcing the patient to continue treatment,

committing to a group of peers to change oneself, the availability of multiple role play partners, and being challenged by peers counter distorted thinking (Heimberg & Becker, 2002). A main advantage in group treatment of panic disorder with agoraphobia is that the group provides the phobic stimulus that causes anxiety or panic attack which creates an in vivo exposure, thus providing a perfect opportunity to learn adaptive coping skills.

The advantages of group treatment would not be complete without mentioning those identified by Yalom in his book, "The Theory and Practice of Group Psychotherapy", a highly popular group psychotherapy text published in 1995. He identifies eleven primary therapeutic factors of group treatment: instillation of hope, universality, imparting information, altruism, the corrective recapitulation of the family group, development of social techniques, imitative behavior, interpersonal learning, group cohesiveness, catharsis (opportunity to express feelings) and existential factors (recognizing one's mortality, to learning to take responsibility for one's own life, no matter how much support others give).

Yalom, Tinklenberg, and Gilula (1968) were among the first to develop a method for assessing therapeutic factors. Twenty group therapy clients placed 60 therapeutic factor Q-sort items into categories ranging from "Least helpful to me in group" to "Most helpful to me in group." Using these categories, Yalom et al., (1968) derived a ranking of the relative client-perceived importance of therapeutic factors.

Specifically, the clients in Yalom et al.'s study ranked the factors from most to least important as follows: (1) interpersonal learning, (2) catharsis, (3) cohesiveness, (4) self-understanding, (5) existential factors, (6) universality, (7) instillation of hope, (8) altruism, (9) family re-enactment, (10) guidance and, (11) identification (Kivlighan & Holmes, 2004).

MacKenzie (1983) developed a questionnaire that was intended to assess the climate of a group. The Group Climate Questionnaire - Short Form (GCQ-S: MacKenzie, 1983) includes a subscale that measures the construct engagement. This subscale is thought to relate to Yalom's (2005) concept of group cohesion. A factor analysis of this questionnaire showed that engagement included both support (group cohesion as a precondition for change) and work (group cohesion as a therapeutic factor)

dimensions of the group. This instrument provides evidence that group cohesion serves in both of these capacities.

There have been many studies on therapeutic factors influencing the outcome of group psychotherapy (Bloch, & Crouch, 1986; Yalom, 1995). Which factors are more important for the therapeutic outcome may differ with various dimensions such as the therapeutic approach, the type of disorders, and so on.

Huh, Choi & Park (2003) aimed to identify which therapeutic factors have crucial influence on treatment outcome in group behavioral therapy with patients with panic disorder. They examined therapeutic factors of group behavioral therapy for panic disorder in 161 patients with panic disorder. After treatment, patients were assessed by Yalom's Curative Factor Questionnaire. The results showed patients with the greatest improvement from treatment rated significantly higher in guidance, group cohesiveness, altruism, identification, and family reenactment factors.

Choi and Park (2006) further investigated which therapeutic factors had the most positive influence on the outcome of cognitive behavioral group treatment for social phobia. Fifty patients with social phobia were asked to complete the Yalom's Curative Factors Questionnaire and Therapeutic Components Evaluation Form at the end of their Cognitive Behavioral Group Treatment (CBGT). Among the 12 therapeutic factors, existential factor, interpersonal learning-output, guidance, and self-understanding showed higher mean scores among all the patients. The patients who showed more improvement rated significantly higher in therapeutic factors such as interpersonal learning-output, guidance, universality and group cohesiveness.

García-Cabeza et al. (2011) also evaluated these therapeutic factors in five studies focused on patients diagnosed with severe mental disorder. All factors were measured with the Yalom Q-sort questionnaire that defines factors based on the value given by the patients. They found that the instillation of hope was most important in patients with severe mental disorders.

According to Yalom & Leszcz (2005), while some beneficial aspects of the group approach also apply to the individual paradigm (e.g., modeling), the phenomenon of social support, social pressure and vicarious learning remain unique to group intervention, thus lending support to the contention that group treatment is the more effective approach.

It seems that group therapy may also offer additional benefits that may not be found in individual therapy because of the unique interactional experiences that take place between those participating in the group. Yalom articulates these therapeutic factors in several sources (e.g., Yalom & Leszcz, 2005; Yalom, Cox & Vinogradov 2008), most notably group cohesion and universality, which collectively describe the connectedness group members experience with each other. These are perhaps the most important benefits of group therapy, being described by numerous authors (e.g., Leszcz & Kobos 2008).

Eidelson (1985) described several potential advantages of group versus individual CBT as follows:

First, group CBT encourages and offers opportunities for vicarious learning or learn from observing other members: members see other group members' attempts to challenge and restructure their thinking and consequently learn how to challenge their own thought processes. Modeling and observational learning can be very powerful and occur readily in groups. The members of group are often learning and may exhibit common traits after a few weeks together.

Second, group CBT provides greater resources or a diversity of viewpoints and maximum resources because all of the other group members that may be harnessed during the process of helping people develop new alternatives. In addition to the therapist(s), contribute to the process; members can draw on more points of view to help challenge their beliefs.

Third, the group format provides a form of strong feelings of belongings, trust, and social connection so that the tendency of the panic disordered person to withdraw from social interaction is offset; the interpersonal support and encouragement that often occurs in successful groups provides a safe environment where individual can share their innermost thoughts and ideas without the fear of being rejected or

ridiculed for them. Furthermore group provides a motivation for the group member to stimulate more interpersonal interactions outside the group setting.

Fourth, group CBT can allow beyond individual therapy in providing direct for more experiential disputation of irrational or dysfunctional beliefs; group members help one another to overcome such typical beliefs as: catastrophic thoughts about normal or anxious physical sensations, i.e., "If I have a panic attack in public I will go crazy and have to be committed." "My heart skipped a beat, I must be having a heart attack." In fact, in the group setting it is the norm that the members do contribute to one another's improvement; just by being there, each member expert when it comes to panic attack, the members are able to make suggestions that contribute to others' progress.

Fifth, one of the main principals behind group CBT is the feedback one gives oneself. Because it becomes obvious throughout the group that other members are distorting reality, members can identify when others in group are making these cognitive distortions, then they are probably doing likewise. Therefore, this factor provides an opportunity to develop a new perspective on oneself and her or his relationships with others.

Sixth, when group members help other group members to correct their distorted, negative thinking, all group members' gain practice rehearsing more positive or adaptive thoughts. In fact, group CBT provide an opportunity to demonstrate the relationship between thought and feelings. In addition, some group members become more aware of their own maladaptive thought patterns and become ready through group practice, to challenge their own beliefs.

Finally, in group CBT format some "loaded" issues such as compliance with homework assignments in psychotherapy, can be handled without engendering extreme defensiveness. It is often the case that more than one member is reporting difficulty with homework or some other problem. These issues can be treated as general problems that everyone can benefit from discussing. In this way, no one member feels singled out. Cognitive tools such as thought records can be used to help members understand and solve their problems.

1.4.2 Previous Research on effect of Group CBT in Panic Disorder

Otto et al., (1999) examined the efficacy of group CBT therapy for patients who fail to respond to pharmacotherapy for PD. They selected samples of patients who were refractory to an adequate dose of medication ('adequately-treated' nonresponders) and patients who had not responded to an inadequate dose of medications ('inadequately-treated' nonresponders). They examined outcome in response to group CBT. The adequately-treated sample consisted of 10 patients and the inadequately-treated sample consisted of 14 patients, CBT was provided in 12 sessions with group format. CBT for the adequately-treated patients resulted in significant decreases in both outcome measures. CGI-severity (clinician global impression of severity) scores decreased from a pretreatment mean of 4.7 to a week-12 score of 2.5. PDSS scores (Panic Disorder Severity Scale) decreased from a composite score mean of 2.1 to a mean of 1.1. Patients in the inadequately-treated sample also improved significantly with treatment. CGI-severity scores decreased from a mean of 5.0 at baseline to a mean of 2.8 at week 12 and PDSS scores decreased from a mean of 2.3 to a mean of 1.2. Forty-three percent of the sample had a CGI-severity score of 1 or 2 at week 12. Heldt et al., (2006) studied the impact of brief group CBT (GCBT) for PD on QoL (Quality of Life) and to identify the clinical features associated with these changes. In their study thirty-six patients with PD refractory to pharmacological treatment took part in a treatment protocol consisting of 12 sessions of GCBT. To evaluate the changes in QoL, the results showed significant improvement in all domains of QoL was observed, which was associated with reductions in general and anticipatory anxiety and agoraphobic avoidance. They concluded GCBT was efficacious in the treatment of PD.

Rufer et al., (2010) conducted a study designed to assess the association of different aspects of panic disorder with quality of life (QoL) and to examine the relationship between QoL and symptomatic outcome following brief group CBT (GCBT). The sample consisted of 55 outpatients with PD who underwent GCBT. QoL was assessed at baseline, posttreatment and six months follow-up. Baseline scores were compared with normative data obtained from a large population sample. They

concluded that treatment responders showed significantly better QoL than non-responders. PD symptom reduction following GCBT was associated with considerable improvement in emotional and physical aspects of QoL.

Rosenburg and Hougaard (2005) evaluated the effectiveness of group CBT for PD with agoraphobia in a clinical setting. The patients randomly divided to group CBT (GCBT) or waiting list group (WL). The applied treatment programme consisted of 14 weekly 1½-h sessions of group CBT with groups of six patients. The results showed, investigation group achieved better outcome on most analyses, (42.2%) found to be panic-free after treatment compared with 12.5% in the control group. Treatment gains were durable with 66.7% without panic attacks at follow-up at 1.5-2 years.

Galassi et al., (2007) studied about the efficacy of group treatment. Seventy-six PD patients were included in the study. The treatment consisted of 14 weekly 2-hr group sessions and included: (a) an educational component, (b) interoceptive exposure, (c) cognitive restructuring, (d) problem solving, and (e) in vivo exposure. The patients achieved significant treatment gains on all dimensions assessed with a high rate of panic remission and significant improvement in the associated symptoms. Furthermore, these gains were maintained at 6-months' follow-up. Notably, there was no control group in this study.

Dannon et al., (2004), evaluated the effectiveness of group CBT in the treatment of PD and to compare the treatment outcome of group CBT versus Paroxetine pharmacotherapy. Fifty seven PD patients were randomly allocated to receive either GCBT or Paroxetine. Follow up was done after four and twelve weeks of treatment in order to compare the efficacy of GCBT versus Paroxetine. Group CBT and Paroxetine were both effective in the short term treatment of PD. Assessments at weeks four and twelve of treatment showed no statistically significant differences between the two groups in terms of treatment outcome. Treatment with group CBT alone for the acute phase of PD appears to be equally efficacious to treatment with Paroxetine alone. Also the study showed that GCBT produced beneficial results, for it was associated

with a reduction in the number and frequency of panic attacks and with an improved feeling of well-being.

Erickson, Janeck & Tallman, (2007) in a study demonstrated that group CBT format is effective in various anxiety disorders, particularly panic disorder. In their study 152 patients were randomly assigned to receive 11-week group CBT or a wait-list control group. Follow-up was done after six months. The result showed reductions in anxiety scores for participants in the group CBT were greater than those for the control group participants. Patients with PD in particular appeared to benefit. Outcomes for the group CBT were superior in terms of clinically significant changes, defined as a 20% or 40% improvement. Reductions in anxiety scores continued to be present six months later.

In another study Lidren et al., (1994) compared bibliotherapy and group CBT in treatment of PD. Thirty-six patients were randomly assigned to 1 of 3 conditions group therapy, bibilotherapy or a waiting list control condition. Interventions lasted 8 weeks and were followed by a posttest, along with 3- and 6- month follow-up assessments. They found that both the bibliotherapy and group treatments were more effective than the waiting list condition in reducing frequency of panic attacks. Both interventions maintained their effects throughout the follow -up periods.

An extensive review on group psychotherapy format studies in panic disorder is presented below (Table 1.8).

Table 1.8: Overview group psychotherapy format studies in panic disorder

Lidren, Watkins Gould, Clum, Asterino, Tulloch (1994)	Participants	Thirty-six patients with PD
	Condition	A comparative study design to evaluate efficacy of GCBT versus bibliotherapy using a Self Help book (SH) in the treatment of PD. Patients randomly assigned to one of three conditions: (a) GCBT, (b) SH) and (c) WL, 8 session weekly/1/5 h.
	F/Up	3- and 6- month
	Outcome	GCBT= SH >WL
Otto, Mark, Pollack,	Participants	Twenty-four PD patients
	Condition	Assessed group CBT for patients failing to respond to pharmacotherapy. Subjects received 12 GCBT sessions. Two groups: (a) the patients inadequately treated that

Susan, Penava, Bonnie & Zucker (1999)		had been treated for a 2 month minimum with a dosage of medication and (b) patients who had not responded to an inadequate dose of medications.
	F/Up	Not reported
	Outcome	GCBT=PHMT
Dannon, Gon- Usishkin, Gelbert, Grunhaus (2004)	Participants	Fifty-seven PD/A patients
	Condition	A comparative study of the efficacy of GCBT versus drug treatment. The patients were randomly allocated to receive either GCBT or Paroxetine (PHMT).
	F/Up	4 week, 6 months
	Outcome	GCBT=PHMT
Rosenburg & Hougaard (2005)	Participants	Forty PD/A patients
	Condition	A longitudinal study designed to investigate the influence of group CBT for PD/A. The patients were randomly divided to group CBT or WL. Treatment program consisted of 14 weekly 1½-h sessions of group CBT with groups of six patients.
	F/Up	4 months 1.5 - 2 years
	Outcome	GCBT>WL
Heldt, Blava, Isolan, Kipper, Teruchkin, et al., (2006)	Participants	Thirty-six PD patients
	Condition	Examined effectiveness of Group CBT on QoL and identified the clinical features associated with these changes in patient's refractory to medication treatment. The treatment protocol consisted of 12 sessions of CBGT. Lack of control group.
	F/Up	Not reported
	Outcome	Significant improvement in all domains of QoL. Reductions in general and anticipatory anxiety and agoraphobic avoidance.
Galassi, Quercioli, Charismas, Niccolai & Barciulli (2007)	Participants	Seventy-eight PD/A patients
	Condition	A randomized, controlled trial to examine efficacy of GCBT for PDA. Consisted of six GCBT groups with 14 weekly 2-hour. Lack of a control group.
	F/Up	6-months
	Outcome	Significant improvement on all dimensions assessed (MIA, STAI, BDI, CGI) with a high rate of panic remission and significant in the associated symptoms.
Erickson, Janeck & Tallman (2007)	Participants	One hundred fifty two patients with anxiety disorders
	Condition	Assessed a GCBT format to treat patients who have different anxiety disorders in the same group. Patients were randomly assigned to treatment in the 11-week GCBT or to a wait-list control group (WL).
	F/Up	6 months
	Outcome	GCBT>WL
Rufer, et al., (2010)	Participants	Fifty-five PD patients
	Condition	A pretest post design to assess the changes in quality of life (QoL) following group CBT for PD. Nine groups

		were conducted; five to seven patients participated in each group, GCBT protocol consisted of five weekly sessions of 150 minutes each. Results of QoL in patients with PD compared to healthy subjects.
	F/Up	Six months
	Outcome	Emotional and physical aspects of QoL improved following CBGT. This improvement was associated with a decrease of PD symptoms.

Note*: GCBT: Group Cognitive Behavior Therapy; PCT: Panic Control Treatment; PHMT: Pharmacotherapy; SH: Self Help bibliotherapy; WL: Waiting List; FU: Follow-Up; BDI: Beck Depression Inventory; CGI: Clinical Global Impression Scale; PDSS: Panic Disorder Severity Symptoms; MIA: Mobility Inventory for Agoraphobia; STAI: State-Trait Anxiety Inventory; QOL: Quality Of Life.

In summary, these studies showed CBT delivered in group format effective in reducing PD symptomatology and catastrophic interpretations in PD. Group CBT and pharmacotherapy had comparable treatment efficacy. Both treatments had similar effects in reducing PD symptoms and were more efficacious than placebo and control group immediately after treatment and follow-up.

1.4.3 Individual Therapy versus Group Therapy

A review of the literature has shown that many studies have been done comparing individual therapy versus group therapy for subjects such as therapeutic factors, process variables, depression, social phobia and OCD, eating disorder, obesity, childhood aggression or other problems, sexually abused women, borderline personality disorder. There is a gap in the literature comparing treatment of panic disorder in an individual therapy modality versus group therapy modality. Only a few studies have examined whether individual and group treatments are equally effective in the treatment of panic disorder (Sharp, Power & Swanson, 2004; Neron, Sylvain, Lacroix, Denis, Chaput & Yves, 1995).

The question whether individual and group treatments are equally effective is important for several reasons, the foremost perhaps being economical. If group therapies are as effective as individual therapies, this could decrease the costs of treatment substantially, since group therapy is considerably less expensive than individual therapy (Vos et al., 2005).

From a clinical and scientific perspective, if these treatments are equally effective, this suggests that the presence of other patients during the treatment does not hinder the treatment of the individual patient. On the other hand, it may also be possible that the treatments result in comparable effects but through different mechanisms (Yalom & Leszcz 2005). For example, in individual treatment the relationship between client and therapist may be stronger, while in group therapy other mechanisms, such as cohesion and social support play the greater role (Yalom & Leszcz 2005). If individual and group treatments are not equally effective, this would suggest that one is not as good as the other in teaching the patient techniques that help reduce panic disorder. Or it could be possible that group processes interfere with the therapeutic process (Yalom & Leszcz 2005). But before these questions can be answered, it first has to be known whether group and individual treatments are indeed equally effective.

There has been a gradual accumulation of research comparing group to individual treatments over the past five decades, and what has been shown is that there are no significant differences between the two treatments format (McRoberts et al, 1998). Research has also shown there are different therapeutic processes in the two modalities (Holmes & Kivlighan, 2000). At the same time however, little is understood about the similarities or difference between the processes in these two treatment modalities (McRoberts et al., 1998), and few studies have examined them (Holmes & Kivlighan, 2000).

Outcomes of empirical studies comparing the effectiveness of individual and group therapy interventions demonstrate that both treatment modalities according to various theoretical orientations are substantially more effective than no treatment or minimal treatments for a variety of psychological disorders and problems (Bednar & Kaul, 1994; Fuhriman & Burlingame, 1994).

Burlingame, MacKenzie, & Strauss (2004), examined 107 studies and 14 meta-analyses published between 1990 and 2002 across six disorders: mood disorder, anxiety, eating disorder, substance abuse, personality disorder and psychosis. They reported that there was adequate evidence to conclude that group therapy is as effective as individual therapy either as the primary treatment or as a part of a

treatment program.

Toseland & Siporin (1986), conducted a meta-analysis of 74 empirical studies which participants were randomly allocated to receive individual or group treatment (for various diagnosis). The same modality and technique were used with all subjects in both the group and individual formats. The results obtained in 75% of the studies two treatment format were equally effective and in 25% of studies group therapy was more effective than individual therapy.

In a meta-analysis of 700 group therapy studies, Fuhriman and Burlingame (1994), concluded that group psychotherapy is as effective as individual therapy in treating a range of psychological problems and across treatment models.

McRoberts et al (1998) conducted a meta-analysis of 23 empirical studies which individual and group therapies were compared directly. Results of this review demonstrated that no treatment outcome differences were found for group versus individual therapy formats; a finding that supports earlier reviews (Berman, & Niemeier, 1990; Tillitski, 1990).

Other meta-analytic studies demonstrate group therapy's effectiveness with a variety of populations in different treatment settings (e.g., Burlingame, et al., 2003; Kösters, Burlingame, Nachtigall, & Strauss, 2006; McDermut, et al., 2001; Payne & Marcus, 2008). These studies implicate that mode of therapy does not appear to affect outcome, with individual and group therapy demonstrating comparable effectiveness (McRoberts et al., 1998). This finding holds true across a number of variables, including "the chronicity of the disorder, gender, or age of the client" (McRoberts et al, 1998, p. 108). Additionally, no significant differences in effectiveness have been observed between theoretical orientations or treatment settings when comparing individual and group therapy (McRoberts et al., 1998). Individuals who participate in group therapy are better off than those on wait lists, with 72-85% of participants demonstrating treatment gains (Burlingame et al., 2003; McDermut et al., 2001).

A conclusion based on Morrison's review (2001), and Petrocelli's meta-analysis

(2002), showed that for the most part there was little difference in results between CBGT and individual CBT treatment studies.

The research shows, although group therapy may be a viable and cost-effective alternative to traditional individual therapy services, nevertheless, what has been shown is that most patients have a strong preference for individual over group treatment (Cuijpers, van Straten & Warmerdam, 2008). Additionally most of the treatment experiences of mental health professionals, about 80%, tend to be in individual therapy, with other modalities being significantly underutilized (Norcross et al., 1988). For example, the numbers of psychotherapists using group therapy as a form of personal therapy are significantly lower than those engaging in individual therapy (Guy et al., 1988). Group therapy is only undertaken by about 4% to 30% of professionals (Norcross et al., 1988).

However, these authors also assert that in some situations individual therapy might represent the more effective treatment setting. For instance, a client may feel more comfortable discussing emotional topics with an individual therapist. This may be especially true when the client is shy, or dislikes talking in front of many people. The individual format may also facilitate discussions related to more intimate issues that may be serving as impediments to treatment progress (Cuijpers, van Straten & Warmerdam, 2008).

Lazarus (1971) proposed that individual treatment may lead clients to experience a greater feeling of involvement, higher motivation, and better adherence. Findings by Subich and Coursal (1985), support these assertions. These authors found that compared to subjects assigned to group therapy, clients in individual treatment expected to be both more open and responsible in therapy. But on the other side, group therapy may also offer additional benefits that may not be found in individual therapy because of the unique interactional experiences that take place between those participating in the group. As compared with individual therapy, in group therapy participants can learn effective social skills and try out new styles of relating with other members of the group (Corey, 2008). In addition, the phenomenon of social support, social pressure and vicarious learning remain unique to a group intervention. As already mentioned Yalom articulates therapeutic factors in several

sources (e.g., Yalom & Leszcz, 2005; Yalom, Cox & Vinogradov 2008), most notably group cohesion and universality, which collectively describe the connectedness group members experience with each other. These are perhaps the most important benefits of group therapy, being described by numerous authors. While some beneficial aspects of the group approach also apply to the individual paradigm (e.g., modeling), the phenomenon of social support, social pressure and vicarious learning remain unique to a group intervention. The added benefits of these variables seem to lend support to the contention that group treatment is an effective approach (Yalom & Leszcz, 2005).

1.4.4 Previous Research on Individual Therapy versus Group Therapy in Panic Disorder

There are a few studies which have evaluated the efficacy of group versus individual therapy in treatment of panic disorder:

Néron, Lacroix and Chaput (1995), compared the efficacy of group CBT versus individual cognitive behavior therapy in the treatment of PD and PDA. Twenty patients with PD or PDA were randomly assigned to group CBT (GCBT) or individual CBT (ICBT) with weekly sessions for 12 or 14 weeks. Sessions (GCBT= 2 hours, ICBT=1 hour) were administered weekly for 12 (GCBT) or 14 weeks (ICBT). In addition GCBT patients were given two individual one hour sessions during their 12-week treatment. The CBT protocol was identical for both treatment modalities.

The results showed that both treatment formats significantly reduced panic frequency at treatment end. However, a differential effect favoring individual CBT (ICBT) over group CBT (GCBT) was observed at the end of the follow-up phase with regards to generalized anxiety symptoms.

Sharp & colleagues (2004) studied the efficacy of group CBT versus individual cognitive behavior therapy in the treatment of PD and PDA. Ninety-Seven PD or PDA was randomly assigned to group CBT (GCBT), individual CBT (ICBT) or waiting List control group. Treatment consisted of 1-hour sessions held once a week for 8 weeks. All patients were seen by the same therapist and all received an identical

treatment manual. Meanwhile, all participants took either anxiolytic or antidepressant medication or a combination of both or were required to continue taking these medications as prescribed throughout the study period. They found that both group and individual CBT were superior to a wait list control group in reduction of anxiety and depression symptoms and agoraphobic avoidance but did not differ significantly from each other. However individual CBT was associated with greater clinical significance (i.e., outcome score at least two standard deviations below the pre-treatment mean for the entire sample), than either group CBT or wait-list control immediately following termination of treatment. However, this advantage for individual treatment was not detectable at 3-month follow-up.

Marchand, et al., (2009) conducted a randomized controlled clinical trial with a wait-list control group to examine the effectiveness of three modalities (brief, group, and standard) of cognitive-behavioral treatment (CBT) for PDA. 100 patients were randomly assigned to each treatment condition: a 14-session individual CBT (n=33), a 14-session group CBT (n=35) and a 7-session brief CBT (n=32). Participants received a self-study manual and were assigned weekly readings and exercises. The results indicated that all three-treatment conditions significantly reduced the intensity of symptoms, increased participants' quality of life, offered high effect sizes, superior maintenance of gains over time, and lower rates of relapse, compared to the wait-list control.

An extensive review on group versus individual psychotherapy format studies in panic disorder is presented below (Table 1.9).

Table 1.9: Overview of group versus individual psychotherapy format in panic disorder

Neron, Lacroix, Chaput (1995)	Participants	twenty patients with PD/A
	Condition	A pretest-posttest comparison group design to evaluate effect of group vs individual CBT. The subjects randomly received either (a) GCBT, (b) ICBT. All patients were seen by the same therapist and all received an identical treatment manual. Sessions GCBT: 12 weekly sessions, 2 hours, ICBT=14 weekly session 1 hour.
	F/Up	3-6 months
	Outcome	GCBT=ICBT in reduction of HAMD, ZDI

		ICBT>GCBT in reduction of BAI, HAMA
Sharp, Power & Swanson (2004)	Participants	Ninty-seven patients PD/ A
	Condition	A comparative study design evaluating efficacy of group versus individual CBT. The participants were randomly allocated to receive (a) GCBT, (b) ICBT, and (c) WL. 8 sessions 1hour. All patients were seen by the same therapist and all received an identical treatment manual.
	F/Up	3 months
	Outcome	GCBT and ICBT=WL in reduction of SRT GCBT = ICBT in reduction of HAMA, MADRS & FQ
Marchand, Roberge, Primiano & Germain (2009)	Participants	One hundred patients PD/ A
	Condition	A long-term clinical outcome study of standard, group and brief CBT for PDA: The participants were randomly allocated to receive (a) 14 session GCBT, (b) 14 sessions ICBT, and (c) 7 sessions brief CBT or (d) WL.
	F/Up	Two year
	Outcome	GCBT, ICBT and BCBT >WL GCBT = ICBT

Note*: BCBT: Brief Cognitive Behavior Therapy; GCBT: Group Cognitive Behavior Therapy; ICBT: Individual Cognitive Behavior Therapy; WL: Waiting List group; BAI: Beck Anxiety Inventory; FQ: Fear Questionnaire; HAMA: Hamilton Anxiety Scale; HAMD: Hamilton Depression Scale; MADRS: Montgomery-Asberg Depression Scale; SRT: Symptom Rating Test; ZDI: Zung Depression Inventory.

In summary, each of these studies found CBT delivered in group format as comparable to those of individual CBT in reducing PD symptomatology and treating PD immediately after treatment and at follow-up. Group therapy is a feasible arrangement and can provide a cost-effective alternative to individual therapy, as the studies by Sharp et al (2004) and Marchand et al (2009) showed.

1.5 Aim of the Study

The primary goals of this research is (a) to evaluate the effectiveness of an fourteen week program of Cognitive Behavioral therapy in two format of group and individual therapy in reducing the cognitive, affective and panic disorder severity, (b) comparison of efficacy of group versus individual CBT in treatment of panic disorder. Therefore, the results of this study provide additional support, along with new insight, to the field of panic disorder and agoraphobia.

Panic disorder with or without agoraphobia is a prevalent clinical disorder which places heavy demands on treatment resources in primary care (Power, Sharp, Swanson, Simpson, 2000). Patients with panic disorder suffer from recurrent panic attacks, anticipatory anxiety, abnormal sensitivity to anxiety and a wide range of alarming symptoms accompanied by catastrophic cognitions, considerable impairment in functioning and depression (Coryell, Pine, Fyer & Klein 2006; Perna, et al. 2004; van Beek &, Griez, 2000). Since people with panic disorder focus increasing attention toward monitoring their body and the outside world for sign of panic, they often develop deficits in multiple life domains. Work, social relationship and quality of life are all negatively affected (Telch et al., 1995).

Clinical evidence suggests that CBT is an effective treatment for PD/A. In particular CBT leads to reductions in anxiety symptoms, anxious cognition, agoraphobic avoidance, and depressive symptoms (Barlow, 2011; Deacon and Abramowitz, 2004; Teachman et al., 2010; Wenzel et al., 2006). There is evidence of Group-based CBT studies that shows the positive effects in reduction of anticipatory anxiety, secondary depression, number and severity of panic attacks and dysfunctional cognitions in PD (Sharp, Power, Swanson, 2004; Marchand et al., 2009; Rufer, Albercht, Schmidt et al, 2010; Rosenburg & Hougaard; 2005., Dannon et al., 2004. To the best of my knowledge there are few reported studies comparing individual versus group therapy in patients with PD. Although, as mentioned previously, Sharp et al., 2004 and Neron et al., (1995) revealed individual and group CBT were equally in reduction of depression in patients with panic disorder in post intervention and

follow-up. But on the other side, Neron et al., (1995) study showed that individual CBT was superior to group CBT in reduction of overall anxiety in patients with panic disorder in post intervention and a six month follow-up, while the study by Sharp et al., (2004) indicated that two treatment format did not differ significantly from each other in reduction of overall anxiety and other panic symptoms after treatment. It must be noted that in both studies all participants took either anxiolytic or anti-depressant medication or combination of both, which may have obscured group differences. In contrast, the present study excluded individuals on psychotropic medication including benzodiazepine or concurrent psychotropic medications, from participation. In addition the current study will measured more specific symptoms related to PD compared with study by Neron et al., and Sharp et al., that a few dependent variables were measured in their study. Hence this study is an attempt to examine and compare the effectiveness of two formats: cognitive behavioral group therapy and individual cognitive behavior therapy without combination with pharmacotherapy in the treatment of panic disorder after 14 sessions of CBT and a 4-month follow-up. This study is a response to changes in format policy in treating panic disorder that have occurred in recent years. It also serves as a prototype intervention for future policy direction. By evaluating the effectiveness of GCBT and ICBT to treat panic disorder this current study offers a model for replication in future interventions not only for panic disorder but other anxiety disorders as well. In addition this treatments format offers a cost-effective intervention which will reduce costs, save money, and thereby allow the allocation of financial resources to address other pressing health concerns.

1.6 Hypotheses and Research questions

1.6.1 Hypotheses

Based on previous empirical studies (Neron et al., 1995; Sharp et al., 2004 & Marchand et al., 2009) that found that was no significant difference between individual and group formats in reduction of some panic symptoms. Therefore, it is expected no differences in effectiveness of CBT for panic disorder with or without agoraphobia delivered in either the individual or group treatment formats. The following hypotheses were formulated:

The following hypotheses were formulated:

Ha 1: Group therapy is affective as individual therapy in reduction of overall negative affect (Depression and Anxiety)

Ha 2: Group therapy is affective as individual therapy in reduction of catastrophizing cognition (agoraphobic cognition and anxiety sensitivity)

Ha 3: Group therapy is affective as individual therapy in reduction of agoraphobic avoidance and panic disorder severity

Ha 4: Greater improvement of group therapy and Individual CBT compared to Wait-list group.

Ha 5: Therapeutic outcomes in group CBT and individual CBT at post-test will be maintained at four months follow-up.

1.6.2 Research Questions

- a) Is there any difference between the outcomes of individual CBT, group CBT groups and waiting list control group in terms of severity of panic attack, anxiety, depression, agoraphobic cognition, anxiety sensitivity, and agoraphobic avoidance at post -treatment?
- b) What are the differences between Individual CBT and Group CBT groups regarding their effects on different panic disorder criterion post-treatment?
- c) What are the differences between Individual CBT and Group CBT in terms of severity of symptoms over the follow-up period (4 month post-treatment)?

Chapter II - Methodology

2.1 Design and procedure

2.1.1 Participants

Participants in this study were 45 outpatients (25 men and 20 women) with a DSM_IV diagnosis of panic disorder with or without agoraphobia. Participants in this study were between the ages of 18 and 65 years old who were residents of the Bandarabbas city, in Iran and applied for treatment of panic disorder. Participants were referred from local emergency room physicians, mental health clinics and private psychiatric offices. The study has been conducted in Ebne-Sina's psychiatric government clinic and five offices in Bandarabbas city.

Of those accepted into the study, four patients had entered treatment but had failed to complete the trial. Four people failed to show up for the first session and could not be reached by phone, and one became ineligible after beginning antidepressants after session 5 of the group cognitive behavior therapy.

The confidentiality of participants was protected by storing all data based on an assigned number rather than the name or other identifying information. The participant was made aware that involvement in the study was voluntary and withdrawal from the study at any time was acceptable without repercussions.

To be included in the study, the participants had to meet the following criteria:

- The participant must be between 18- 65 years old, and either male or female.
- The participants must give informed consent.
- The participant must fulfill DSM-IV criteria for panic disorder with or without agoraphobia
- The participant must have suffered panic disorder for at least 1 month
- The participant must have panic disorder as the primary problem

Individuals were excluded from participation for any of the following reasons:

- 1) A lifetime diagnosis of psychosis, bipolar disorder, organic mental disorder or other psychiatric disorder and current diagnosis of substance abuse or

dependence, a current co-principal diagnosis of a depressive disorder, or any medical condition that might compromise their health or influence their abilities to benefit from the protocol. Such medical conditions included: cardiovascular (heart or circulation) condition, respiratory disease, (such as asthma), seizure disorders, diabetes, hypertension, hyperthyroid, head injury or surgeries, and evidence of organic brain syndrome or mental retardation.

- 2) Psychotropic medication (for a psychiatric or psychological condition) including benzodiazepine.
- 3) A history of previous same treatments.
- 4) The unwillingness or inability to give informed consent.

The inclusion and exclusion criteria were reviewed with each participant prior to his or her enrollment and 8 people were excluded after the initial screening based on the excluding criteria.

The flowchart of participants in the study is presented in Figure 2.1:

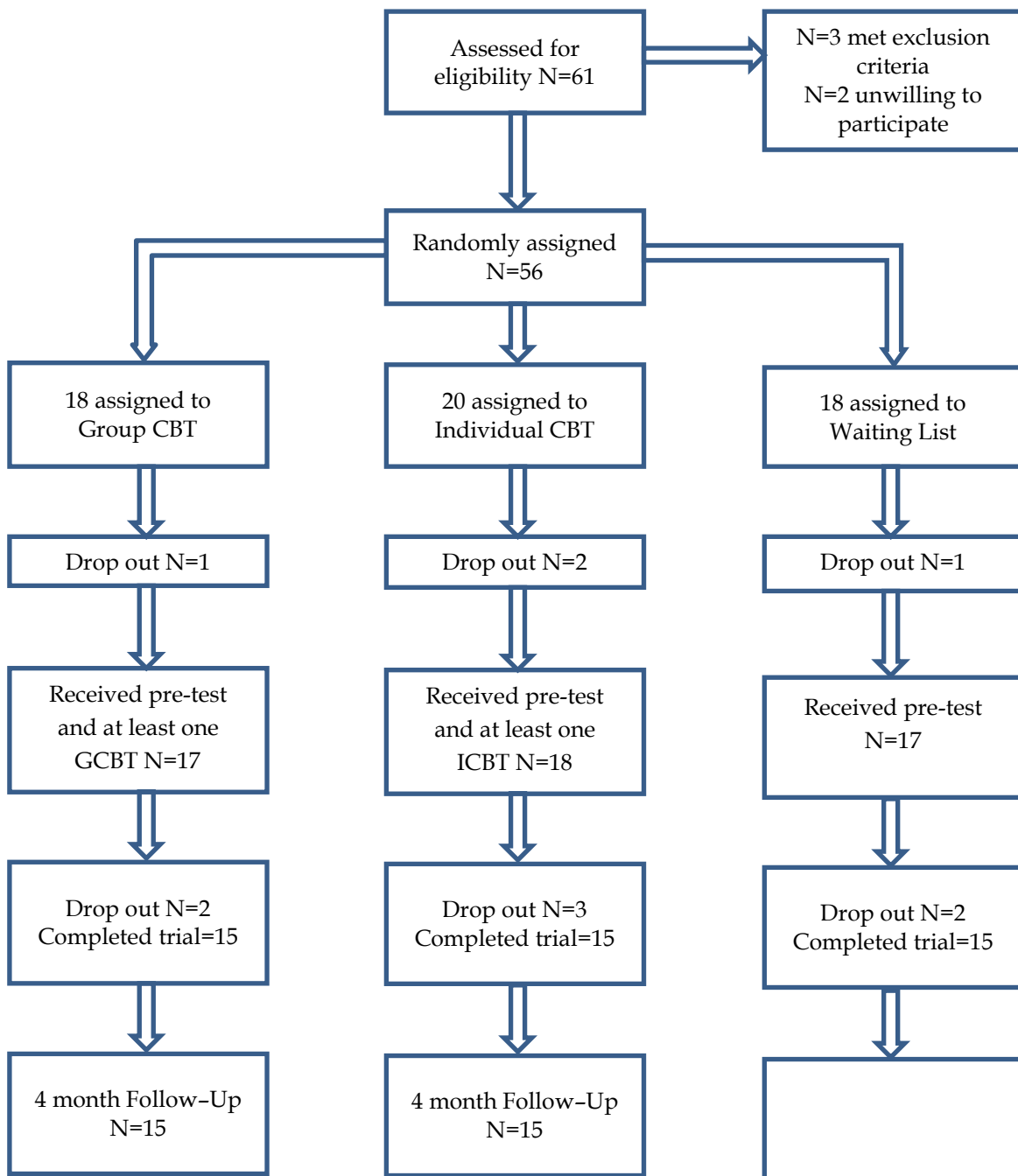


Figure 2.1: Flowchart of study participants, point of random assignment and dropouts

2.1.2 Study Design and Procedure

This study uses a Quasi-experimental design with a non-equivalent control group design with pre-post post-test samples. This design is used whenever the true experimental design is not feasible and availability permits subject's selection.

Prior to entering the study, all prospective participants were privately interviewed by the primary investigator of the study who administered the general overview and panic disorder section of the Structured Clinical Interview for DSM-IV Disorders (SCID) (Spitzer et al., 1997). A demographic questionnaire was also used to obtain relevant information pertaining to their panic history and other medical history.

At the first encounter participants were told that the purpose of the study was to test the efficacy of a non-medication treatment for panic disorder. If they were interested to partake they would be randomly placed into one of two treatment groups or waiting list group.

The prospective participants were told that participation was voluntary and that they could withdraw at any time. The time commitment for the study was also explained. If the participant was interested, an appointment was then scheduled for the participant to be seen by the primary investigator of the study.

Eligible candidates were randomly assigned to three groups: Group Cognitive-Behavioral Therapy (N=15), Individual Cognitive-Behavioral Therapy (N=15) or a waiting -list group (as control group) (N=15).

In the two treatment conditions (Group CBT and Individual CBT), patients met with a therapist and received 14 weekly sessions of treatment.

Control group participants were regularly checked once a week to make sure that none of them had received any kind of psychological, psychiatric or counseling intervention.

Treatment effectiveness of individual and group CBT was compared with each other and the untreated wait-list control group with a pretest post-test design on the same measures. Follow-up testing to evaluate long term benefit was conducted at 4 month post treatment. It was carried out by both a telephone call and a letter that was

mailed to all participants following the completion of the study. It is diagrammed as below:

	N		Treatments week		FU 4 months
QI	15	Assessment pre	14 week group CBT	Assessment post	Telephone and E-mail
QII	15	Assessment pre	14 week individual CBT	Assessment post	Telephone and E-mail
QIII	15	Assessment pre	TAU	Assessment post	-

There is one independent variable, the treatment condition (Group CBT, Individual CBT, and wait-list control) and two measurement occasions (pre-treatment, post-treatment) with an additional follow-up, or in other words, a 3 (group) × 2 assessment phase (pre, post assessment) and a 2 (group) × 3 (pre, post and follow-up assessment phase) design. The dependent variables are panic disorder severity score, frequency of catastrophic cognitions score, anxiety sensitivity score, avoidance of situation related to fear score, anxiety score and depression score. Additional information including age, gender, marital status, occupational status, level of education, age of onset and duration of illness were also collected as descriptive independent variables.

2.1.3 Treatment Protocol

Individual CBT group (ICBT) received a maximum of fourteen, one hour sessions and group CBT (GCBT) received a maximum of fourteen, 1.5 hour sessions and Waiting List group (WL) waited 3 months, and then also received a maximum of fourteen, one hour sessions of ICBT.

The therapy was conceptualized as a program of individual and group therapy based upon Cognitive-Behavioral therapy. The treatment package included:

- (a) education about the nature and causes of panic,
- (b) self-monitoring and awareness of cues,
- (c) identification of different response components, understanding the physiology of panic and learning physical control such as breathing retraining or progressive muscle relaxation training (PMR),
- (d) self statement analysis and cognitive restructuring,
- (e) prediction testing,
- (f) interoceptive and naturalistic exposure to feared physical sensations, and
- (g) how to maintain progress.

The present study followed Barlow's treatment protocol. The treatment program completed 1 session per week and consisted of 14 one hour sessions of individual and group cognitive behavioral therapy. The patients in both individual and group formats were seen by the same therapist and all received an identical treatment manual. The main treatment components during each of the fourteen sessions are listed below:

Session 1:

1. Introduction
2. Psychoeducation (fear and anxiety and causes, physiological aspects of anxiety and symptoms of panic attacks, review of the function of the central nervous system and profile of a person with panic disorder).
3. Brief description of the treatment program (cognitive techniques, relaxation, exposure therapy, retraining breathing).

4. Treatment schedule (once a week for the next 14 weeks).
5. Distribution of Weekly Record sheet. The weekly sheet contains of record of Panic Situation, Physical symptoms Situation, Physical symptoms, Emotion/s, (Rate intensity of emotion (0-100%)), Unhelpful Thoughts or Images, (Rate intensity of belief (0-100%)) Response to Thought, (Rate of intensity believe to this different perspective 0-100%) Outcome: Describe of emotion, (Re-rate intensity of emotion 0-100%).

Session 2:

1. Review weekly record.
2. Introduce cognitive restructuring (automatic thoughts and techniques for monitoring cognitions).
3. Introduce progressive muscle relaxation (PMR) exercise – 16 muscle groups.

Session 3:

1. Review weekly record.
2. Explore alternative explanations for cognitive self-statements.
3. PMR (16 muscle groups) with discrimination training.

Session 4:

1. Review weekly record.
2. Identify logical errors in thinking and introduce analysis of faulty logic (Evidence, Overgeneralizing, Certainties versus Possibilities, All-or-Nothing Thinking, and Absolutistic Thinking).
3. PMR (8 muscle groups) with discrimination training.

Session 5:

1. Review weekly records and discuss progress/problems.
2. Repetition of PMR (8-muscle groups).
3. Presentation of didactic instructions on:
 - a) Decatastrophizing
 - b) Rescue factors
 - c) Reattribution

d) Hypothesis testing

Session 6:

1. Review weekly records.
2. Introduce PMR (4 muscle groups) procedures.
3. Present the rationale for exposure therapy.
4. Develop of an exposure hierarchy.
5. Begin imaginary practice for covert rehearsal and application of cognitive strategies during graded visualization of anxiety.

Session 7:

1. Review weekly records.
2. Repetition of PMR (4 muscle-groups).
3. Introduction and rationale of breathing exercise: hyperventilation example and training of diaphragmatic breathing.
4. Imaginal exposure and panic symptom induction; breathing retraining.
5. Hypothesis testing and cognitive coping strategy practice (assigns a behavioral experiment in a low-level anxiety-provoking situation and use self - instruction to manage the situation).

Session 8:

1. Review weekly records.
2. Imaginal exposure and self-exposure homework (assign a behavioral experiment in a low-level anxiety-provoking situation and use self - instruction to manage the situation).
3. Introduce 4-muscle group procedure with recall relaxation.
4. Hypothesis testing, thought stopping and diversionary techniques for anxiety management.

Session 9:

1. Review weekly records.
2. Relaxation by recall (attention to breathing and vocalizing "relax" with exhalations and released the tension from particular muscle group).

3. Continue imaginal exposure and self-exposure practice (spend approximately 30 minutes practicing visualizing moderate-anxiety items with the client).
4. Hypothesis testing and cognitive management practice.

Session 10:

1. Review weekly records.
2. Imaginal exposure and self-exposure practice (spend approximately 30 minutes practicing the visualization procedures with items from the anxiety hierarchy).
3. Introduce and practice cue-controlled relaxation (Attention to breathing, then take a deep breath and think the word “relax” with exhalation).
4. Hypothesis testing and cognitive management practice (application of cognitive coping strategies and cue- controlled relaxation during exercise).

Session 11:

1. Review weekly records.
2. Imaginal exposure and self-exposure homework (with high anxiety hierarchy items).
3. Repetition of cue- controlled relaxation.
4. Hypothesis testing and cognitive management practice.

Session 12:

1. Review weekly records.
2. Imaginal exposure and self-exposure homework (with high anxiety hierarchy items).
3. Hypothesis testing and cognitive management practice.

Session 13:

1. Review the weekly record and treatment progress.
2. Begin generalization practice to help the client generalize coping strategies to a great variety of life situations and integrate the cognitive coping strategies with the in vivo exposure treatments.
3. Encourage the client to verbalize his/her understanding of the importance of

practice in various situations.

Session 14:

1. Review the weekly record and the client's progress in the previous weeks.
2. Continue generalization practice and relapse prophylaxis issues (practicing what client has learned in confrontation with new situations).
3. Briefly review the cognitive procedures and rationales used during this treatment program, focusing most on those procedures that have been most useful to the client. Include comments on the following:
 - The three response model of anxiety and the role of "false alarms" in panic symptoms
 - The importance of using coping procedures to facilitate continuing exposure to fearsome situations
 - Relaxation procedures (16 muscle groups, 8 muscle groups, 4 muscle groups, Discrimination training, Recall relaxation, Cue-controlled relaxation)
 - Diaphragmatic breathing
 - Automatic thinking
 - Analysis of faulty logic
 - Decatastrophizing
 - Exploring alternatives
 - Reattribution
 - Rescue factors
 - Hypothesis testing
 - Self-statements
4. Schedule the post-treatment assessments.

2.2 Measures

1. **Demographic questionnaire:** The demographic questionnaire was used in this study to obtain information about personal characteristics of participants, including age, gender, marital status, occupational status and education level. In addition, the patient's history of panic disorder including number of months or years of the disorder and panic attack frequency including how many panic attacks the person has per week were also requested.
2. **Panic Disorder Severity Scale (PDSS)** (Shear et al., 2001): The PDSS was administered to assess severity of diagnosis in participants. The Panic Disorder Severity Scale (Shear et al., 2001b) is a brief, clinician-rated, 7-item scale that assesses seven specific dimensions that comprise the key features of PDA, which are rated on a 4 point scale (0, none;4, extreme). The seven items include frequency of panic, anxiety focused on future panic, distress during panic, interoceptive avoidance, situational avoidance, interference in social functioning, and interference in work functioning. The PDSS was found to have excellent interrater reliability ($\kappa = .87$). It has fair internal consistency, with a Cronbach's alpha of .65, in view of the fact that the key features of PDA vary considerably from patient to patient. The total score on the PDSS was significantly correlated with the clinical severity ratings for PD on the ADIS-IV ($r = .55$; Shear et al., 1997). This measure has demonstrated both convergent and discriminant validity with other panic and anxiety assessment tools (Shear, Masser, 1994). Shear, et al., (2001b) evaluated the internal consistency of PDSS in 198 patients according to DSM-III-R panic disorder. The internal consistency yielded a Cronbach's alpha of 0.64. Joint reliability ranged from 0.84 to 0.88 for trained raters. The validity of PDSS total score showed moderate correlations with both panic disorder severity ratings of the Anxiety Disorders Interview Schedule – Revised (ADIS-R) ($r = 0.54$) (DiNardo & Barlow, 1988) and severity ratings of the Clinical Global Impression (CGI) Scale ($r = 0.66$). Individual PDSS item scores were strongly associated ($r = 0.60-0.78$) with ADIS-R items of similar content and less strongly associated ($r = 0.35-0.47$) with CGI Scale and ADIS-R severity

ratings. The PDSS items most highly correlated with similar ADIS-R items were panic frequency ($r = 0.71$), anticipatory anxiety ($r = 0.78$), agoraphobic fear and avoidance ($r = 0.73$), and sensation fear and avoidance ($r = 0.69$). The PDSS has proved to be sensitive to change with treatment.

- 3. The Beck Anxiety Inventory (BAI)** (Beck et al., 1988): The BAI was administered to assess general anxiety symptoms in participants. The BAI is a standard 21 item measure of emotional and somatic symptoms and has scores from 0 to 63 (Beck et al., 1988b). Participants are asked to assess their level of intensity on a four-point scale (not at all, mildly, moderately, and severely) during the past week for each of the symptoms. The BAI is considered to have high internal consistency. The BAI holds high internal consistency ($\alpha=.92$) and test retest reliability over one week ($r=.75$). These data indicate that the BAI is highly effective for determining the presence of anxiety disorders (Fydrich, Dowdall & Chambless, 1992). In Iran, Kaviani & Mousavi (2008) investigated anxiety levels in clinical and non-clinical populations. They examined the validity and reliability of the BAI in the Iranian normal population as well as in clinically anxious patients. In their study 1,513 non-clinical respondents were randomly recruited and completed the Beck Anxiety Inventory (BAI). Of this population, 112 respondents were randomly selected and re-tested in order to measure test-retest reliability with a one-month interval time between first and second tests. Furthermore, 261 clinically anxious patients were tested. In order to measure validity, 150 patients were interviewed. Results showed that the Persian version of the BAI had a good reliability ($r=0.72$, $p<0.001$), a very good validity ($r=0.83$, $p<0.001$), and an excellent internal consistency ($\text{Alpha}=0.92$). Steer, Ranieri, Beck & Clark (1993) provided further information about the psychometric characteristics of the Beck Anxiety Inventory (BAI). The BAI was administered to 470 outpatients with mixed psychiatric disorders along with the revised Beck Depression Inventory (BDI) and the SCL-90-R. The BAI's internal consistency was high ($\text{alpha}=.92$). The BAI was significantly correlated with the SCL-90-R Anxiety subscale ($r=.81$) and less with the SCL-90-R Depression subscale ($r=.62$) and the BDI ($r=.61$). The mean BAI scores of the 141 (30.0%) outpatients with mood disorders and the 86 (18.3%)

outpatients with anxiety disorders were comparable, but higher than the mean BAI score of the 243 (51.7%) outpatients with other disorders. Fydrich, Dowdall & Chambless (1992) and Hoyer et al., (2002) carried out further psychometric research. In these two studies the test-retest reliability and internal consistency of the scale were examined with a sample of 40 outpatients having anxiety disorders. The BAI proved highly internally consistent (cronbach's alpha=.94) and acceptably reliable over an average time lapse of 11 days ($r=.67$).

4. Fear Questionnaire-Agoraphobia subscale (FQ-AG) (Marks & Mathew, 1979):

This test was administered to assess avoidance of situations related to agoraphobia and social phobia in participants. The FQ (Marks & Mathew, 1979) is a standard measure of fear and avoidance. The FQ contains three item subscales: Agoraphobia, Blood Injury, and Social phobia. Marks & Mathew (1979), reported good psychometric properties for each subscale. Scores of 12 on each subscale are considered subclinical. The total score on this measure can range between zero and 100. The test-retest reliability is reported to be $r = .89$. Cox, Swinson & Shaw, (1991) examined the usefulness of the FQ in differentiating and social phobia in 68 patients suffering from PDA, 50 social phobics, 75 subjects with 'non-clinical' panic attacks and 188 non-panicking controls. The FQ agoraphobia and social subscales had satisfactory internal consistency and were accurate (82%) in correctly differentiating the patients. The highest level of social fear was reported by social phobics and the highest level of agoraphobic fear was reported by patients with panic disorder and agoraphobia. Five items from these two subscales significantly differentiated social phobia from panic disorder with agoraphobia. The results support the reliability and validity of the FQ.

5. Beck Depression Inventory Second Edition (BDI-II) (Beck, Steer, & Brown,

1996): The BDI was administered to assess depressive symptoms in participants. The BDI is a widely used self-report method for assessing depressive symptomatology. It consists of 21 self-report questions with four possible responses for each. Each item is a list of four statements arranged in increasing severity about a particular symptom of depression. According to Kendall and

Watson (1989) the internal consistency of the BDI has an averaged of $\alpha = .86$ across numerous studies. Test-retest reliability for one to three months is $r = .74$ and the scale has an internal consistency between $\alpha = .76$ to $.95$ (Riskind, Steer, Beck, & Brown, 1987). Kühner et al., (2007), examined the content validity of the BDI-II that has improved by meeting DSM-IV symptom criteria. Internal consistency was satisfactorily high ($\alpha \geq 0.84$), and retest reliability exceeded $r > 0.75$ in nonclinical samples. Associations with construct-related scales (depression, dysfunctional cognitive constructs) were high; The BDI-II differentiated well between different grades of depression and was sensitive to change.

- 6. Anxiety Sensitivity Index (ASI)** (Peterson & Reiss, 1993): The ASI test assesses anxiety aroused by symptoms of fear in participants (Peterson & Reiss, 1993). It is a 16-item scale and includes such questions as: "It scares me when I feel shaky", and "It scares me when I'm nervous". Participants rate their agreement with each anxiety-related symptom using a five point Likert scale (0-Very Little, 4-Very Much). The ASI measures sensitivity to sensations of anxiety distinct from state or trait anxiety (McNally, 1989; Reiss, Peterson, Gursky, & McNally, 1986). The ASI has shown adequate internal consistency ($\alpha = .82$, Telch, et al., 1989c) and good split-half reliability ($r = .85$, Peterson & Heilbronner, 1987). Retest reliability has been found to be within the $r = .71-75$ range and the ASI total score has demonstrated validity (Reiss et al, 1986). Mantar, Yemez & Alkın (2010), investigated the validity and reliability of the ASI in 150 healthy individuals without any psychiatric disorder and 300 patients with an anxiety disorder and/or major depressive disorder according to DSM-IV criteria. All subjects included in the study were evaluated by the ASI, State-Trait Anxiety Inventory-Trait form (STAI-T), BDI and Somatosensory Amplification Scale (SAS). The results showed that the scale differentiated the healthy group from all patient subgroups. ASI was found to be moderately correlated to STAI-T ($r = 0.68$), BDI ($r = 0.57$) and SAS ($r = 0.47$). In fact analysis, ASI was found to be compared of 3 factors: physical, cognitive and social. The Cronbach alpha value for these sub items was calculated to be 0.89 for physical symptoms; 0.88 for cognitive symptoms and 0.82 for the social symptoms. It was also found that ASI had a

high internal consistency (Cronbach alpha=0.93) and the scale had a fairly good test-retest reliability ($r=0.64$, $p<0.001$).

- 7. Agoraphobic Cognition Questionnaire (ACQ)** (Chambless & Gillis., 1993): The ACQ was administered to measure catastrophic cognition and fear of fear in participants (Chambless & Gillis, 1993). ACQ is a 14-item self-administered questionnaire concerning maladaptive thoughts regarding negative consequences associated with anxiety. The items are rated on a five point (1-5) scale ranging from the "thought never occurs" to the "thought always occurs when I am nervous. According to Chambless, et al. (1985), the ACQ has good internal consistency with alpha = .80. The scale is stable over time. A test-retest correlation of .75 was found with a one month interval between pre and post-test administration. The ACQ scale has good discriminant validity as it is able to distinguish between groups (i.e., agoraphobics, "normals", and clients with other depression and anxiety disorders). The ACQ is sensitive to behavioral and cognitive changes with treatment. Thirty-five clients not partaking in the reliability study took the ACQ before and after treatment. Scores on the ACQ showed a change in avoidance and panic [$t(34) = 4.08$, $p < .001$] (Chambless et al., 1985). The reliability and validity of the ACQ was also addressed in a study by Rapee, Craske, Brown, and Barlow (1996), who explored the lack of perceived control over internal emotional responses and externally threatening events in anxious individuals. Participants included 250 individuals seeking treatment for a variety of anxiety disorders in an outpatient clinic. Results indicated that the ACQ can be conceptualized as a unitary measure, and test-retest reliability was high for a one month period over three times. The following correlations over time were reported: Time 1-2 ($r=.88$), Time 1-3 ($r=.82$) and Time 2-3 ($r=.84$).

2.3 Statistical Data Analyses

All statistical analyses were carried out using the program Statistical Package for the Social Sciences (SPSS for Windows, version 20 SPSS Inc). The results were considered significant when $p < 0.05$.

Demographic and Clinical Measures

Differences in categorical variables such as gender, marital status, education, occupation status, panic disorder duration and panic attack frequency were tested with the chi square test. Continuous variables such as age, BAI, BDI, PDSS, ACQ, ASI and FQ-AG were investigated with one-way analyses of variance (ANOVA).

The assumption of homogeneity of variances is examined through Levene's test of equality to make sure that there are no significant differences in the mean scores on the dependent variable and confounding variable among the three groups in pretreatment.

Pretreatment, posttreatment scores on the questionnaires were analyzed using repeated measures ANOVA with the factors 3 (Group: ICBT, GCBT, WL) \times 2 (Time: pretreatment, posttreatment) and a 2 (Group: ICBT, GCBT) \times 3 (Time: pretreatment, posttreatment) repeated measures design.

Repeated measures analyses were also tested for sphericity (using Mauchly sphericity test). Heterogeneity of variance was calculated using the Greenhouse-Geisser correction.

Bonferroni adjustments of p values were used to correct for multiple comparisons. Effect sizes are indicated in terms of η^2 . All effects are reported as significant at $p < .05$. Pearson product-moment correlation coefficients were computed to assess the relationship between variables.

Chapter III - Results

3.1 Introduction

This chapter presents the data analysis, the comparison two treatment formats, Individual Cognitive Behavior Therapy (ICBT), Group Cognitive Behavior Therapy (GCBT) and the Wait-list control group (WL) before and after the treatment. This chapter is divided into two sections. The first section aims to examine sample comparability before treatment. In order to ensure the lack of pre-existing differences between the groups, and ensure the randomization of participants in groups, Chi-square tests for six categorical variables (gender, level of education, marital status, occupational status, panic duration and frequency of panic) and one-way between groups ANOVA for age variable and six dependent variables (Depression, Anxiety, Severity of Panic Disorder, Agoraphobic Cognition, Anxiety sensitivity and Agoraphobic avoidance) were utilized in this section.

Then a Univariate Analysis of Variance (ANOVA) with repeated measures was performed to test for effects of group \times time. In case of significant interaction group \times time effects, post- hoc analyses were carried out. Participants who were initially in the WL group were excluded from the four months follow-up due to initiation of treatment at post testing.

3.2 Group comparison pre-treatment

The three groups were compared with regard to demographic characteristics. The following demographic variables were included in the analysis: age, gender, marital status, occupational status and level of education. Furthermore, the following panic disorder related variables were included: panic disorder duration (how long the person has experienced panic attacks) and panic attack frequency (how many panic attacks the person has per week). These variables were selected to provide a means of assessing the severity of the disorder.

3.2.1 Demographic data

Age: According to results shown in Table 3.1, the mean age of participants is (M=32.98, SD=10.62). The groups did not differ significantly with regard to age.

Table 3.1: Descriptive Statistics and ANOVA results for Age

Demographic Variables	Group	N	Mean	SD	SD Error	Min	Max	F (df=2, 42)	P*
Age (years)	Individual Therapy	15	32.07	11.04	2.85	18	56	0.16	0.86
	Group Therapy	15	34.20	12.30	3.17	19	61		
	Waiting List	15	32.67	8.86	2.29	21	48		
	Total	45	32.98	10.62	1.58	18	61		

Note*: Sig.p<0.05

Table 3.2 presents a comparison of the three groups according to selected demographic characteristics.

Table 3.2: Chi-Square Test of Demographic Variables by group

Demographic Variables	Values	Individual Therapy		Group Therapy		Waiting List		Stat. Test	
		N	%	N	%	N	%	χ^2	p
Gender	Female	7	47%	5	33%	8	53%	1.260	0.533
	Male	8	53%	10	67%	7	47%		
Marital Status	Single	9	60%	7	47%	6	40%	5.54	0.477
	Married	4	27%	7	47%	9	60%		
	Sep/Divorced	1	7%	1	7%	0	0%		
	Widowed	1	7%	0	0%	0	0%		

Education	Less H.S diploma	3	20%	3	20%	3	20%	3.03	0.932
	H.S diploma	7	47%	9	60%	7	47%		
	Undergraduate	2	13%	1	7%	2	13%		
	Bachelors	2	13%	2	13%	3	20%		
	Masters	1	7%	0	0%	0	0%		
Occupational Status	Employee	8	53%	6	40%	4	27%	4.8	0.904
	Self-employment	2	13%	4	27%	3	20%		
	Military	2	13%	1	7%	2	13%		
	Student	2	13%	1	7%	3	20%		
	Housewife	1	7%	2	13%	2	13%		
	Unemployed	0	0%	1	7%	1	7%		
Panic Disorder duration	Less than 6 month	3	20%	2	13%	2	13%	1.04	0.903
	6 months to 1 year	7	47%	8	53%	6	40%		
	More than 1 year	5	33%	5	33%	7	47%		
Panic Attack Frequency	≤ 2 per week	10	67%	9	60%	10	67%	0.194	0.908
	≥ 3 per week	5	33%	6	40%	5	33%		

Table 3.2 illustrates that the three groups are not significantly different with regard to key demographic variables.

Gender: As depicted in Table 3.2, of 45 participants, 20 (44%) are female and 25 (56%) are male. The Chi-Square test revealed no significant group differences.

Marital Status: As depicted in Table 3.2, 22 (49%) of participants were single, 20 (44%) were married, 2 (4%) were separated or divorced and 1 (2%) was widowed. The Chi-Square test revealed no significant group differences.

Education: As shown in Table 3.2, 9 (20%) of 45 participants had less than a high school education, 23 (51%) had a high school diploma, 5 (11%) were undergraduates, 7 (16%) had a Bachelors degree and 1 (2%) had a Masters degree. The Chi-Square test revealed no significant group differences.

Occupational Status: According to Table 3.2, of 45 participants 18 (40%) were employees, 9 (20%) were self-employed, 5 (11%) were military, 6 (13%) were students, 5 (11%) were housewives and 2 (4%) were unemployed. The Chi-Square test showed no significant group difference.

Panic Disorder Duration: As shown in Table 3.2, of 45 participants 7 (16%) had a history of panic disorder of less than 6 months and 21 (47%) had a history of panic

disorder of 6 months to 1 year, and 17 (38%) had a history of panic disorder of more than 1 year. The Chi –square analysis revealed no significant group difference.

Panic attack frequency: As shown in Table 3.2, of 45 participants 29 (64%) had 2 panic attacks or less, per week and 16 (36%) had 3 panic attacks or more per week. Chi-square analysis revealed no significant group difference.

Summary

The results showed that the three groups did not differ significantly with regard to demographic variables or history of disorder at pre-treatment.

3.2.2 Pre-treatment comparison of questionnaire data

The three groups were compared with regard to pre-treatment scores of the following dependent variables: Beck Anxiety Inventory (BAI) score, Beck Depression Inventory (BDI), Panic Disorder Severity Scale (PDSS), Agoraphobic Cognition Questionnaire (ACQ), Anxiety Sensitivity Index (ASI), Fear Questionnaire – agoraphobia scale (FQ-AG) Means and SDs are presented in Table 3.3.

Table 3.3: Means and SDs of variables (BAI, BDI, PDSS, ACQ, ASI, and FQ-AG) in pre-treatment

Variable	Group	N	Mean	SD	SD Error	Min	Max
BAI	Individual Therapy	15	33.07	8.08	2.09	22	53
	Group Therapy	15	30.20	5.36	1.38	22	41
	Waiting List	15	31.33	5.73	1.48	24	48
	Total	45	31.53	6.46	0.96	22	53
BDI	Individual Therapy	15	23.73	4.71	1.22	18	32
	Group Therapy	15	22.67	4.53	1.17	17	30
	Waiting List	15	22.53	5.30	1.37	16	32
	Total	45	22.98	4.78	0.71	16	32
PDSS	Individual Therapy	15	20.27	2.63	0.68	16	24
	Group Therapy	15	19.20	2.14	0.55	15	22
	Waiting List	15	21.27	2.22	0.57	17	25
	Total	45	20.24	2.44	0.36	15	25
ACQ	Individual Therapy	15	40.53	5.83	1.50	28	48
	Group Therapy	15	41.40	4.81	1.24	34	52
	Waiting List	15	39.33	7.06	1.82	29	54
	Total	45	40.42	5.89	0.88	28	54
ASI	Individual Therapy	15	39.07	5.36	1.39	32	47
	Group Therapy	15	37.80	3.53	0.91	32	43

	Waiting List	15	41.13	6.32	1.63	28	51
	Total	45	39.33	5.27	0.79	28	51
FQ-AG	Individual Therapy	15	17.67	4.56	1.18	11	26
	Group Therapy	15	17.47	3.91	1.01	10	24
	Waiting List	15	18.20	4.21	1.09	12	25
	Total	45	17.78	4.15	0.62	10	26

Since one-way ANOVA relies on the test of homogeneity of variance, the underlying assumption of homogeneity of variance was examined with the Levene's test for homogeneity of variances. Table 3.4, represents the results of Levene's test of Equality of Variance of the three groups in pre-test.

Table 3.4: Levene's Test of Equality of Variance for all variables at pretest

Variable	Levene's statistic	df1	df2	p*
BAI	1.407	2	42	0.256
BDI	0.249	2	42	0.781
PDSS	0.481	2	42	0.622
ACQ	0.948	2	42	0.396
ASI	2.522	2	42	0.092
FQ-AG	.360	2	42	0.700

Note*: Sig.p<0.05

The data were submitted to ANOVA comparing the three groups. None of the variables showed significant results. The ANOVA results are shown in table 3.5.

Table 3.5: One-way ANOVA for all variables in pre-test

Variable	Source	Sum of Squares	df	Mean Square	F	p*
BAI	Between Groups	62.533	2	31.267	0.740	0.483
	Within Group	1774.667	42	42.254		
	Total	1837.200	44			
BDI	Between Groups	12.978	2	6.489	0.275	0.761
	Within Group	992	42	23.619		
	Total	1004.978	44			
PDSS	Between Groups	32.044	2	16.022	2.922	0.065
	Within Group	230.267	42	5.483		
	Total	262.311	44			

ACQ	Between Groups	32.311	2	16.156	0.453	0.639
	Within Group	1496.667	42	35.635		
	Total	1528.978	44			
ASI	Between Groups	84.933	2	42.467	1.569	0.220
	Within Group	1137.067	42	27.073		
	Total	1222	44			
FQ-AG	Between Groups	4.311	2	2.156	0.120	0.887
	Within Group	753.467	42	17.940		
	Total	757.778	44			

Note*: Sig.p<0.05

BAI: As shown in Table 3.3, there was no significant group difference pre-treatment with regard to Anxiety scores as measured with the Beck Anxiety Inventory (BAI). The mean score indicated a severe level of anxiety (scores ranging from 26 to 63 represent severe anxiety).

As shown in Table 3.4 the homogeneity of variance assumption was met.

BDI: As shown in Table 3.3, there was no significant group difference pre-treatment with regard to Beck Depression Inventory (BDI). The scores indicated a moderate level of depression (scores ranging from 20 to 28 represent moderate depression). As shown in Table 3.4, the homogeneity of variance assumption was met.

PDSS: As shown in Table 3.3, there was no significant group difference pre-treatment with regard to Panic Disorder Severity Scale (PDSS). The mean score indicated a severe level of Panic Disorder Severity (scores ranging from 14 and above represent severe panic disorder).

As shown in Table 3.4, the homogeneity of variance assumption was met.

ACQ: As shown in Table 3.3, there was no significant group difference pre-treatment with regard to Agoraphobic Cognition (ACQ).

As shown in Table 3.4 the homogeneity of variance assumption was met.

ASI: As shown in Table 3.3, there was no significant group difference pre-treatment with regard to Anxiety Sensitivity Index (ASI). The scores indicated a high level of anxiety sensitivity severity. Donnell and McNally (1990) defined high Anxiety

Sensitivity as an ASI score of 27 or higher.

According to Table 3.4, the homogeneity of variance assumption was met.

FQ-AG: As shown in Table 3.3, there was no significant group difference pre-treatment with regard to agoraphobic avoidance (FQ-AG). Marks and Mathews (1979) defined scores of less than 12 on FQ-AG subscale are considered normative. As shown in Table 3.4, the homogeneity of variance assumption was met.

Summary

The results indicate that there are no significant group differences with regard to demographic data and clinical variables at pre-treatment.

3.3 Effect of treatments pre-post and pre-post-follow-up

Questionnaire data were submitted to ANOVA with a 3 (groups: ICBT, GCBT, WL) x 2 (time: pretest, posttest) and a 2 (groups: ICBT, GCBT) x 3 (time: pretest, posttest, 4 month follow-up) repeated measures design. Partial Eta² was used to evaluate effect size.

3.3.1 Beck Anxiety Inventory (BAI)

3.3.1.1 Treatment (ICBT/GCBT/WL) by time (pre/posttest)

Data were submitted to repeated measures ANOVA with a design of 3 (group: ICBT, GCBT, WL) x 2 (time: pretest, posttest). In addition to the F ratio partial eta² was extracted to assess the effect size.

The BAI means and standard deviations of the BAI are presented in Table 3.6.

Table 3.6: Mean and SDs of BAI in Pre-treatment and Post-treatment

Group	pre-test			post-test	
	N	M	SD	M	SD
ICBT	15	33.07	8.07	12.13	2.92
GCBT	15	30.20	5.36	17.33	3.35
Waiting list	15	31.33	5.73	29.80	5.98
Total	45	31.53	6.46	19.76	8.59

The results of analysis of variance of the BAI are shown in Table 3.7.

Table 3.7: Results of the ANOVA of Group, Time and Time by Group of BAI from Pre-treatment to Post-treatment

Source	Sum of Squares	df	Middle of Squares	F	p	η ²
Group	1110.689	2	555.344	10.920	0.001	.342
Time	3121.111	1	3121.111	314.961	0.001	.882
Time x Group	1424.689	2	712.344	71.885	0.001	.774
Error	416.200	42	9.910			

There was a significant main effect for group and time and a significant interaction effect of time x group. Partial eta² indicates a large effect size for time and a medium effect size for time x group interaction.

Post - hoc tests were used to compare groups with respect to the mean difference between pre-post BAI scores (Table 3.8).

Table 3.8: Pairwise comparisons among Three Groups for BAI Scores

Group I	Group J	Mean Differences	Std. Error	p
ICBT	GCBT	-5.200	1.571	0.006
ICBT	Waiting List	-17.667	1.571	0.001
GCBT	Waiting List	-12.467	1.571	0.001

As shown in Table 3.8, patients who participated in both treatment groups showed significantly more reduction in BAI severity scores between pretest and posttest than the Wait-list group, while the significant difference between two treatments modalities indicated that ICBT is more efficacious in reducing anxiety severity. The findings are shown in Figure 3.1.

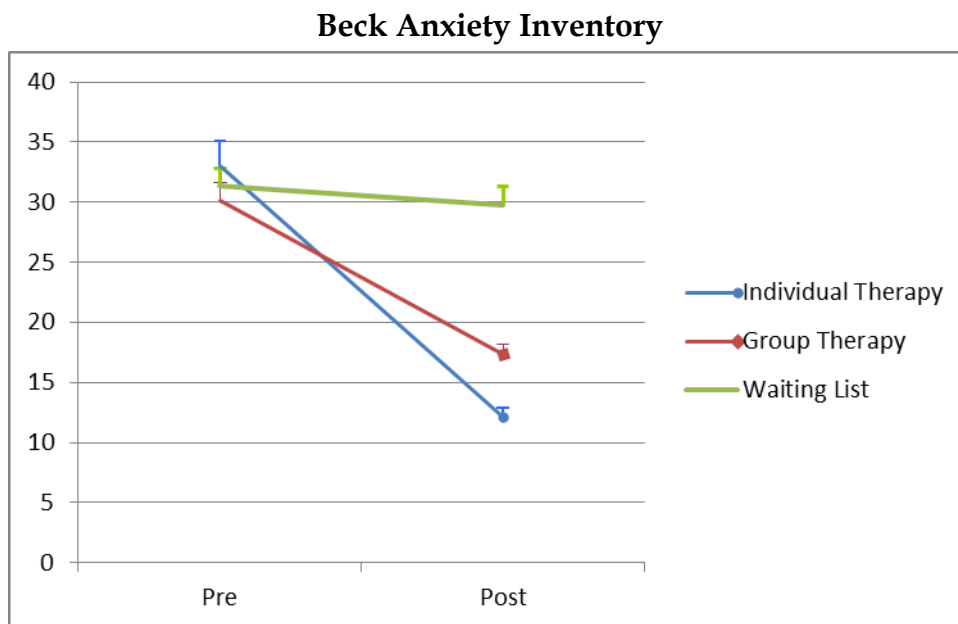


Figure 3.1: Means and standard errors for the Beck Anxiety Inventory (BAI) of groups at pre and post-test

Summary

Both treatment groups (Individual CBT, Group CBT) showed significantly more improvement with regard to the Beck Anxiety Inventory (BAI) compared to the wait-list control group from pretest to posttest. In addition, Individual CBT was more effective than Group CBT in reduction of anxiety severity.

3.3.1.2 Treatment (ICBT/GCBT) by time (pre/post/four-month follow-up)

Data were submitted to repeated measures ANOVA with a design of 2 (Group: ICBT, GCBT) \times 3 (Time: pretest, posttest, follow-up). In addition to the F ratio partial eta² was extracted to assess the effect size.

The group means and standard standard deviations of the BAI are presented in Table 3.9.

Table 3.9: Mean and SDs of BAI in Pre-treatment, Post-treatment and Follow-up in ICBT and GCBT

Group	N	pre-test		post-test		Follow-up	
		M	SD	M	SD	M	SD
ICBT	15	33.07	8.07	12.13	2.92	9.00	2.90
GCBT	15	30.20	5.36	17.33	3.35	12.80	2.73
Total	30	31.63	6.89	14.73	4.07	10.90	3.38

The results of the ANOVA for BAI scores are shown in Table 3.10.

Table 3.10: Results of the ANOVA of Group, Time and Time by Group of BAI from Pre-treatment, Post-treatment to Follow-up

Source	Sum of Squares	df	Middle of Squares	F	p	η^2
Group	94.044	1	94.044	2.335	.138	.077
Time	7301.756	2	3650.876	297.645	0.001	.914
Time x Group	278.689	2	139.344	11.360	0.001	.289
Error	686.889	56	12.266			

There was a significant main effect for time and a significant interaction effect of group x time. Partial eta² indicates a large effect size for time. Furthermore the significant difference between two treatments modalities indicated that ICBT is more efficacious in reducing anxiety severity. The findings are shown in Figure 3.2.

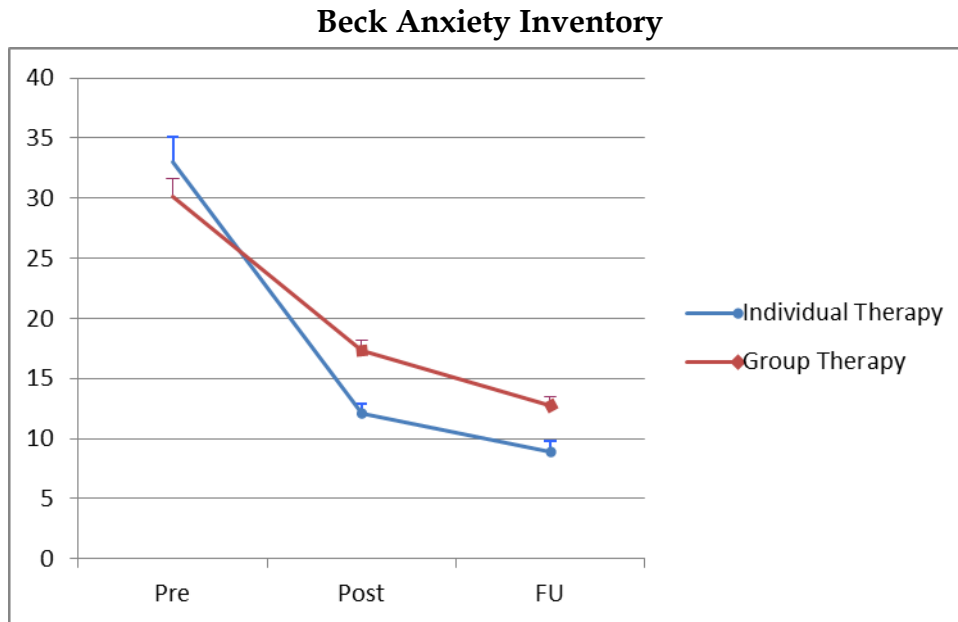


Figure 3.2: Means and standard errors for the Beck Anxiety Inventory (BAI) of treatment groups at pretest, posttest and follow-up

Summary

Participants in both treatment groups (Individual CBT, Group CBT) showed significantly more improvement with regard to Beck Anxiety Inventory (BAI) from pre to posttest than the waiting list control group. Furthermore, individual CBT led to greater improvement than group CBT from pretest, posttest to follow-up.

3.3.2 Beck Depression Inventory (BDI)

3.3.2.1 Treatment (ICBT/GCBT, WL) by time (pre/posttest)

Data were submitted to repeated measures ANOVA with a design of 3 (group: ICBT, GCBT, WL) x 2 (time: pretest, posttest). In addition to the F ratio partial eta² was extracted to assess the effect size.

The BDI means and standard deviations of three groups are presented in Table 3.11.

Table 3.11: Mean and SDs of BDI in Pre-treatment and Post-treatment

Group	N	pre-test		post-test	
		M	SD	M	SD
ICBT	15	23.73	4.71	11.27	2.66
GCBT	15	22.67	4.53	13.27	2.46
Waiting list	15	22.53	5.30	22.93	4.21
Total	45	22.98	4.78	15.82	6.03

The results of analysis of variance of the BDI are shown in Table 3.12.

Table 3.12: Results of the ANOVA of Group, Time and Time by Group of BDI from Pre-treatment to Post-treatment

Source	Sum of Squares	df	Middle of Squares	F	p	η ²
Group	503.267	2	251.633	8.864	.001	.297
Time	1152.044	1	1152.044	208.141	.001	.832
Time x Group	677.489	2	338.744	61.201	.001	.745
Error	232.467	42	5.535			

There was a significant main effect for group, time and a significant interaction effect of time x group. Partial eta² indicates a large effect size for time and a medium effect size for time x group interaction.

Post - hoc tests were used to compare groups with respect to the mean difference between pre- post BDI scores (Table 3.13).

Table 3.13: Pairwise comparisons among Three Groups for BDI Severity Scores

Group I	Group J	Mean Differences	Std. Error	p
ICBT	GCBT	-2.000	1.172	0.095
ICBT	Wait-list	-11.667	1.172	0.001
GCBT	Waiting list	-9.667	1.172	0.001

As shown in Table 3.13 patients who participated in the both treatment groups showed significantly more reduction in BDI severity scores between pretest and posttest compared to the Wait-list group, while not significantly differing from each other. The findings are shown in Figure 3.3.

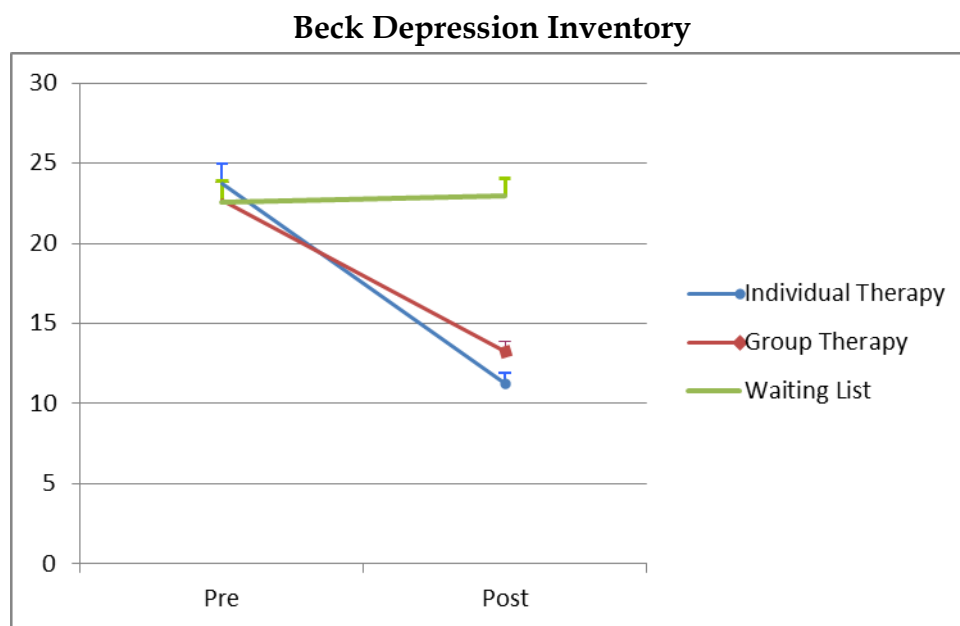


Figure 3.3: Means and standard errors for the Beck Depression Inventory (BDI) of groups at pretest, posttest

Summary

Both treatment groups (Individual CBT, Group CBT) showed significantly more improvement with regard to the Beck Depression Inventory (BDI) compared to the wait-list control group, while not significantly differing from each other.

3.3.2.2 Treatment (ICBT/GCBT) by time (pre/post/four-month follow-up)

Data were submitted to repeated measures ANOVA with a design of 2 (Group: ICBT, GCBT) x 3 (Time: pretest, posttest, follow-up) to evaluate the change in depression symptoms (BDI) in two groups. In addition to the F- ratio, partial eta² was extracted to assess the effect size.

The group means and standard deviations of the BDI are presented in Table 3.14.

Table 3.14: Mean and SDs of BDI in Pre-treatment, Post-treatment and Follow-up in ICBT and GCBT

Group	pre-test			post-test		Follow-up	
	N	M	SD	M	SD	M	SD
ICBT	15	23.73	4.71	11.27	2.66	9.80	3.59
GCBT	15	22.67	4.53	13.27	2.46	11.93	2.712
Total	30	23.20	4.57	12.27	2.72	10.87	3.31

The results of analysis of variance of the BDI are shown in Table 3.15.

Table 3.15: Results of the ANOVA of Group, Time and Time by Group of BDI from Pre-treatment, Post-treatment to follow-up

Source	Sum of Squares	df	Middle of Squares	F	p	η ²
Group	23.511	1	23.511	.822	.372	.029
Time	2736.089	2	1368.044	289.363	.001	.912
Time x Group	49.156	2	24.578	5.199	.008	.157
Error	264.756	56	4.728			

There was a significant main effect for time and a significant interaction effect of group x time. Partial eta² indicates large effect size for time. Furthermore the significant difference between two treatment modalities indicated that ICBT is more efficacious in reducing depression. The findings are shown in Figure 3.4.

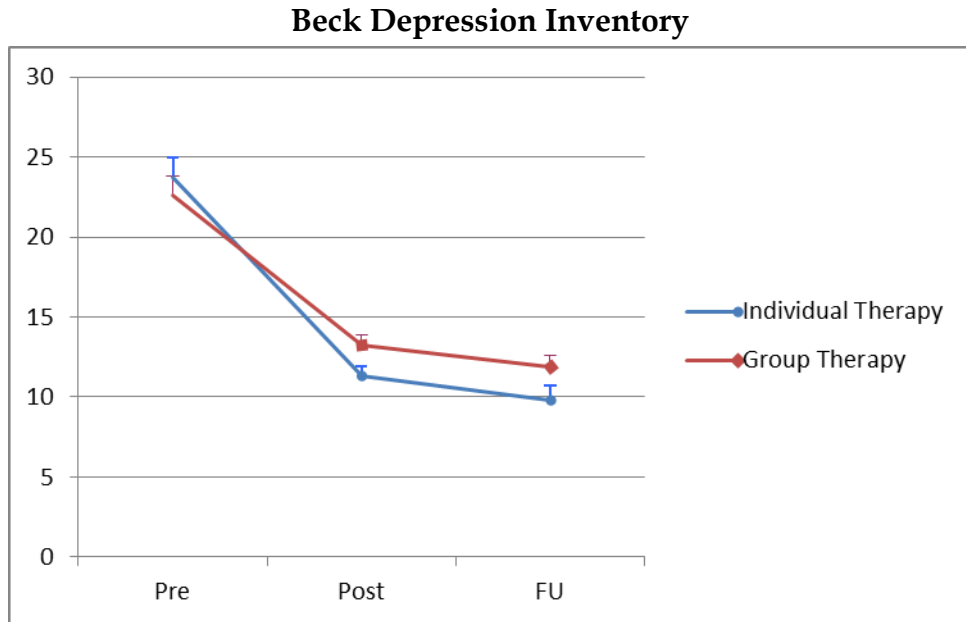


Figure 3.4: Means and standard errors for the Beck Depression Inventory (BDI) of treatment groups at pretest, posttest and follow-up

Summary

Participants in both treatment groups (Individual CBT, Group CBT) showed significantly more improvement with regard to Beck Depression Inventory (BDI) from pretest, posttest to 4 months follow-up. Furthermore, individual CBT led to greater improvement than group CBT.

3.3.3 Panic Disorder Severity Scale (PDSS)

3.3.3.1 Treatment (ICBT/GCBT, WL) by time (pre/posttest)

Data were submitted to repeated measures ANOVA with a design of 3 (group: ICBT, GCBT, WL) x 2 (time: pretest, posttest). In addition to the F ratio partial eta² was extracted to assess the effect size.

The PDSS means and standard deviations of three groups are presented in Table 3.16.

Table 3.16: Mean and SDs of PDSS in Pre-treatment and Post-treatment

Group	N	pre-test		post-test	
		M	SD	M	SD
ICBT	15	20.27	2.63	9.20	1.93
GCBT	15	19.20	2.14	11.47	1.60
Waiting list	15	21.27	2.22	20.40	2.59
Total	45	20.24	2.44	13.69	5.30

The results of analysis of variance of the PDSS are shown in Table 3.17.

Table 3.17: Results of the ANOVA of Group, Time and Time by Group of PDSS from Pre-treatment to Post-treatment

Source	Sum of Squares	df	Middle of Squares	F	p	η ²
Group	678.200	2	339.100	40.323	0.001	.658
Time	966.944	1	966.944	690.675	0.001	.943
Time x Group	405.756	2	202.878	144.913	0.001	.873
Error	58.800	42	1.400			

There was a significant main effect for group, time and a significant interaction effect of time x group. Partial eta² indicates a medium effect size for group and a large effect size for time and time x group interaction.

Post - hoc tests were used to compare groups with respect to the mean difference between pre- post PDSS scores in Table 3.18.

Table 3.18: Pairwise comparisons among Three Groups for PDSS Scores

Group I	Group J	Mean Differences	Std. Error	p
ICBT	GCBT	-2.27	0.760	0.014
ICBT	Wait-list	-11.20	0.760	0.001
GCBT	Waiting list	-8.93	0.760	0.001

As shown in Table 3.18 patients who participated in the ICBT and GCBT groups showed significantly more reduction in PDSS severity scores between pretest and posttest compared to the Wait-list group, while the significant difference between two treatments modalities indicated that ICBT is more efficacious in reducing severity of panic disorder. The findings are shown in Figure 3.5.

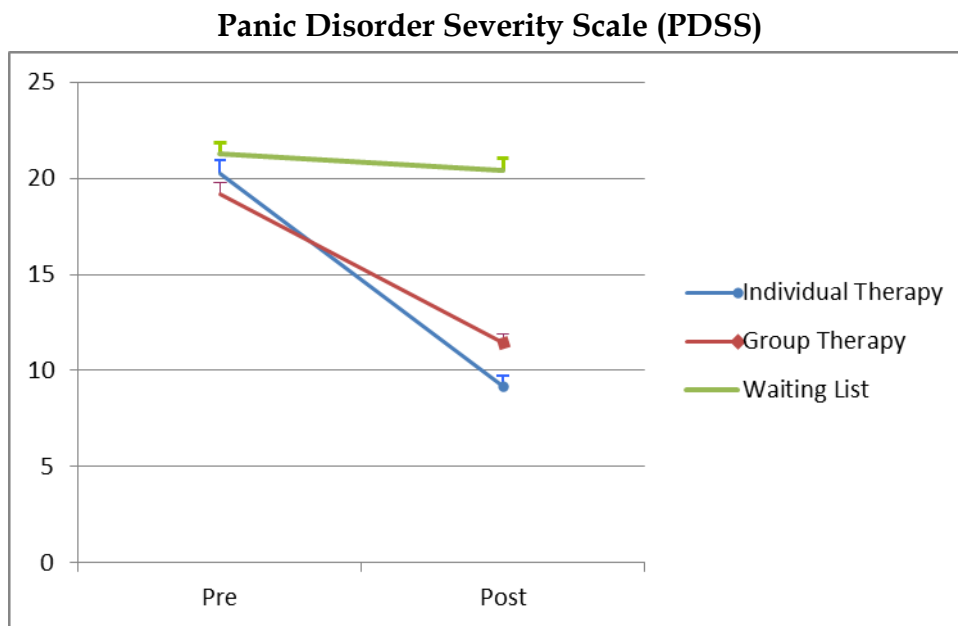


Figure 3.5: Means and standard errors for the Panic Disorder Severity Scale (PDSS) of groups at pretest, posttest

Summary

Both treatment groups (Individual CBT, Group CBT) showed significantly more improvement with regard to the panic disorder severity (PDSS) compared to the wait-list control group from pre to posttest. Furthermore individual CBT led to greater improvement than group CBT.

3.3.3.2 Treatment (ICBT/GCBT) by time (pre/post/four-month follow-up)

Data were submitted to repeated measures ANOVA with a design of 2 (Group: ICBT, GCBT) x 3 (Time: pretest, posttest, follow-up)

The group means and standard deviations of the PDSS are presented in Table 3.19.

Table 3.19: Mean and SDs of PDSS in Pre-treatment, Post-treatment and Follow-up in ICBT and GCBT

Group	N	pre-test		post-test		Follow-up	
		M	SD	M	SD	M	SD
ICBT	15	20.27	2.63	9.20	1.93	6.80	1.32
GCBT	15	19.20	2.14	11.47	1.60	8.80	1.21
Total	30	19.73	2.42	10.33	2.09	7.80	1.61

The results of analysis of variance of the PDSS are shown in Table 3.20.

Table 3.20: Results of the ANOVA of Group, Time and Time by Group of PDSS from Pre-treatment, Post-treatment to Follow-up

Source	Sum of Squares	df	Middle of Squares	F	p	η^2
Group	25.600	1	25.600	3.388	0.076	.108
Time	2371.822	2	1185.911	802.927	0.001	.966
Time x Group	51.467	2	25.733	17.423	0.001	.384
Error	82.711	56	1.477			

There was a significant effect for time and a significant interaction effect of group x time. Partial η^2 indicates a large effect size for time. Furthermore individual CBT led to greater improvement than group CBT. The findings are shown in Figure 3.6.

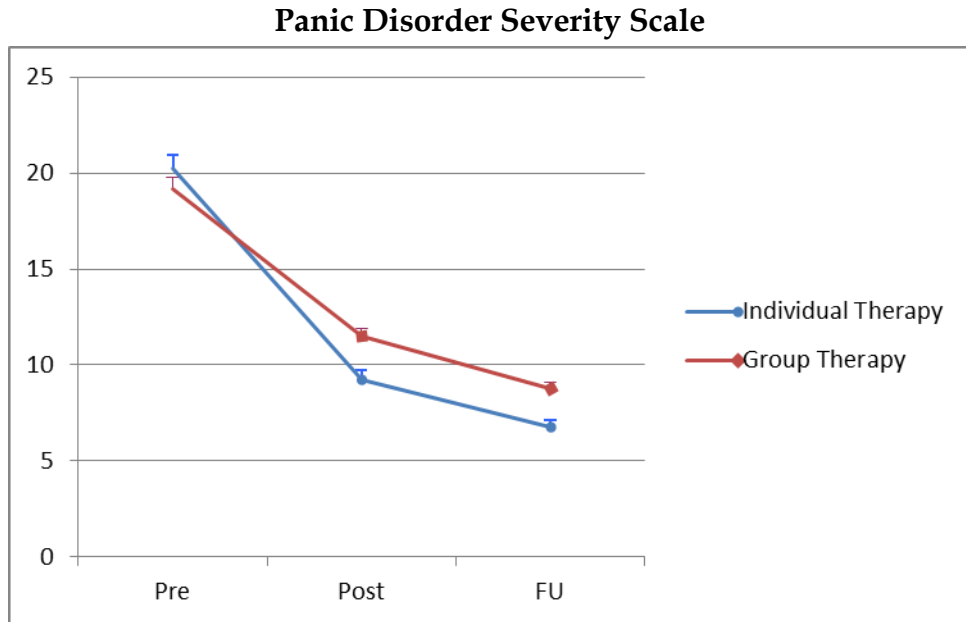


Figure 3.6: Means and standard errors for the Panic Disorder Severity Scale (PDSS) of treatment group at pretest, posttest, and follow-up

Summary

Participants in both treatment groups (Individual CBT, Group CBT) showed significantly more improvement with regard to Panic Disorder Severity Scale (PDSS) from pretest, posttest to 4 months follow-up. Furthermore, individual CBT led to greater improvement than group CBT.

3.3.4 Agoraphobic Cognition (ACQ)

3.3.4.1 Treatment (ICBT/GCBT, WL) by time (pre/posttest)

Data were submitted to repeated measures ANOVA with a design of 3 (group: ICBT, GCBT, WL) x 2 (time: pretest, posttest). In addition to the F ratio partial eta² was extracted to assess the effect size.

The ACQ means and standard deviations of the PDSS are presented in Table 3.21.

Table 3.21: Mean and SDs of ACQ in Pre-treatment and Post-treatment

Group	N	pre-test		post-test	
		M	SD	M	SD
ICBT	15	40.53	5.83	19.80	5.29
GCBT	15	41.40	4.81	22.67	5.31
Waiting list	15	39.33	7.06	39.00	7.37
Total	45	40.42	5.89	27.16	10.41

The results of analysis of variance of the ACQ are shown in Table 3.22.

Table 3.22: Results of the ANOVA of Group, Time and Time by Group of ACQ from Pre-treatment to Post-treatment

Source	Sum of Squares	df	Middle of Squares	F	p	η ²
Group	1353.689	2	676.844	9.847	.001	.319
Time	3960.100	1	3960.100	1055.357	.001	.962
Time x Group	1896.800	2	948.400	252.746	.001	.923
Error	157.600	42	3.752			

There was a significant main effect for group, time and a significant interaction effect of time x group. Partial eta² indicates a large effect size for time and time x group interaction.

Post - hoc tests were used to compare groups with respect to the mean difference between pre- post ACQ scores in Table 3.23.

Table 3.23: Pairwise comparisons among Three Groups for ACQ Scores

Group I	Group J	Mean Differences	Std. Error	p
ICBT	GCBT	-2.87	2.217	0.609
ICBT	Wait-list	-19.20	2.217	0.001
GCBT	Waiting list	-16.33	2.217	0.001

As shown in Table 3.23 patients who participated in the ICBT and GCBT groups showed significantly more reduction in ACQ severity scores between pretest and posttest compared to the Wait-list group, while not significantly different from each other. The results of pairwise comparison show that there is no significant difference between treatment groups in reducing ACQ.

The findings are shown in Figure 3.7.

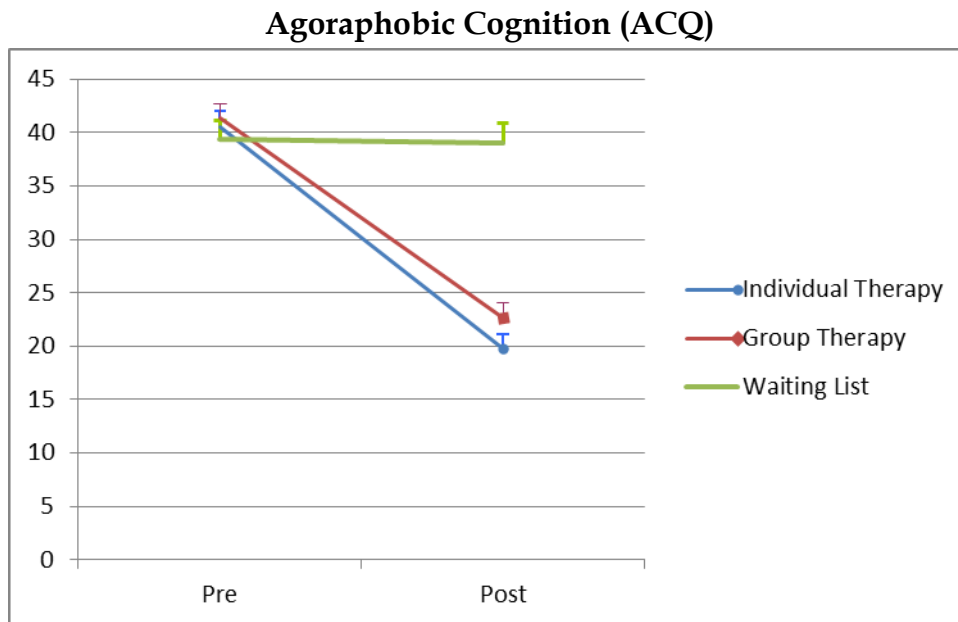


Figure 3.7: Means and standard errors for the Agoraphobic Cognition (ACQ) of groups at pretest, posttest

Summary

Both treatment groups (Individual CBT, Group CBT) showed significantly more improvement with regard to the Agoraphobic Cognition (ACQ) compared to the wait-list control group from pre to posttest, while not significantly differing from each other.

3.3.4.2 Treatment (ICBT/GCBT) by time (pre/post/four-month follow-up)

Data were submitted to repeated measures ANOVA with a design of 2 (Group: ICBT, GCBT) x 3 (Time: pretest, posttest, follow-up). In addition to the F ratio partial eta² was extracted to assess the effect size.

The group means and standard deviations of the ACQ are presented in Table 3.24.

Table 3.24: Mean and SDs of ACQ in Pre-treatment, Post-treatment and Follow-up in ICBT and GCBT

Group	N	pre-test		post-test		Follow-up	
		M	SD	M	SD	M	SD
ICBT	15	40.53	5.83	19.80	5.29	15.73	4.77
GCBT	15	41.40	4.81	22.67	5.31	17.67	4.89
Total	30	40.97	5.27	21.23	5.41	16.70	4.85

The results of analysis of variance of the ACQ are shown in Table 3.25.

Table 3.25: Results of the ANOVA of Group, Time and Time by Group of ACQ from Pre-treatment, Post-treatment to Follow-up

Source	Sum of Squares	df	Middle of Squares	F	p	η ²
Group	80.278	1	80.278	1.122	.299	.039
Time	9988.267	2	4994.133	1174.871	.001	.977
Time x Group	15.022	2	7.511	1.767	.180	.059
Error	238.044	56	4.251			

There was only a significant effect for time and partial eta² indicates a large effect size for time. Furthermore there is no significant difference between treatment groups in reducing ACQ. The findings are shown in Figure 3.8.

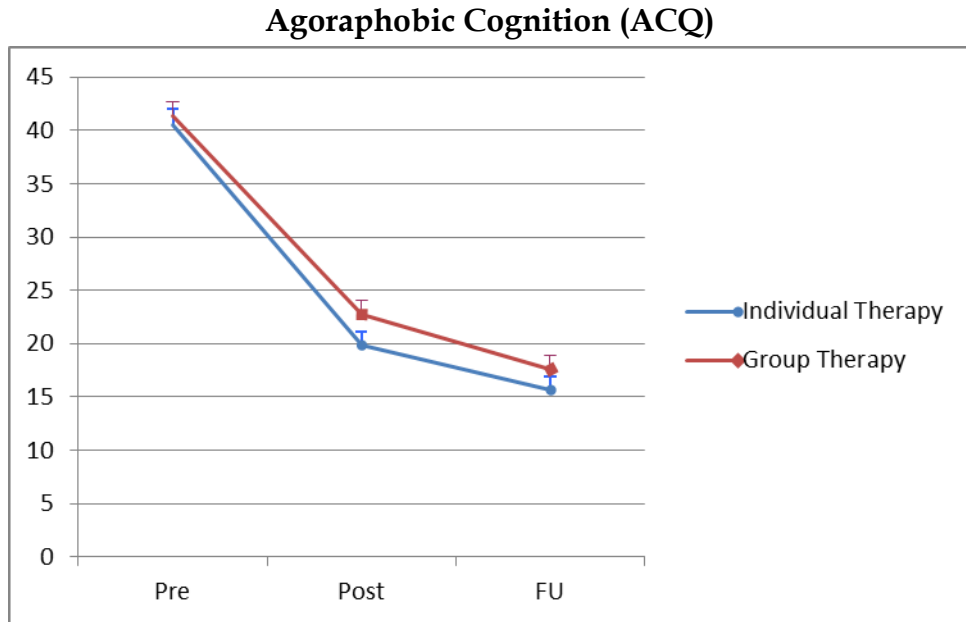


Figure 3.8: Means and standard errors for the Agoraphobic Cognition (ACQ) of treatment groups at pretest, posttest, and follow-up

Summary

Participants in both treatment groups (Individual CBT, Group CBT) showed significant improvement with regard to Agoraphobic Cognition (ACQ) from pretest, posttest to 4 months follow-up, while not significantly differing from each other.

3.3.5 Anxiety Sensitivity Severity (ASI)

3.3.5.1 Treatment (ICBT/GCBT, WL) by time (pre/posttest)

Data were submitted to repeated measures ANOVA with a design of 3 (group: ICBT, GCBT, WL) x 2 (time: pretest, posttest). In addition to the F ratio partial eta² was extracted to assess the effect size.

The ASI means and standard deviations are presented in Table 3.26.

Table 3.26: Mean and SDs of ASI in Pre-treatment and Post-treatment

Group	N	pre-test		post-test	
		M	SD	M	SD
ICBT	15	39.07	5.36	20.67	6.00
GCBT	15	37.80	3.53	22.47	3.94
Waiting list	15	41.13	6.32	40.80	7.12
Total	45	39.33	5.30	27.93	10.82

The results of analysis of variance of the ASI are shown in Table 3.27.

Table 3.27: Results of the ANOVA of Group, Time and Time by Group of ASI from Pre-treatment to Post-treatment

Source	Sum of Squares	df	Middle of Squares	F	p	η ²
Group	2406.422	2	1203.211	21.491	.001	.506
Time	2901.344	1	2901.344	561.206	.001	.930
Time x Group	1402.022	2	701.011	135.596	.001	.866
Error	217.133	42	5.170			

There was a significant main effect for group, time and a significant interaction effect of time x group. Partial eta² indicates a large effect size for time and time x group interaction.

Post - hoc tests were used to compare groups with respect to the mean difference between pre- post ASI scores in Table 3.28.

Table 3.28: Pairwise comparisons among Three Groups for ASI Scores

Group I	Group J	Mean Differences	Std. Error	p
ICBT	GCBT	-1.800	2.132	.403
ICBT	Wait-list	-20.133	2.132	.001
GCBT	Waiting list	-18.333	2.132	.001

As shown in Table 3.28 patients who participated in the ICBT and GCBT groups showed significantly more reduction in ASI severity scores between pretest and posttest compared to the Wait-list group, while not significantly differing from each other. The findings are shown in Figure 3.9.

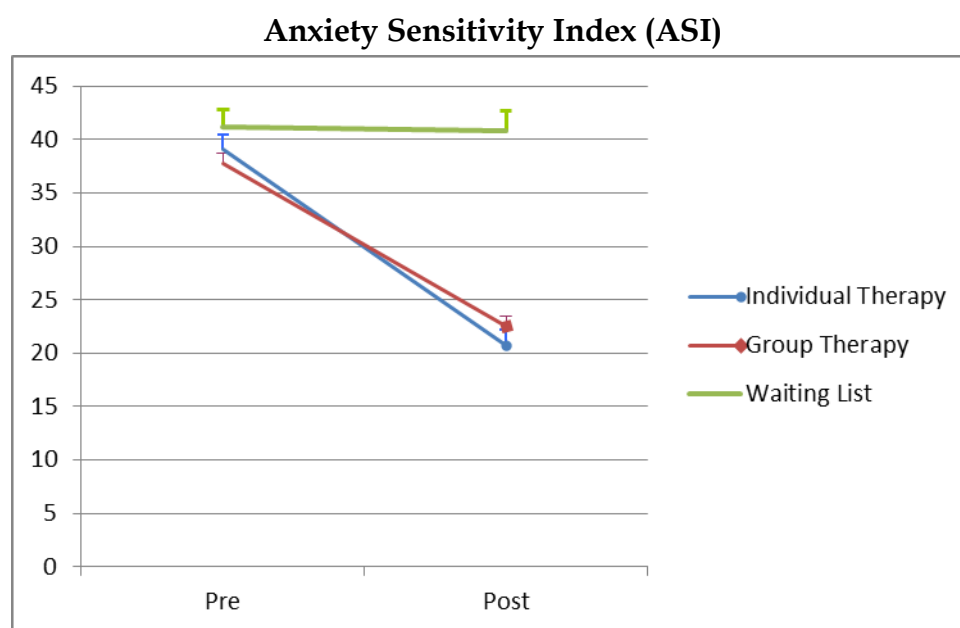


Figure 3.9: Means and standard errors for the Anxiety Sensitivity (ASI) of groups at pretest and posttest

Summary

Both treatment groups (Individual CBT, Group CBT) showed significantly more improvement with regard to the Anxiety Sensitivity Index (ASI) compared to the wait-list control group from pre to posttest, while not significantly differing from each other.

3.3.5.2 Treatment (ICBT/GCBT) by time (pre/post/four-month follow-up)

Data were submitted to repeated measures ANOVA with a design of 2 (Group: ICBT, GCBT) x 3 (Time: pretest, posttest, follow-up). In addition to the F ratio partial eta² was extracted to assess the effect size.

The group means and standard deviations of the ASI are presented in Table 3.29.

Table 3.29: Mean and SDs of ASI in Pre-treatment, Post-treatment and Follow-up

Group	N	pre-test		post-test		Follow-up	
		M	SD	M	SD	M	SD
ICBT	15	39.07	5.36	20.67	6.00	16.27	3.30
GCBT	15	37.80	3.53	22.47	3.94	18.80	2.68
Total	30	38.43	4.51	21.57	5.07	17.53	3.22

The results of analysis of variance of the ASI are shown in Table 3.30.

Table 3.30: Results of the ANOVA of Group, Time and Time by Group of ASI from Pre-treatment, Post-treatment to Follow-up

Source	Sum of Squares	df	Middle of Squares	F	p	η ²
Group	23.511	1	23.511	.533	.463	.019
Time	7375.622	2	3687.811	572.458	.001	.953
Time x Group	60.956	2	30.478	4.731	.013	.145
Error	360.756	56	6.442			

There was a significant effect for time and a significant interaction effect of time x group. Partial eta² indicates a large effect size for time. Furthermore individual CBT led to greater improvement than group CBT in reducing ASI. The findings are shown in Figure 3.10.

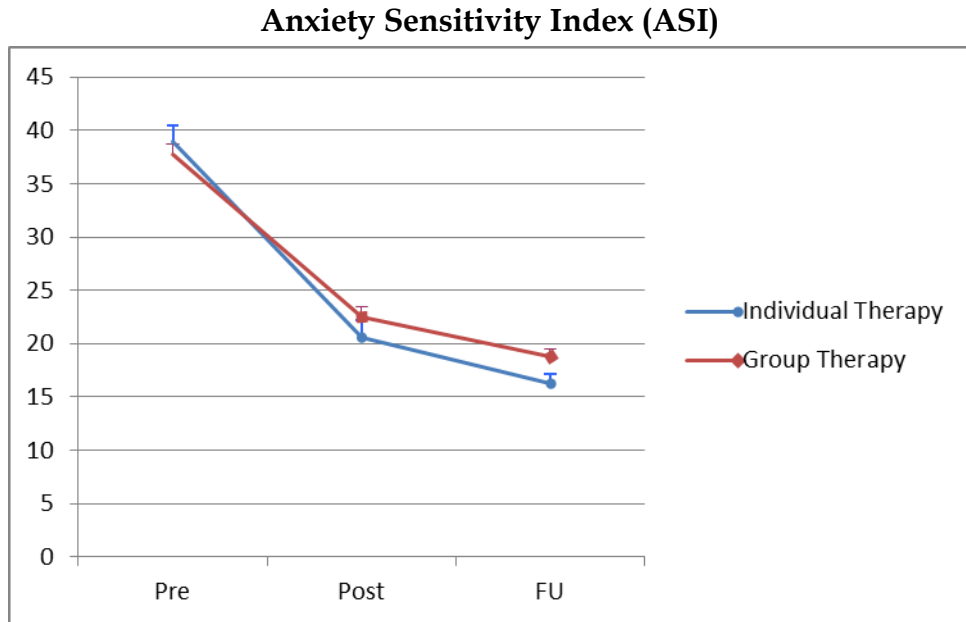


Figure 3.10: Means and standard errors for the Anxiety Sensitivity (ASI) of treatment groups at pretest, posttest, and follow-up

Summary

Participants in both treatment groups (Individual CBT, Group CBT) showed significant improvement with regard to Anxiety Sensitivity (ASI) from pretest, posttest to 4 months follow-up. Furthermore, individual CBT led to greater improvement than group CBT.

3.3.6 Agoraphobic Avoidance Severity (FQ-AG)

3.3.6.1 Treatment (ICBT/GCBT, WL) by time (pre/posttest)

Data were submitted to repeated measures ANOVA with a design of 3 (group: ICBT, GCBT, WL) x 2 (time: pretest, posttest). In addition to the F ratio partial eta² was extracted to assess the effect size.

The FQ-AG means and standard deviations of the FQ-AG are presented in Table 3.31.

Table 3.31: Mean and SDs of FQ-AG in Pre-treatment and Post-treatment

Group	N	pre-test		post-test	
		M	SD	M	SD
ICBT	15	17.67	4.56	11.60	3.54
GCBT	15	17.47	3.91	12.60	3.04
Waiting list	15	18.20	4.21	17.93	4.30
Total	45	17.78	4.15	14.04	4.55

The results of analysis of variance for severity of agoraphobic avoidance are shown in Table 3.32.

Table 3.32: Results of the ANOVA of Group, Time and Time by Group of FQ-AG from Pre-treatment to Post-treatment

Source	Sum of Squares	df	Middle of Squares	F	p	η ²
Group	211.489	2	105.744	3.559	.036	.145
Time	313.600	1	313.600	188.699	.001	.818
Time x Group	140.600	2	70.300	42.301	.001	.668
Error	69.800	42	1.662			

There was a significant main effect for group, time and a significant interaction effect of time x group. Partial eta² indicates a large effect size for time and a medium effect size for time x group interaction.

Post - hoc tests were used to compare groups with respect to the mean difference between pre- post FQ-AG scores in Table 3.33.

Table 3.33: Pairwise comparisons among Three Groups for FQ-AG Scores

Group I	Group J	Mean Differences	Std. Error	p
ICBT	GCBT	-1.00	1.34	.459
ICBT	Wait-list	-6.33	1.34	0.001
GCBT	Waiting list	-5.33	1.34	0.001

As shown in Table 3.33 patients who participated in the ICBT and GCBT groups showed significantly more reduction in FQ-AG severity scores between pretest and posttest compared to the Wait-list group, while not significantly differing from each other. The findings are shown in Figure 3.11.

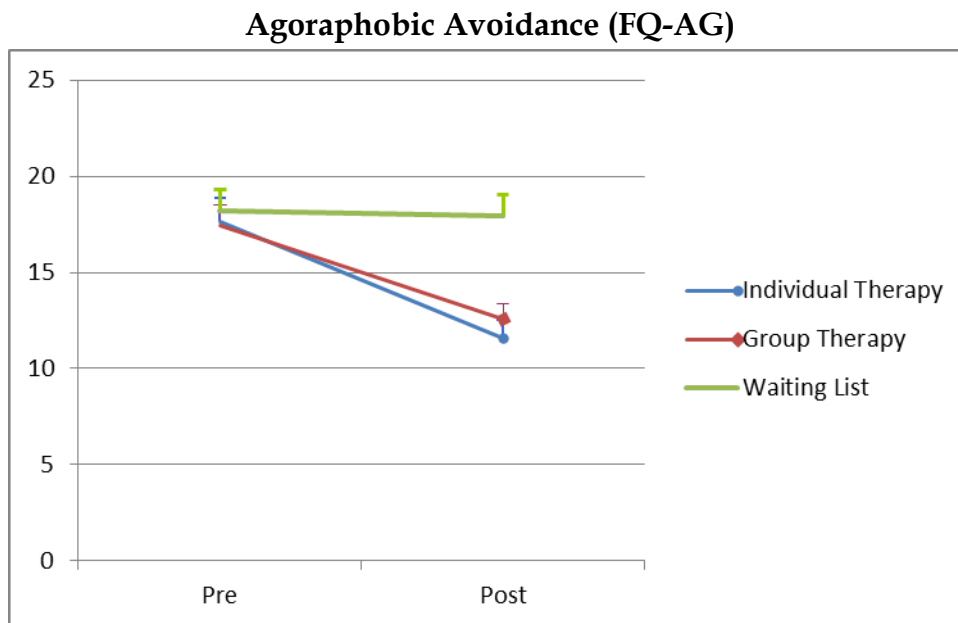


Figure 3.11: Means and standard errors for the agoraphobic avoidance (FQ-AG) of groups at pretest and posttest

Summary

Both treatment groups (Individual CBT, Group CBT) showed significant improvement with regard to the agoraphobic avoidance (FQ-AG) compared to the wait-list control group from pre to posttest, while not significantly differing from each other.

3.3.6.2 Treatment (ICBT/GCBT) by time (pre/post/four-month follow-up)

Data were submitted to repeated measures ANOVA with a design of 2 (Group: ICBT, GCBT) x 3 (Time: pretest, posttest, follow-up).

The group means and standard deviations of the FQ-AG are presented in Table 3.34.

Table 3.34: Mean and SDs of FQ-AG in Pre-treatment, Post-treatment, Follow-up in ICBT and GCBT

Group	N	pre-test		post-test		Follow-up	
		M	SD	M	SD	M	SD
ICBT	15	17.67	4.56	11.60	3.54	9.33	2.66
GCBT	15	17.47	3.91	12.60	3.04	10.87	2.61
Total	30	17.57	4.17	12.10	3.28	10.10	2.71

The results of analysis of variance of the FQ-AG are shown in Table 3.35.

Table 3.35: Results of the ANOVA of Group, Time and Time by Group of FQ-AG from Pre-treatment, Post-treatment to Follow-up

Source	Sum of Squares	df	Middle of Squares	F	p	η^2
Group	13.611	1	13.611	.427	.519	.015
Time	896.356	2	448.178	220.501	.001	.887
Time x Group	11.822	2	5.911	2.908	.063	.094
Error	113.822	56	2.033			

There was only a significant effect for time and partial η^2 indicates a large effect size for time. Furthermore there is no significant difference between treatment groups in reducing FQ-AG. The findings are shown in Figure 3.12.

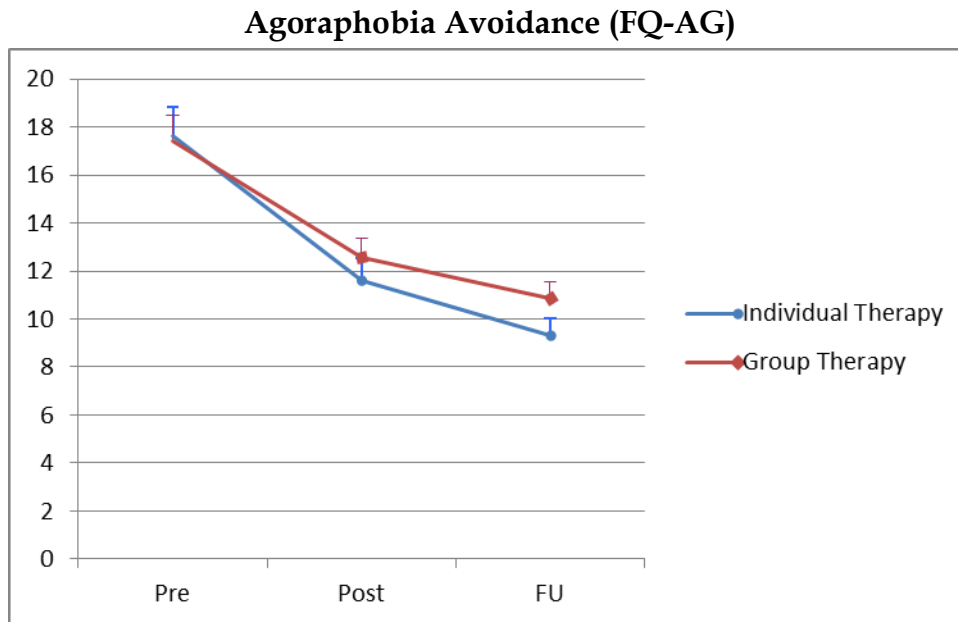


Figure 3.12: Means and standard errors for the Agoraphobic avoidance (FQ-AG) of treatment groups at pretest, posttest, and follow-up

Summary

Participants in both treatment groups (Individual CBT, Group CBT) showed significant improvement with regard to Agoraphobic avoidance (FQ-AG) from pretest, posttest to 4 months follow-up, while not significantly differing from each other.

3.4 Correlations among pretest measures

In order to determine the relationship among variables, a Pearson product-moment correlation coefficient matrix was computed with regard to pretest measures. The correlation coefficients are presented below in Table 3.36.

Table 3.36: Pearson product-moment correlation between dependent variables at pretest N = 45

variable		BDI	PDSS	ACQ	ASI	FQ-AG
BAI	r	0.555**	0.620**	0.618**	0.414**	0.446**
	p	0.001	0.001	0.001	0.005	0.002
BDI	r		0.328*	0.536**	0.309*	0.272
	p		0.028	0.001	0.039	0.070
PDSS	r			0.397**	0.326*	0.367*
	p			0.007	0.029	0.013
ACQ	r				0.307*	0.418**
	p				0.040	0.004
ASI	r					0.343*
	p					0.021

* Correlation is significant at the 0.05 level (2-tailed)

** Correlation is significant at the 0.01 level (2-tailed)

Results the correlational analysis between pretest measures indicated that there was a significantly positive correlation between the BAI and all other measures. The following scatterplots show that the significant correlations are not due to outliers.

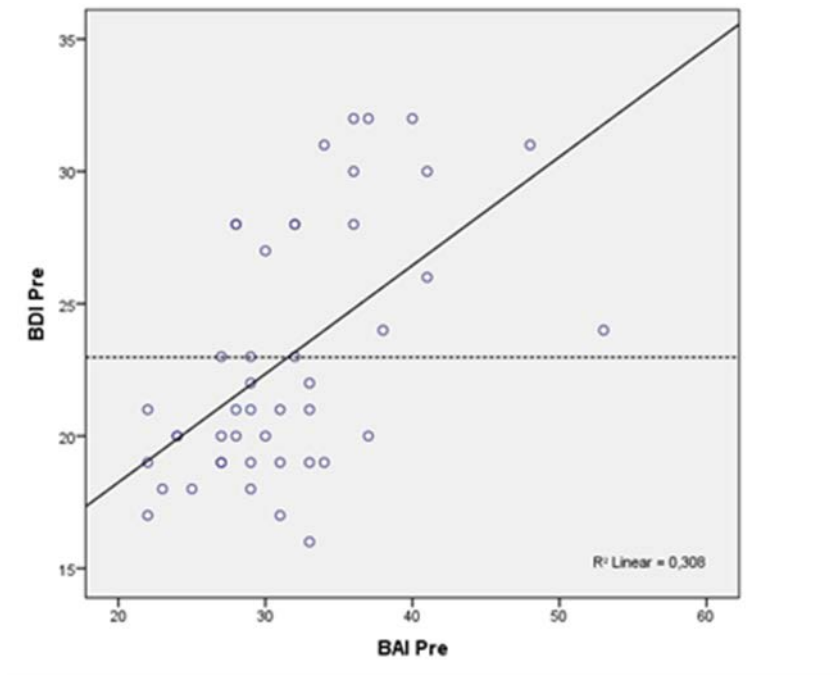


Figure 3.13: Scatterplot between BAI and BDI

There is a high significant positive correlation between anxiety (BAI) and depression (BDI), ($r = 0.55$, $p = .001$). This correlation indicates that increases in BAI were correlated with increases in BDI.

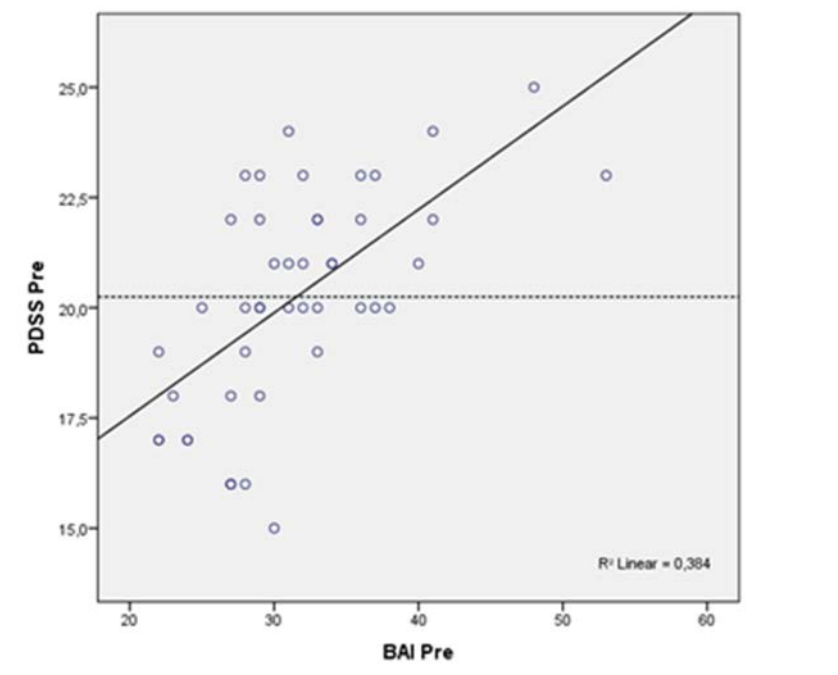


Figure 3.14: Scatterplot between BAI and PDSS

There is a high significant positive correlation between anxiety (BAI) and panic disorder severity (PDSS), ($r = 0.62$, $p = .001$). This correlation indicates that increases in BAI were correlated with increases in PDSS.

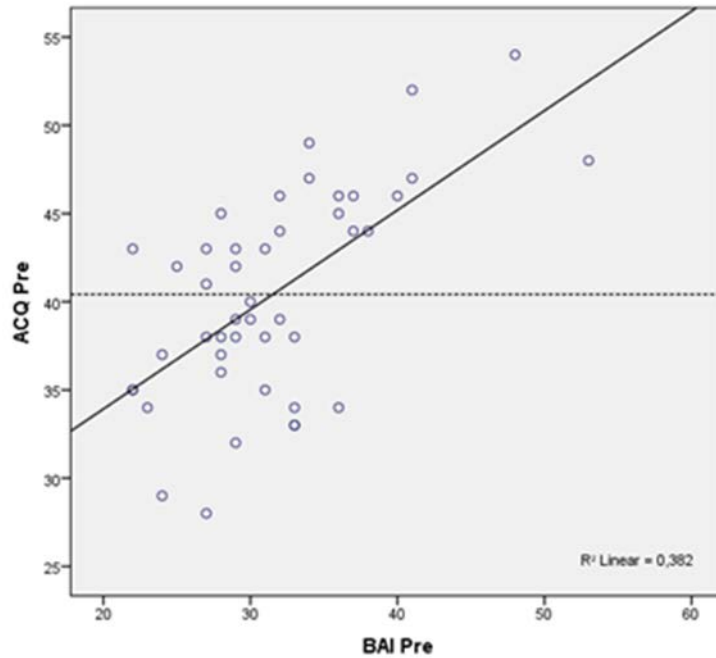


Figure 3.15: Scatterplot between BAI and ACQ

There is a high significant positive correlation between anxiety (BAI) and agoraphobic cognition (ACQ), ($r = 0.62$, $p = .001$). This correlation indicates that increases in BAI were correlated with increases in ACQ.

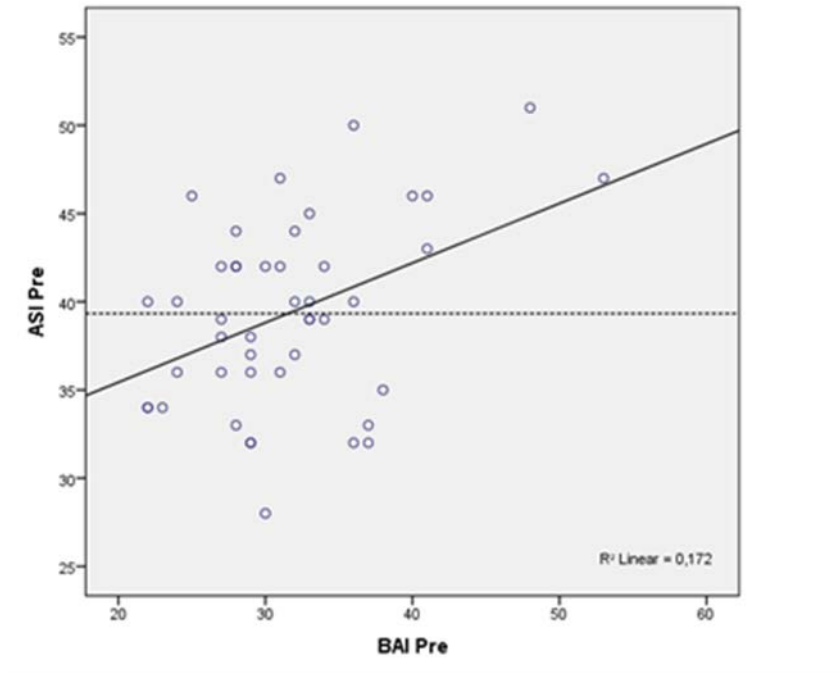


Figure 3.16: Scatterplot between BAI and ASI

There is a high significant positive correlation between anxiety (BAI) and anxiety sensitivity (ASI), ($r = 0.41$, $p = .005$). This correlation indicates that increases in BAI were correlated with increases in ASI.

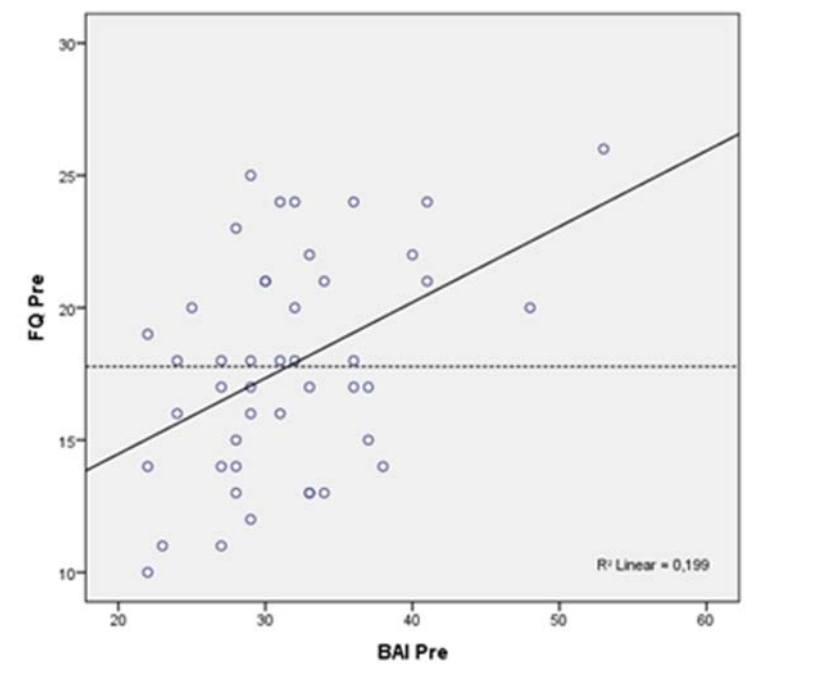


Figure 3.17: Scatterplot between BAI and FQ-AG

There is a high significant positive correlation between anxiety (BAI) and agoraphobic fear (FQ-AG), ($r = 0.45$, $p = .002$). This correlation indicates that increases in BAI were correlated with increases in FQ-AG.

The BDI was also significantly positively correlated with all measures apart from the FQ-AG. The following scatterplots illustrate the correlations.

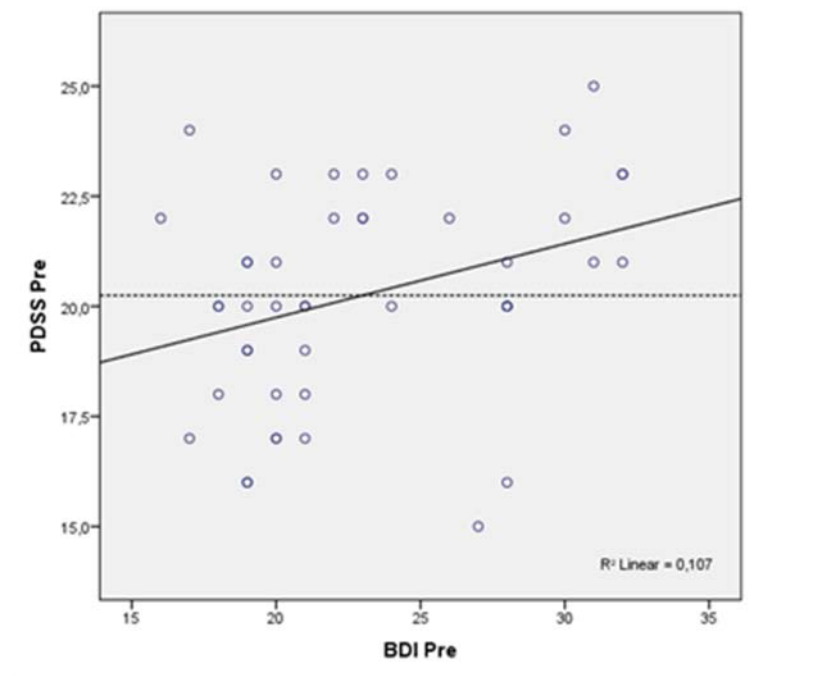


Figure 3.18: Scatterplot between BDI and PDSS

There is a significant positive correlation between depression (BDI) and panic disorder severity (PDSS), ($r = 0.33$, $p = .028$). This correlation indicates that increases in BDI were correlated with increases in PDSS.

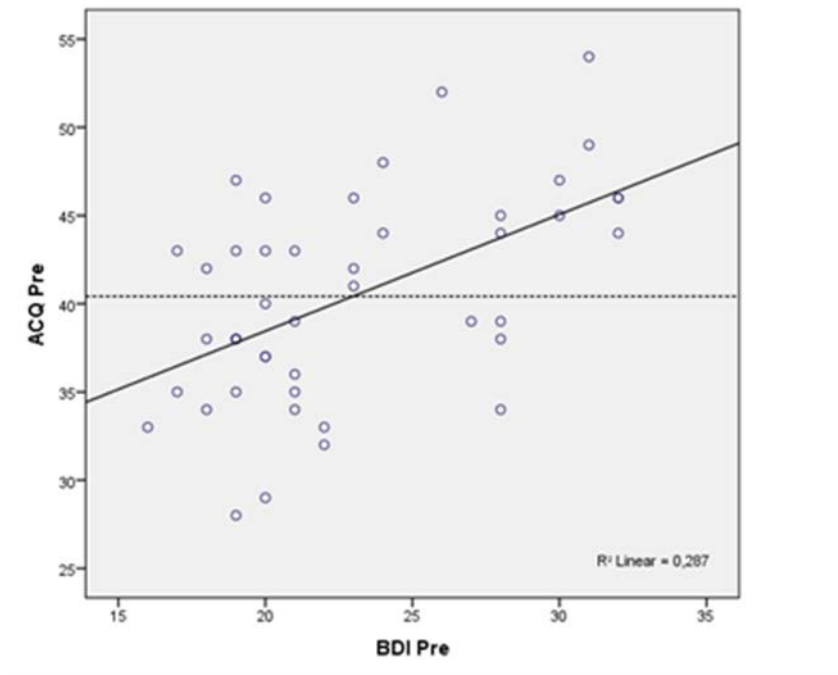


Figure 3.19: Scatterplot between BDI and ACQ

There is a high significant positive correlation between depression (BDI) and panic agoraphobic cognition (ACQ), ($r = 0.54$, $p = .001$). This correlation indicates that increases in BDI were correlated with increases in ACQ.

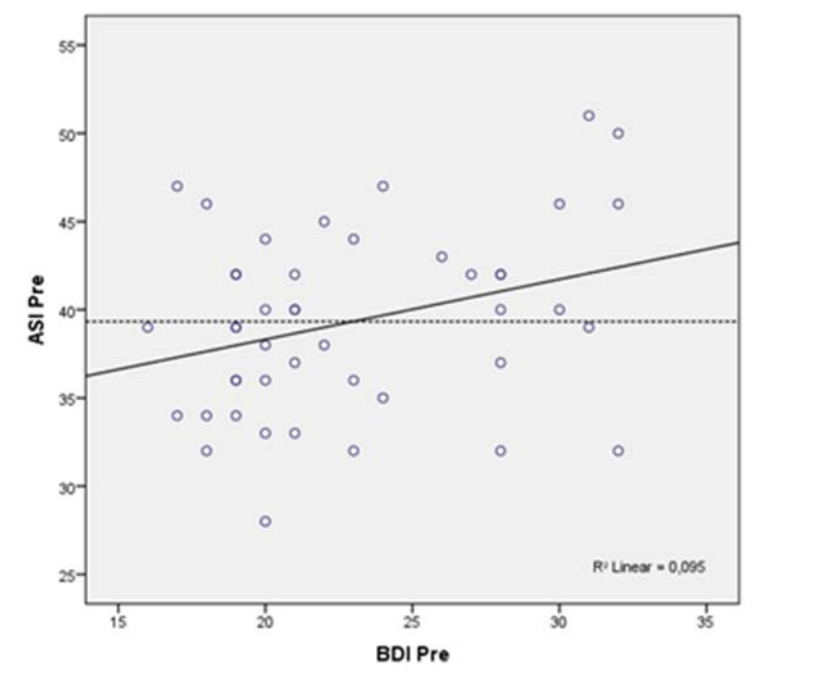


Figure 3.20: Scatterplot between BDI and ASI

There is a significant positive correlation between depression (BDI) and panic agoraphobic cognition (ACQ), ($r = 0.31, p = .039$). This correlation indicates that increases in BDI were correlated with increases in ASI.

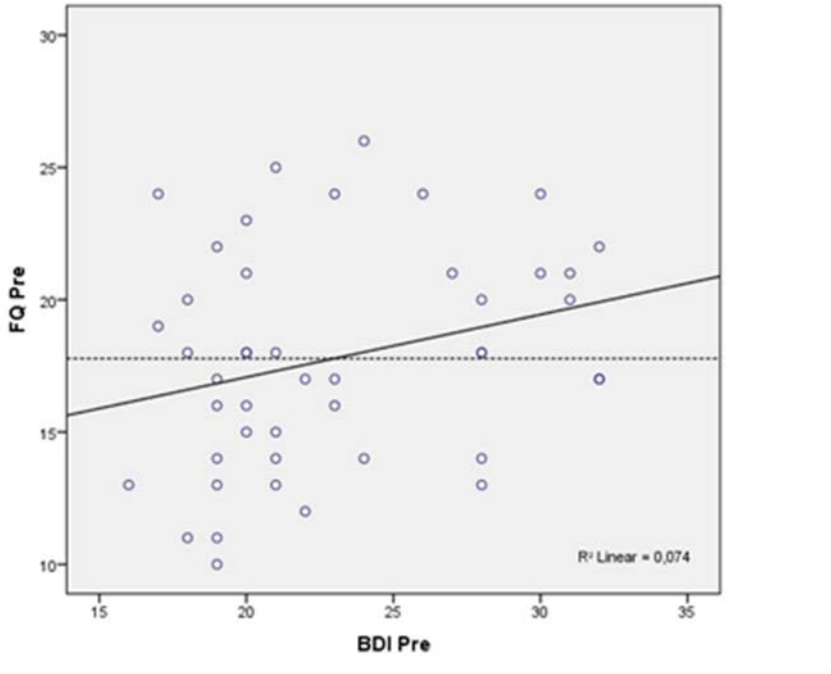


Figure 3.21: Scatterplot between BDI and FQ-AG

There was a significantly positive correlation between the PDSS and all other measures. The following scatterplots show that the significant correlations are not due to outliers.

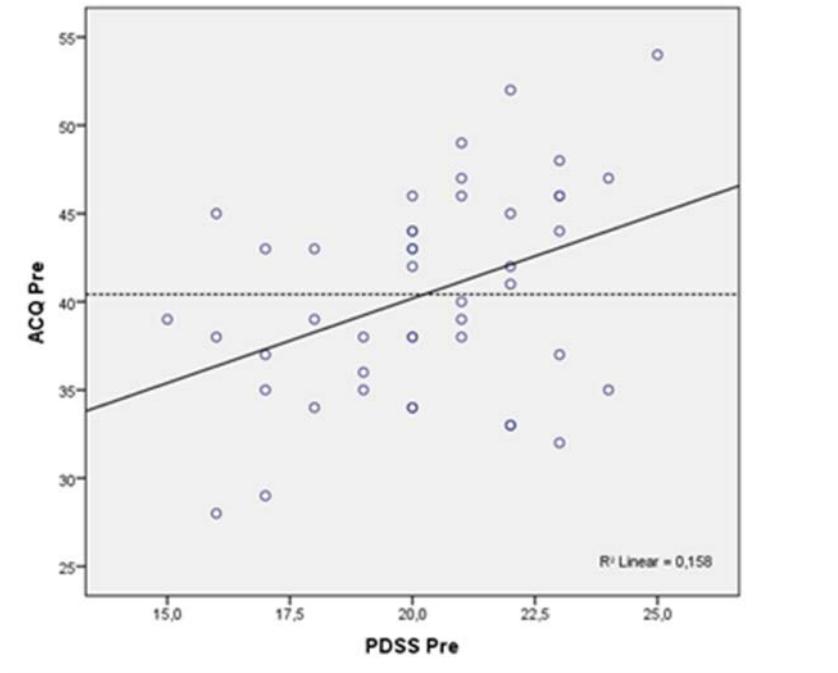


Figure 3.22: Scatterplot between PDSS and ACQ

There is a high significant positive correlation between panic disorder severity (PDSS) and agoraphobic cognition (ACQ), ($r = 0.40$, $p = .007$). This correlation indicates that increases in PDSS were correlated with increases in ACQ.

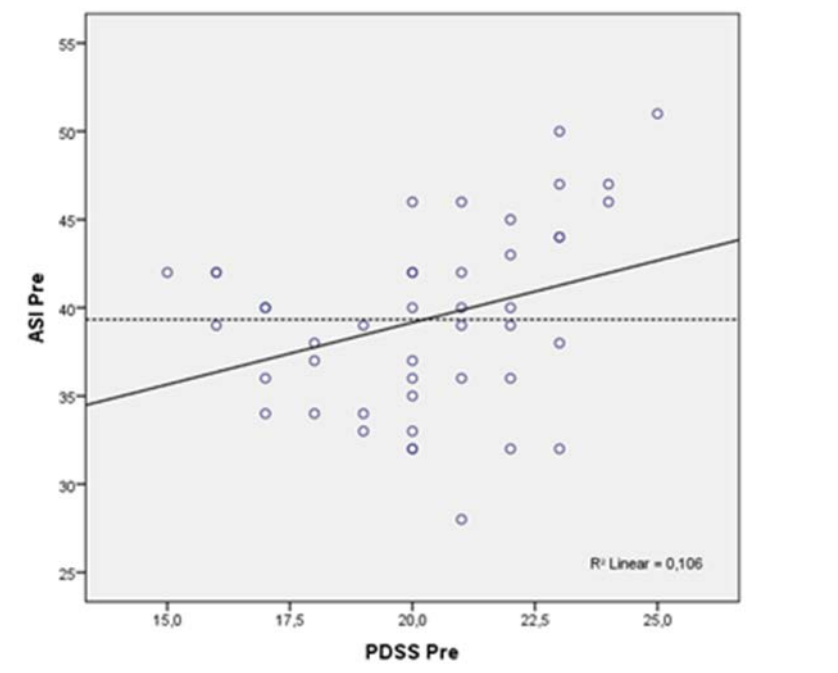


Figure 3.23: Scatterplot between PDSS and ASI

There is a significant positive correlation between panic disorder severity (PDSS) and

anxiety sensitivity (ASI), ($r = 0.33, p = .029$). This correlation indicates that increases in PDSS were correlated with increases in ASI.

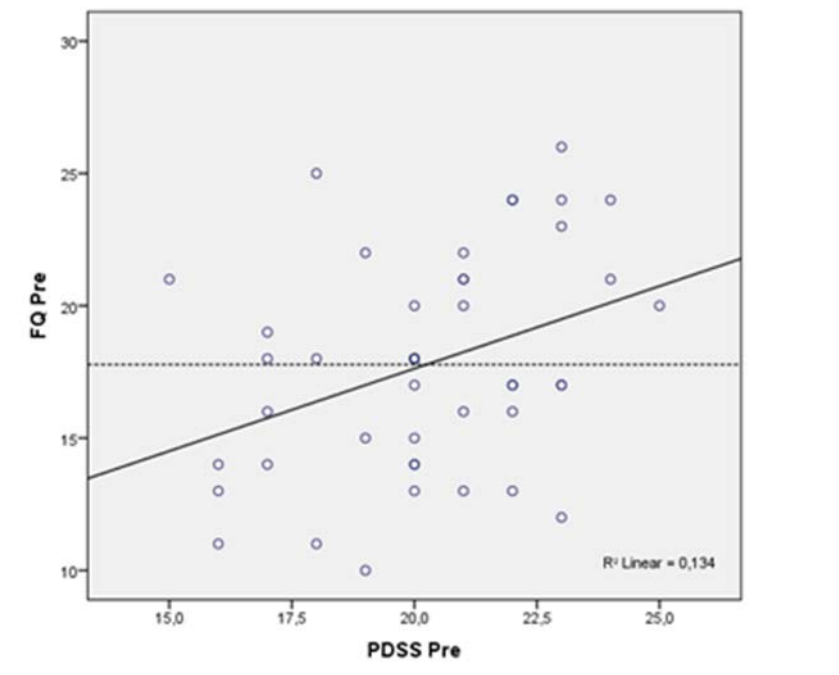


Figure 3.24: Scatterplot between PDSS and FQ-AG

There is a significant positive correlation between panic disorder severity (PDSS) and agoraphobic fear (FQ-AG), ($r = 0.37, p = .013$). This correlation indicates that increases in PDSS were correlated with increases in FQ-AG.

There was a significantly positive correlation between the ACQ and all other measures. The following scatterplots show that the significant correlations are not due to outliers.

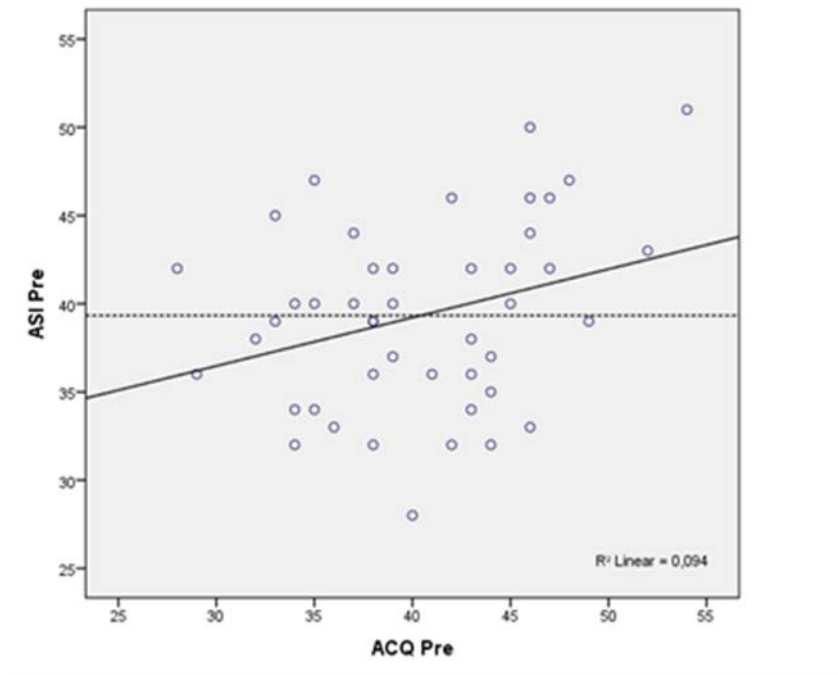


Figure 3.25: Scatterplot between ACQ and ASI

There is a significant positive correlation between agoraphobic cognition (ACQ) and anxiety sensitivity (ASI), ($r = 0.31, p = .040$). This correlation indicates that increases in ACQ were correlated with increases in ASI.

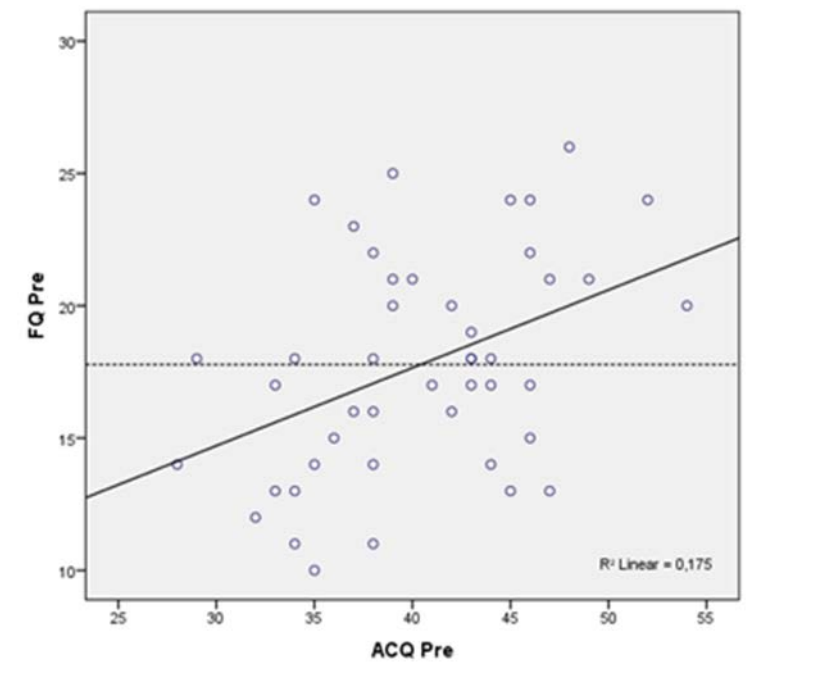


Figure 3.26: Scatterplot between ACQ and FQ-AG

There is a high significant positive correlation between agoraphobic cognition (ACQ)

and agoraphobic fear (FQ-AG), ($r = 0.42$, $p = .004$). This correlation indicates that increases in ACQ were correlated with increases in FQ-AG.

There was a significantly positive correlation between the ASI and all other measures. The following scatterplots show that the significant correlations are not due to outliers.

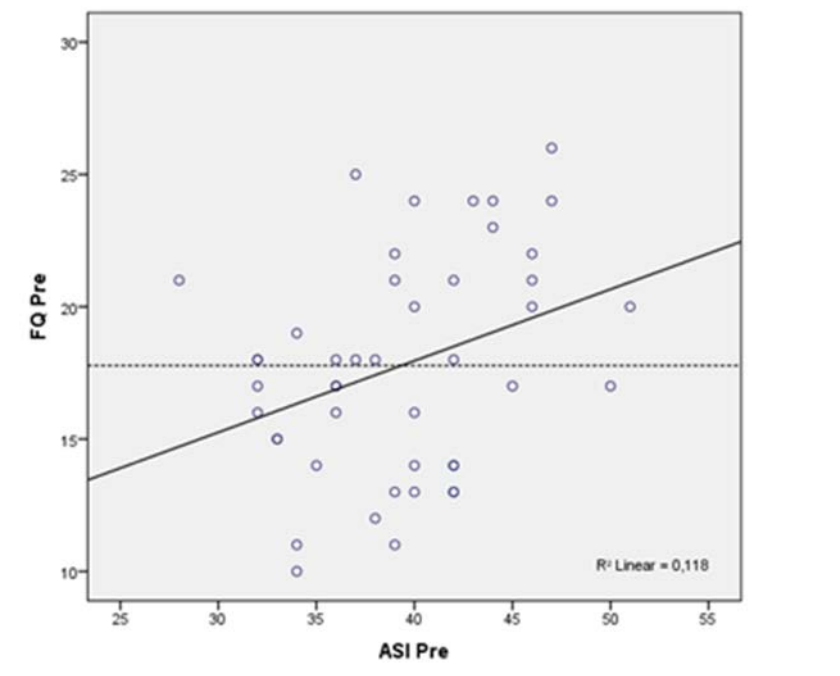


Figure 3.27: Scatterplot between ASI and FQ-AG

There is a significant positive correlation between anxiety sensitivity (ASI) and agoraphobic fear (FQ-AG), ($r = 0.34$, $p = .021$). This correlation indicates that increases in ASI were correlated with increases in FQ-AG.

Summary

The results of correlational analysis indicated that there were a significant positive correlation between all measures apart from BDI and the Fear-Agoraphobia Questionnaire (FQ-AG).

Chapter IV - Discussion

Although a growing literature supports the effectiveness of cognitive-behavioral therapies for patients with panic disorders in general, less is known about the efficacy of individual compared to group CBT programs for patients with PD. In addition there have been no previous studies comparing the effectiveness of these formats with this type of psychotherapy in an Iranian population. Hence the present study investigated the comparative efficacy and difference between CBT implemented in an individual /group format in a sample of patients with panic disorder with or without agoraphobia. These two formats of treatments were compared with a waiting list control group.

The principal findings of the current investigation are the following: Compared with the waiting list group, both of the active treatment conditions (group CBT and individual CBT) resulted in a significant greater decrease from pre to post treatment in Depression, Anxiety, Agoraphobic Cognitions, Agoraphobic avoidance, Panic Disorder Severity Scale, and Sensitivity to Anxiety.

There was a significant difference between the two treatment groups from pre to post treatment, and 4 month follow-up. Data analysis revealed that, compared with the waiting list control group, the participants in both CBT formats showed significant improvement after treatment, while, participants in both treatment formats were equally effective in the reduction of, depression (BDI), agoraphobic cognition (ACQ), sensitivity of anxiety (ASI) and agoraphobia (FQ-AG), but individual CBT led to greater improvement than group CBT in relation to the reduction of overall anxiety (BAI), and panic disorder severity (PDSS) in post treatment. Furthermore participants in both treatment groups is maintained their improvement at 4 months follow-up phase, while, individual CBT group led to greater improvement than group CBT in relation the reduction of overall anxiety (BAI), depression (BDI), panic disorder severity (PDSS) and sensitivity to anxiety (ASI) at 4 months follow-up.

4.1 Severity of PD

The results of the present study indicated that all participants in the three conditions exhibited severe levels of anxiety (cut-off score: of 26 and above) and moderate depression (cut-off score: of 28 and above) in baseline assessments, while the BAI and BDI baseline scores of the three groups did not differ significantly.

Patients with panic disorder suffer from a wide range of anxiety, stress and depression and approximately 60% of patients report depressive and anxiety symptoms (Cameron, 2007). Anxiety and depressive symptoms are often comorbid with each other. The comorbidity of depressive and anxiety symptoms are associated with barriers to treatment and worse psychiatric outcomes, including treatment resistance, increased risk for suicide, greater chance for recurrence, and greater utilization of medical resources, (Aina & Susman, 2006). As Grillon et al. (2008) stated, in panic disorder, persistent symptoms of anxiety are caused by anticipation of the next uncued (unpredictable) panic attack. Anticipatory anxiety is a strong predictor for the "autonomic" subtype, and a reverse predictor for the cognitive subtype in panic disorder (Sarp, et al., 2010). Some support for this position is found in studies of the BAI where individuals with panic disorder attain significantly higher scores on the BAI than those with other anxiety disorders (e.g., Leyfer, Ruberg, Woodruff-Borden, 2006).

Grillon et al., (2008) in a study showed patients with panic disorder are overly sensitive to unpredictable aversive events and exhibit severe anxiety in the unpredictable condition.

Similar results were found in a study by King et al (2011). They reported patients with panic disorder suffer from a severe level of anxiety. They reported severe mean scores ($M=34.9$) for BAI scale in 50 patients with PD at baseline.

The findings of the current study are consistent with the findings of Beck & Steer (1990). They reported in the manual, the BAI total score means and standard deviations for panic disorder is ($M= 27.27, SD=13.11$).

The results of this study indicated that the BDI baseline scores of the three groups did not differ significantly. The BDI total mean score for three groups indicated

moderate depression (cut-off score 20 and above).

Individuals diagnosed with panic disorder tended to yield lower quality of life and depression scores than anxiety disorders expect PTSD (Pollock & Kuo, 2004).

Analysis of depression in PD can be explained by a reduction in positively reinforced behaviors and in an increase in negatively reinforced escape and avoidance behaviors, including also verbal behaviors like complaining (Bergström, et al., 2010).

The results of study by Salkovskis, Hackmann, et al., (2006) and Chambless (1985) also showed a moderate rate of depression as is assessed with BDI in patients with PDA. The authors stated that avoidance behaviors may also act as risk factors in the onset of depression.

The unpredictability of panic attacks and the ongoing symptomatology often lead to feelings of helplessness and maladaptive coping strategies and as a result patients show elevated levels of depression (Lepöla, Koponen & Leinonen, 1996).

Gregor, et al. (2005) in a study of 39 PD patients found increased impairment in both family/home responsibilities, social functioning and less participation in life activities led to incidences of depression and reduction of quality of life. This correlation may exist because panic attacks can be so debilitating that they interfere with life functioning and can subsequently result in a decreased sense of worth and symptoms of depression. Hence, depression is likely to be secondary to agoraphobic anxieties, anticipatory anxiety or other symptoms related to panic disorder.

Therefore when panic symptoms begin to decrease, life functioning and social integration may improve and result in a decrease in depressive symptoms as well.

The results of this study indicated that the PDSS baseline scores of the three groups did not differ significantly. The PDSS total mean score for the three groups indicated severe level of panic disorder severity (cut-off score 14 and above).

The Panic Disorder Severity Scale (PDSS) assesses the severity of seven dimensions of PD symptoms and functional impairment: 1) frequency of panic attacks, 2) distress during panic attacks, 3) anticipatory anxiety, 4) agoraphobic fear/avoidance, 5) interoceptive fear/avoidance, 6) impairment/interference in work function and 7) impairment/interference in social functioning.

Similar results were found in a study by Choi et al (2012). They reported patients

with panic disorder suffer from a severe level of panic disorder (PDSS) scale. They reported severe mean scores for PDSS scale in 119 patients with PD at baseline.

The results of this study indicated that the ACQ baseline scores of the three groups did not differ significantly. The ACQ total mean score for the three groups indicated a severe level of agoraphobic cognition severity.

According to Clark & Beck (2009), the mean ACQ total score for panic disorder is approximately 28, with post-treatment scores dropping to 19.

Similar levels of ACQ were reported by Hoffart et al., (2008), Salkovskis, Hackmann, et al., (2006), Michelson, et al., (1990), Manjula et al., (2009). They reported patients with panic disorder suffer from a severe level of Agoraphobic Cognition (AC) before beginning treatment.

The agoraphobic cognition questionnaire (ACQ) assessed "fear of fear", and the frequency of maladaptive thought and catastrophic consequence about both the physical and social consequences (e.g., fainting, choking, heart attack, loss of self-control) when experiencing panic attack.

The findings of the current study are consistent with various clinical studies that indicated that most individuals with panic disorder report thoughts or images of physical or mental catastrophe in response to internal stimuli during panic episodes. According to Hofmann et al., (2007) catastrophic appraisals play a key role in the pathogenesis of panic attacks and PD. The catastrophic misinterpretation of bodily sensations and symptoms was postulated as the main cognitive mechanism in panic disorder. Goldstein and Chambless (1978) labeled this fear of experiencing anxiety or panic attacks as "fear of fear". This leads to hypervigilance about bodily sensations, increased arousal of the sympathetic nervous system, more physical sensations and heightened anxiety, which then spiral into a panic attack and as a result of these catastrophic cognitions the symptoms are maintained.

The results of this study indicated that the patients in three groups exhibited high anxiety sensitivity on ASI (cut-off score: of 27 and above) and there was no significant difference between groups in the pretreatment.

Prospective studies have demonstrated that elevated AS is a risk factor for the

subsequent development of panic attacks (Hayward, et al., 2000; Plehn & Peterson, 2002). The results of a study by Dixon et al., (2013) also indicated that ASI scores often predict panic symptoms in response to biological challenges (e.g., carbon dioxide inhalation) that provoke feared bodily sensations. Prospective longitudinal studies indicate that scores on the ASI predict subsequent spontaneous attacks, indicating that elevated anxiety sensitivity is a risk factor for panic disorder.

The results of a meta-analysis Olatunji, Wolitzky-Taylor (2009), that included 38 studies, revealed panic disorder associated with greater AS compared to other anxiety disorders except for posttraumatic stress disorder. These findings suggest that AS is central to the phenomenology of panic disorder.

Similar levels of ASI were reported by Manjula et al., (2009), Hecker et al., (2004) and Teachman et al. (2008). They reported patients with panic disorder suffer from a severe levels of Anxiety Sensitivity (AS) scale before beginning intervention.

Research on the psychopathology of panic disorder suggests that patients with panic disorder have a psychological predisposition to respond fearfully to physiological cues of arousal and various reviews also support that individuals with panic disorder are significantly more likely to misinterpret bodily sensations in terms of a serious impending threat or danger than non-panic comparison groups (see Casey et al., 2004b). Moreover, there is considerable empirical evidence that panic disorder is characterized by elevated scores on the ASI fear of somatic sensations subscale (e.g. Deacon & Abramowitz, 2006, Rector et al., 2007, Taylor, Zvolensky, et al., 2007).

Schneider and Schulte (2008) found that individuals with panic disorder exhibited a significantly higher automatic priming effect for ideographically selected anxiety symptom primes followed by catastrophic interpretations than nonclinical controls.

The authors interpret this automatic priming effect as a consequence of strong idiographic associations produced by the relation of catastrophic thoughts to bodily symptoms during panic attacks.

According to Peterson and Reiss (1993), high levels of anxiety sensitivity should increase the frequency of panic attacks by contributing to the tendency to interpret bodily sensations in a catastrophic manner, thus increasing the chances that a panic attack will occur. They further argued that anxiety sensitivity should increase the

intensity of panic attacks, since individuals with high anxiety sensitivity should be especially frightened by panic sensations. They stated that anxiety sensitivity would reduce a person's capacity to cope with panic attacks, as people with low anxiety sensitivity would be able to dismiss panic attacks as temporary events while those with high anxiety sensitivity would interpret panic attacks as a sign of possible mental or physical illness.

According to Beck, anxiety conditions are created and maintained by faulty cognitive processes that exaggerate physical and psychosocial dangers. In other terms, patients with panic disorder have significant negative perceptions of their physical health and increased fear of autonomic arousal. Hence they display more negative health perceptions and higher levels of anxiety sensitivity (Markowitz et al., 1989; Schmidt, Telch, & Joiner, 1996).

The results of this study indicated that the patients in the three groups exhibited high agoraphobic avoidance on FQ-AG and there was no significant difference between groups in the pretreatment.

The main feature of panic disorder is anxiety about being in a situation or place from which escape may be difficult, or in which help may not be easily available should a panic attack or panic-like symptoms occur. This anxiety usually leads to safety behaviors or avoidance of a variety of feared situations because they are used by panic patients to "prevent" a panic attack. Situations which are commonly avoided by individuals with PDA include: being alone away from home; being home alone; crowded areas; malls, travelling in buses, trains, cars, or planes; going to a new place, closed spaces and open spaces. Some individuals are able to face these situations but usually do so with reluctance and dread or sometimes the individual feels more comfortable about being in these situations if accompanied by someone else.

4.2 Effectiveness of treatment (pretest to posttest)

The results from this study indicated that compared with the waiting list control group, patients who participated in the individual CBT and group CBT showed a significant improvement in reducing overall anxiety severity from pretest to post treatment, however further improvement with ICBT showing better gains in reducing of the anticipatory anxiety (BAI). As anticipatory anxiety scores moved from severe anxiety in pretreatment to mild anxiety in ICBT and moderate anxiety in GCBT after treatment.

Many studies have found the positive effects of CBT treatment in reductions of depression and anxiety scores when panic severity and frequency decreased (i.e., Sharp, Power, Swanson, 2004., Soares et al., 2013., Deacon & Abramowitz, 2006).

In a group consisting of 454 patients with panic disorder, Allen et al., (2010) examined the relationship of between depression and anxiety to treatment outcome cognitive-behavior therapy for panic disorder. They found CBT responders showed greater reductions on measures of anxiety and depressive symptoms. These data suggest that successful treatment of panic disorder is associated with reductions of comorbid anxiety and depressive symptoms.

Bohni et al., (2009) have substantiated that group CBT produced significant decreases in overall anxiety (BAI) scores in thirty-nine patients with panic disorder. The improvements correspond to a large effect size.

In agreement with results of this study Neron, Lacroix, Chaput, (1995) also found ICBT and GCBT significantly effective in reducing anxiety symptoms in total BAI and HAMA (Hamilton Anxiety) scores in post treatment. However, a differential effect favouring individual CBT over group CBT was observed with regards to symptoms other than panic, such as generalized anxiety and depressive symptoms. Thus our study replicated the finding of by Néron, Lacroix & Chaput (1995).

The present finding is consistent with Sharp, Power & Swanson (2004) who obtained a substantial improvement in reduction of anxiety symptoms in a similar study comparing individual therapy and group therapy over 8 sessions with waiting list control group. At treatment end-point, in terms of statistical significance, both formats of treatment were significantly superior to waiting list control but on the

other hand, this result is not consistent with their results who obtained improvement in reduction of anxiety symptoms in individual therapy and group therapy with no significant difference between each other. At treatment end-point, in terms of statistical significance, both the formats of treatment were significantly superior to waiting list control but did not differ significantly from each other, but when clinical significance of outcome at treatment end-point was considered, individual CBT showed a significant advantage over both group CBT and waiting list control. It must be noted that their study had some methodological limitations, such as patients taking concurrent psychotropic medications were not excluded from the study, but were required to continue taking these medications as prescribed throughout the study period. In contrast the present study excluded individuals on psychotropic medication including benzodiazepine or concurrent psychotropic medications, from participation. It is likely that this difference in samples accounted for the differing results. In addition, it must be noted that measures of anxiety and depression (Hamilton Anxiety Scale and the Montgomery Asberg Depression) in their study were rated by the psychologist rather than self-report measures. This might also account for the differences.

These results also are not consistent with a study conducted by Marchand, et al., (2009). They compared 14-session standard CBT, 14-session group CBT and 7-session brief CBT in the treatment of patients with moderate to severe PDA taking either anxiolytic or antidepressant medication or a combination of both. They reported all three-treatment formats significantly reduced the anticipatory anxiety (BAI) symptoms with high effect sizes, and there were no statistical differences between them after treatment. It must be noted that in their study all participants took either anxiolytic or antidepressant medication or a combination of both. Again, the use of patients on medications may account for the results of their study. As previously mentioned the present study excluded individuals from participation for use of psychotropic medication.

The results of a study by King et al., (2011), Beck, Sokol, Clark, Berchick, Wright (1992) and Sokol, Beck, Greenberg, et al., (1989) on group of patients with PD reported that individual CBT produced significant decreases in overall anxiety (BAI)

scores in the CBT group compared with control group by the end of treatment. Similar results were found for CBT interventions delivered in group format. The results of a study by Kim et al., (2010) and Telch, et al., (1993) on group of patients with PD also reported that group CBT produced more significant decreases in overall anxiety scores (BAI) compared with control groups.

The results from this study also indicated that patients who participated in the ICBT and GCBT groups demonstrated significantly greater reduction in the severity of depression symptoms compared to the Wait-list control group from pretest to post treatment, while there was no significant difference between each other. Most notably, participants in two treatment formats moved from moderate levels of depression at pre-treatment to mild range of depression at end of treatment.

Consistent with this study's results, Sharp, Power, Swanson (2004) and Marchand, et al., (2009) and Neron, Lacroix, Chaput, (1995) also showed the effectiveness of ICBT and GCBT in treating PD symptoms related to depression and concluded that ICBT and GCBT were significantly effective in reducing total depression scores in post treatment with no significant difference between each other.

Consistent with this study's results, a meta-analysis (in 23 studies) conducted by Oei, Llamas & Devilly (1999) showed the effectiveness of CBT in treating fear symptoms related to depression and avoidance in panic disorder patients and suggested that both group and individual format of CBT can be regarded as the established treatment of PD to reduce depression and avoidance compare with no-treatment control groups at post-treatment.

The effect of CBT on depression symptoms has been shown by Emmrich et al., (2012), Clark et al., (1999), Teachman, Marker & Smith-Janik (2008) and Tsao, Mystkowski, Zucker, and Craske (2002). They found individual CBT is more effective in treating depressive symptoms comorbid with panic disorder in patients with PDA compared with waiting list control group. The results suggested that CBT can be regarded as an established treatment of depression or depressive symptomatology in panic disorder. A study conducted by Carter, Sbrocco, Gore, et al., (2003) reported group CBT program had a more positive impact in reducing depression levels after termination of treatment in 25 patients with panic disorder than waiting list control group.

The results of this study indicated that both treatment formats demonstrated significantly greater reduction in the severity of panic attacks compared to the wait-list control group in posttreatment, however, participants in ICBT group showed significantly greater improvement than GCBT in post treatment. The results showed that severity of panic disorder (PDSS) scores moved from severe range in pretreatment to non-clinical range in ICBT and moderate range in GCBT in posttreatment.

Results from some studies suggested that reduction of panic severity was associated with both decreases in danger related cognitions and increases in sense of self-efficacy or effectiveness in dealing with such panic situations (Clark et al., 1999; Teachman, et al., 2008). However, studies that report post-treatment changes in both factors leave open the possibility that changes in one factor may be simply a co-effect of changes in the other factor (Bandura, 1988).

These results also are not consistent with a study conducted by Marchand et al., (2009). They found ICBT and GCBT were equally effective in reducing severity of panic disorder (PDSS) scores at post treatment. Thus our study did not replicate the finding of Marchand et al. As previously mentioned, the differing results might be due to use of a medicated sample group.

In agreement with results of this study, similar findings have been reported by Nakano et al., (2008), Manjula, et al., (2009), Meulenbeek, et al., (2010) and Bergström et al., (2010) who showed a significant reduction in panic disorder severity (PDSS) among group of patients with PD. They found that participants in group CBT condition improved more in reduction of PDSS than control condition in post treatment.

The findings of the current study are consistent with the findings of Beck, Sokol, Clark, Berchick & Wright (1992) and Hofmann, et al., (2007) they examined changes in panic disorder severity among group of patients with panic disorder. They have demonstrated that individual CBT led to a significant impact on reduction of severity of panic disorder (PDSS) compared with control group.

The results from this study indicated that patients who participated in the ICBT and GCBT groups demonstrated significantly greater reduction in the severity of

agoraphobic cognition (AC) scores compared to the Wait-list control group, while there was no significant difference between each other.

Reduction in catastrophic agoraphobic cognition or behavioral avoidance could result from a generalization of anxiety coping skills learnt during CBT. Therefore, patients might use these skills in the posttest period to reduce behavioral avoidance and fears.

These results also are consistent with a study conducted by Marchand et al., (2009). They found ICBT and GCBT were equally effective in reducing agoraphobic cognition (ACQ) scores at post treatment and maintained at two years follow-up. Thus our study replicated the finding of Marchand et al.

Many studies suggest that successful treatment was associated with a reduction in catastrophic cognitions (AC) (Noda et al., 2007; Taylor, 2000; Hofmann et al., 2007). These studies reported that numerous variants of CBT intervention for PDA successfully reduced catastrophic cognitions and symptomatic improvement in the majority of cases and therefore regarded as a first-line treatment.

Taylor (2000) reported that modifying patients' catastrophic misinterpretations of bodily sensations resulted in significant reductions in panic disorder.

Recent works (e.g. Hofmann et al., 2007; Smits, Powers, Cho & Telch, 2004) discuss the role of CBT in changes of catastrophic cognitions (AC) during treatment of PDA. Production of the catastrophic misinterpretation will increase panic symptoms in panic disorder individuals, whereas correction of the misinterpretation will prevent panic attacks.

Hofmann et al., (2007) suggest that catastrophic cognitions relating to physical, mental, and social concern were mediators of treatment change for individuals with PDA who received CBT as a component of their treatment while, Smits et al., (2004) showed that CBT effects on PDA were partially mediated by the reduction of fear of fear that led to reduction of agoraphobia. The results of their study indicated that CBT improved the adjustment level in patients with PDA in overt behaviors, cognitions, and somatic sensations.

Casey, et al., 2004b) investigated the role of both negative and positive cognitions in predicting panic severity in an international sample of 149 PD patients. They found

that catastrophic misinterpretation of bodily sensations predicted high panic severity while positive cognitions led to better management of panic attacks.

Exposure is considered the essential element of CBT for anxiety disorders especially reducing agoraphobic cognition in patients with PD (Moscovitch, Antony, & Swinson, 2009, Malbos et al., 2013). Beck and Shipherd (1997) found that fear sensitization and habituation of fear-anxiety are important in the success of CBT in reducing the frequency and severity of fear of bodily sensations and agoraphobic cognitions in treatment of PD patients.

The findings of the current study are also consistent with the findings of Noda, Nakano et al., (2007). They examined changes in agoraphobic cognition severity among 95 patients with PD. They demonstrated that group CBT led to significant impact on reduction of severity of Agoraphobic cognition, panic-related fear and avoidance and reduced their functional impairment in posttreatment.

Gloster, Wittchen, Einsle et al., (2011), Hendriks et al., (2010) King et al., (2011) found that individual CBT formats was more effective than a wait-list control group in the improvement and reduction of agoraphobic avoidance to modify catastrophic cognition among groups of PD patients.

The results from this study indicated that patients who participated in the ICBT and GCBT groups demonstrated significantly greater reduction in anxiety sensitivity (ASI) compared to the Wait-list control group in posttest, while there was no significant difference between each other. As the participants in two treatment formats moved from severe levels of sensitivity to anxiety at pre-treatment to moderate range at end of treatment.

The current study provides support for the effectiveness of CBT intervention at lowering anxiety sensitivity and extends the work of previous studies. Some studies suggest that the reduction in anxiety sensitivity is specific for CBT treatment (Deacon & Abramowitz, 2006; Hofmann et al., 2007; Smit et al., 2008a).

These results also are consistent with a study conducted by Marchand et al., (2009). They found ICBT and GCBT were equally effective in reducing anxiety sensitivity (ASI) scores at post treatment. Thus our study replicated the finding of Marchand et al.

A meta-analysis (Smits, et al., 2008b), that included 16 studies, revealed a large AS reduction effect size ($d = 1.40$) for CBT interventions in individuals with PD and other Axis I pathology. Additional analyses revealed that the average participant receiving CBT improved more than 92% of control group participants. These results suggest that CBT treatments aimed at ameliorating panic and other related disorders also lead to reductions in AS levels.

The results of study by McNally and Lorenz (1987), Taylor & Cox, (1998), Smits, et al., (2004), Smits et al., (2008a) and Hofmann et al. (2007) also indicated an overall reduction of anxiety sensitivity in those who had successfully completed individual cognitive-behavioral treatment for panic disorder. As expected, treatment participants experienced a reduction in AS levels from the clinical to non-clinical range, compared with the non-treatment control group at posttreatment.

Additionally, the current results regarding the effectiveness of group CBT on reducing ASI support findings from previous studies. Bohni et al., (2009) Penava et al., (1998) , Carter et al., (2003) and Schmidt, Trakowski, and Staab (1997), found a reduction in anxiety sensitivity among group of PD patients with high AS following group CBT interventions compared with the waiting list control group at posttreatment. These results showed that group CBT can reduce AS levels from the clinical range for panic disorder with or without agoraphobia into the normal range.

The results from this study indicated that patients who participated in the ICBT and GCBT groups demonstrated significantly greater reduction in agoraphobic avoidance severity (FQ-AG) compared to the Wait-list control group in posttest.

These results also are consistent with a study conducted by Sharp, Power & Swanson (2004) and Marchand et al., (2009). They found ICBT and GCBT were equally effective in of avoidance and agoraphobia (FQ-AG) scores at post treatment.

Consistent with the prediction, some studies suggest that the reduction in agoraphobic avoidance and fear severity is specific for CBT intervention in treatment of PD (Bandelow et al., 2007; Roy-Byrne et al., 2005b; Shear, et al., 2001a; Vincelli et al., 2003).

Consistent with the results of this study, a meta-analysis conducted by Oei, Llamas & Devilly (1999) showed the effectiveness of CBT in treating fear symptoms related to

phobic anxiety and avoidance in PD patients and suggested that CBT can be regarded as the established treatment of PD in reducing fear and avoidance. This study showed that fear and avoidance measures (in 27 studies) improved at post-treatment and/or follow-up.

The results of a study by Vincelli et al., (2003) and Gloster, Wittchen, Einsle et al., (2011) Pelissolo et al., (2012) also showed the effectiveness of individual CBT in patients with PDA in significantly reducing fear (FQ-AG) response criterion. They found that individual CBT was more effective than a wait-list control group in the improvement and reduction of agoraphobic avoidance to modify catastrophic cognition in PD patients.

Additionally, the current results regarding the effectiveness of group CBT on reducing FQ-AG support findings from previous studies. The results of a study by Ross et al. (2005) and Carter et al., (2003) revealed that PD participants in group CBT condition improved more in reduction of agoraphobic avoidance compared with waiting list control group immediately post treatment.

4.3 Effectiveness of treatment (Pretest-Posttest-Follow-up)

The participants in ICBT and GCBT treatments not only maintained their therapeutic gains on six dependent variables (anxiety, depression, panic disorder severity, agoraphobic cognition, anxiety sensitivity and fear) but also continued to improve during the four month follow-up. However the results from this study showed significantly greater improvements in ICBT than GCBT in some measures in post treatment to four months follow up.

The results showed that anticipatory anxiety scores moved from severe anxiety in pretreatment to mild anxiety in ICBT and moderate anxiety in GCBT in posttreatment. In addition, these two treatment formats showed continued significant reduction in rate of anxiety, to mild anxiety, at the 4 month post intervention; however, ICBT group was likewise significantly more effective compared with GCBT in reducing of the anticipatory anxiety (BAI) at the end of the follow-up phase.

In agreement with results of this study Neron, Lacroix, Chaput, (1995) also found ICBT and GCBT significantly effective in reducing anxiety symptoms in total BAI and HAMA (Hamilton Anxiety) scores in post treatment and at a 6 month follow-up. However, a differential effect favouring individual CBT over group CBT was observed with regards to generalized anxiety and depressive symptoms. This differential effect favouring individual therapy was also observed at the end of the follow-up phase. Thus our study replicated the finding of by Néron, Lacroix & Chaput (1995).

This result is not consistent with results from a study conducted by Sharp, Power & Swanson (2004) and Marchand, Roberge, Primiano, Germain (2009) who obtained improvement in reduction of anxiety symptoms in individual therapy and group therapy which were maintained at a three month and 2 years follow-up, respectively, with no significant difference between each other. The previously mentioned limitations of these two studies.

This outcome parallels the findings from Erickson, Janeck, Tallman, (2007), Clerkin, et al., (2008), Telch et al., (1993), Sokol, et al., (1989) Heldt, et al., (2010) and Moller & Hegna (2001). They found participants with PD in CBT group were more

effective in treatment and maintained their improvement in reduction of anxiety (BAI) scores, with a continued reduction after end of treatment to respectively to six months, 1-year, 2- years and three years follow-up and majority of the treated patients met criteria for recovery.

The results from this study also indicated that the participants in both treatment groups moved from moderate depression levels at pretreatment to minimal range in post treatment. In addition, the two treatment formats showed a continued significant reduction in rate of depression at 4 months post intervention, however further improvement with ICBT showing better gain in reducing of depression. This indicates that even at the four month follow-up, CBT programs had effectively helped patients deal with anxiety, and moreover, reduced factors such as sensitivity to autonomic arousal, catastrophic thoughts, and intensity of symptoms associated with panic thus preventing negative emotion of panic disorder. In other words, both groups showed increased self-efficacy and were effectively able to deal and cope with new stressors following treatment termination.

This result is not consistent with results from a study conducted by Sharp, Power & Swanson (2004), Marchand et al., (2009) and Neron, Lacroix, Chaput, (1995) who obtained improvement in reduction of depression symptoms in individual therapy and group therapy which were maintained at a three month, 2 years and a 6 month follow-up respectively, with no significant difference between each other. The previously mentioned limitations of these two studies.

The results of studies by Telch et al., (1993) Sokol et al., (1989) and Ruwaard et al., (2010) also reported reductions in depression (BDI) scores in group CBT were maintained at a 6 month, 1-year and three year follow-up respectively.

The results showed that severity of panic disorder (PDSS) scores moved from severe range in pretreatment to mild range in ICBT and moderate range in GCBT in posttreatment. In addition, these two treatment formats showed continued significant reduction in rate of severity of panic disorder (PDSS), to mild range at the 4 month post intervention; however, ICBT group was likewise significantly more effective compared with GCBT in reducing severity of panic disorder at the end of

the follow-up phase.

These results also are not consistent with a study conducted by Marchand et al., (2009). They found ICBT and GCBT were equally effective in reducing severity of panic disorder (PDSS) scores at two year follow-up. Thus our study did not replicate the finding of Marchand, Roberge, Primiano and Germain. As previously mentioned, the differing results might be due to use of a medicated sample group.

This is consistent with previous findings Otto, Deveney, (2005), Taylor, (2000), , Smit et al., (2004), that panic patients through the CBT program could significantly reduce severity of panic disorder (PDSS) at the end of treatment and maintain this improvement at long term follow-up.

The study Noda et al., (2007), Meulenbeek et al., (2010) and Heldt et al., (2006) and Nakano et al., (2008) also concluded that the improvement in reduction severity of panic disorder (PDSS) in group CBT was maintained at 3 months, 6 months and one year follow-up, respectively.

Hofmann et al., (2007), Clerkin et al., (2008) also reported that individual CBT produced significant improvement in reduction of severity of panic disorder in post treatment and maintenance over 24 weeks and 6 months follow-up, respectively.

The results from this study also indicated that patients in the ICBT and GCBT groups not only demonstrated significantly reduction in catastrophic misinterpretation (ACQ) from pretest to posttest but also continued to improve during the four month follow-up with no significant difference between each other.

It is likely that participants in both CBT interventions continued to use the strategies learned in sessions after they finished treatment and therefore the treatment effect persisted and became greater over time.

These results also are consistent with a study conducted by Marchand, Roberge, Primiano, Germain (2009). They found subjects in two treatment groups maintained their gains in reducing agoraphobic avoidance (ACQ) scores at two years follow-up, while not differing significantly from each other. Thus our study replicated the finding of Marchand, Roberge, Primiano, and Germain.

The study Craske, Farchione, Allen (2007) also concluded that the improvement in reduction agoraphobic cognition (ACQ) in CBT groups was maintained and even

improved at 6 and 12 months later (follow-up).

This result is consistent with results from study by Hofmann et al., (2007), who obtained improvement in reduction of agoraphobic cognition in individual CBT group which maintained at a six month follow-up.

Agoraphobic cognition was found to improve with group CBT and the improvement was maintained at 3 months (Noda et al., 2007) up to a 6 months follow-up (Hecker, Melinda, Losee1, et al., 2004).

Nakano et al (2008) reported that group CBT program was successful in reducing catastrophic misinterpretation and agoraphobic cognition in posttreatment. The result showed the average agoraphobic cognition (ACQ) score fell from 13.3 at baseline to 5.3 post-treatment (47% reduction). This effectiveness was sustained for 1 year.

The results of this study also found a significant reduction in anxiety sensitivity from pretest to posttest which was maintained at four months follow-up. The results of this study also revealed that the improvement in reduction of Anxiety Sensitivity (AS) in the two treatment formats maintained the rate of severity to mild at the four month follow up, but ICBT showed greater improvement than GCBT in at four months follow up.

Participants in both groups learned to conceptualize panic as an extreme end of a continuum of the body's natural response to threat. It follows that they were less likely to view panic as a "weakness" or permanent problem, but rather as a hypersensitive alarm mechanism that was capable of being readjusted. As a result, CBT participants in both formats as a whole probably felt fewer stigmas with the experience of panic and consequently may have been more comfortable admitting that they had experienced a panic attack at the four month follow-up assessment. In a study by Antony (2001), panic cognition measures mean scores (e.g., ASI, ACQ) and fear and avoidance (FQ) at pretreatment were consistent with clinical samples diagnosed with severe panic disorder and avoidance. However in posttreatment and follow-up, with improved functionality after progressively reduced catastrophic misinterpretation of arousal-related body sensations and reduced agoraphobic fear and avoidance, scores were similar to non-clinical samples at the four month follow-

up with no significant differences between treatment conditions.

Several clinical trials of CBT for panic disorder have shown the expected lowering of anxiety sensitivity among patients successfully treated with CBT at follow-up (McNally & Lorenz, 1987; Smit et al., 2008a; Smits et al., 2008b., Deacon, Lickel, Possis, Abramowitz, Taylor, 2012).

These results also are not consistent with a study conducted by Marchand, Roberge, Primiano, Germain (2009) where improvements in reduction of anxiety sensitivity in individual therapy and group therapy were maintained at 2 years follow-up, with no statistically significant difference from each other.

Consistent with this study's results, a meta-analysis (in 31 studies targeted PD) conducted by Öst (2008) showed the effectiveness of group or individual format of CBT in treating maladaptive cognitions and behaviors (i.e., catastrophic misinterpretations of physical symptoms) in the end of treatment and maintain this improvement at follow-up.

The study by, Smits, et al., (2008a) and Arch., Eifert., Davies., (2012) also concluded that the improvement in reduction anxiety and bodily sensations (ASI) in individual CBT format was maintained at the 3-week and 6 - and one year follow-ups respectively.

Anxiety sensitivity and anxiety cognitions were found to improve with group CBT and the improvement were maintained at a six weeks (Bergström et al., 2010), 4 months (Hecker, et al., 2004), six months (Clerkin, 2008) up to a 12 months follow-up (Martinsen, Olsen, Tonset, Nyland, Aarre, 1998).

The results from this study also indicated that patients in the ICBT and GCBT groups not only demonstrated significantly reduction in agoraphobia, and situational avoidance (FQ-AG) from pretest to posttest but also continued to improve during the four month follow-up with no significant difference between each other.

These results also are consistent with a study conducted by Sharp, Power & Swanson (2004) and Marchand, Roberge, Primiano, Germain (2009) where improvements in reduction of avoidance and agoraphobia in individual therapy and group therapy were maintained at, 3 months and 2 years follow-up respectively, with no

statistically significant difference from each other.

This is consistent with previous findings Addis et al., (2006) and Nakano et al., (2008) Craske, Farchione, Allen (2007) who obtained improvement in reduction of severity of fear and agoraphobia (FQ-AG) in group CBT program were maintained at 5 months and one year follow-up, respectively.

Similar results have also been reported by Evans, Holt, Oei (1991) that panic patients through the individual CBT program could significantly reduce severity of fear and agoraphobia (FQ-AG) at 1 year after the treatment.

In general, these findings appear to substantiate the conceptualization of panic proposed in the study and lend support to the argument that the intervention was successful in reducing anxiety sensitivity and consequently reducing the tendency to attribute threatening meaning to anxiety or panic.

These follow-up results can be contrasted to results from alternative pharmacological treatment studies for PD. More than 30 percent of panic sufferers who stop taking tricyclic antidepressants experience a relapse that requires additional treatment (Clum, 1990). The average relapse rate across all studies is approximately 40% (Barlow, 1988). Although the current study did not directly compare ICBT or GCBT to pharmacological intervention, it seems clear from the literature cited, that one of the most important findings for this study involves the virtual lack of relapse across a number of variables relevant to PD. Increase in confidence in one's personal ability to manage PD may be the key factor in maintaining treatment effects across time. This confidence may be lacking in persons who undergo pharmacological interventions and attribute improvements in their condition to the medication versus acquired cognitive behavioral skills.

Summary

Results of this study demonstrated significant improvements in reduction of severity of panic disorder, negative affects (depression, anxiety), agoraphobic avoidance, negative automatic thoughts and sensitivity to anxiety in patients that participate in two treatment formats (individual and group CBT) interventions, while individual CBT group led to greater improvement than group CBT in reducing of anxiety

anticipatory anxiety (BAI) and severity of panic disorder (PDSS) after treatment interventions. These improvements were maintained at 4 months follow-up, while patients in individual CBT led to greater improvement than group CBT in relation to reduction of anticipatory anxiety (BAI), depression (BDI), severity of panic disorder (PDSS) and sensitivity to anxiety (ASI), but two treatment formats were equally effective in the reduction of agoraphobic cognition (ACQ) and agoraphobia (FQ-AG) in post treatment and at the 4 months follow-up. The improvements indicate that these programs are a promising intervention for patients with PD.

4.4 Conclusions

This study examined the efficacy of CBT in individual and group formats for the treatment of panic disorder in Iranian participants. The results obtained suggest that CBT produced significantly greater decreases than waiting list control group in panic disorder symptoms as measured by the BAI; BDI; PDSS; ACQ; ASI and FQ-AG.

From the experience and insights gained through all the hypotheses of this study, it can be concluded that cognitive behavioral therapy is an effective treatment for reducing a wide range of symptoms, including depression, anxiety, panic disorder severity, agoraphobic cognition, anxiety sensitivity and fear in patients with PD.

Compared to the waiting list control group, two treatment formats also were found to be effective in significantly reducing symptoms of panic disorder in post treatment and at 4 months follow-up. These findings were consistent with the analysis of statistical significance, in which the proportion of participants who moved from a dysfunctional or clinical range to a non-clinical range was greatest for the CBT treatment condition (ICBT or GCBT). Hence cognitive behavioral therapy (CBT) should be the treatment of choice for PD.

Cognitive behavioral therapy (CBT) is close to Iranian culture and therapists can educate their clients on the logics of techniques and assumptions underlying them more easily. Thus, the clients can accept them with no trouble (Khoshbooi, 2012). Health professionals and policy makers may notice the effectiveness of cognitive behavior therapy and its adaptation to Iranian culture in the treatment of PD.

The second conclusion of this study is that individual CBT showed a stronger therapeutic response in reduction of anticipatory anxiety, depression, severity of panic disorder, sensitivity to anxiety than group CBT format. While, two treatment modalities were equally effective in reducing agoraphobic cognition and agoraphobia avoidance from pretest to posttest and maintained these levels at 4 month follow-up.

Although all sessions of treatment in this study were delivered by the same therapist and same manual, but what should be considered is that essentially CBT treatment in this study was an educational and instructional type and has been designed mainly for individual treatment format. Therefore, caution should be exercised in generalizing our results to other types of group therapy such as groups with a other approach and more psychotherapeutic focus.

The most common format in traditional cognitive-behavioral therapy is the individual format (Sharp, Power & Swanson, 2004) but individual CBT is undoubtedly the most costly of the treatment delivery modalities and also has implications for service delivery, particularly in terms of availability of qualified therapists. It is clear that financial concerns are predominant in patients' reasons for choosing to not engage in therapy (Marchand, et al., 2004, Sharp, Power & Swanson, 2004) even when they see a need to do so.

However, the results of this study suggests that there were some differences in relation to effectiveness between the group and individual modalities but the group treatment is as effective as individual treatment in reduction of symptoms of panic., hence the group format may be chosen to be the standard kind of therapy to be offered in a service and a good option to reduce costs. This is particularly beneficial for low-income families who struggle to pay the cost of mental health care. For example in Iran, there are a large number of patients in need of treatment and limited budgets to provide it. However, the option of individual treatment should also be maintained in order to address specific needs and to respect patients' preferences. Cost-effectiveness of group therapy encourages and increases the number of patients willing to seek treatment for panic disorder. The mental health community should recognize this population as significantly underserved and work to make therapy

services not only more available, but also more affordable to therapists-in-training. It seems, increasing the availability of group therapy may be one option, as it is just as effective as individual therapy and even offers some unique benefits (Frankel, 2002; Leszcz, 2008), usually at a much cheaper cost (McCrone et al., 2005).

4.5 Limitations of the Present Study

Although the present study contributes to an understanding of the treatment of panic disorder, it is not without limitations. The main limitations are expressed as follows:

First, although it appears that the individual and group treatment are effective, it must be noted that nearly all dependent measures were self-report measures rather than behavioral observations or physiological indices, so there were potential confounds such as social desirability effects.

Second, in the present study, a structured clinical interview was not conducted at post-treatment as well as at follow-up. Therefore, the researcher could not confirm the rate of recovery of the participants. The researcher could only report the reduction of PD symptoms criteria based on the questionnaire.

Third, the therapist and researcher was the same person, which may have biased the results. However, group differences emerged only at follow-up when the therapist was no longer in attendance.

Fourth, in the present research the final evaluation of PD symptoms criteria was conducted 4 months after post-treatment, which is a relatively short duration. Other limitations of this study include (a) This study was conducted on small size (b) many people with panic symptoms are comorbid with other mental health problems, especially depression, another anxiety disorder, substance abuse, but the present study excluded individuals with this comorbid disorders. These factors may affect the generalizable of results.

Fifth, panic disorder patients seem to be more sensitive to hyperventilation than normal volunteers. But the present study lacked of psychophysiological tests to assess sensitive to hyperventilation and physiologically abnormal responses to respiratory function in participants.

4.6 Future Directions of Research

This study was conducted on a small sample, therefore, similar studies with larger sample size should be conducted to examine whether these findings can be confirmed.

In the present study, a structured clinical interview was not conducted at post-treatment as well as at follow-up. Therefore, the researcher could not confirm the rate of recovery of the participants. The researcher could only report the reduction of PD symptoms criteria based on the questionnaire. Therefore, future research should employ a diagnostic clinical interview in order to evaluate the rate of recovery of participants in each treatment modality.

Additionally, future research should have long term follow-up evaluation in order to determine the long term effects of the therapies. In the present research the final evaluation of PD symptoms criteria was conducted 4 months after post-treatment, which is a relatively short duration.

Casey et al., (2004b) concluded in their study that is necessary to include measures of positive cognition (e.g. self efficacy in dealing with anxiety thought) in assessing the impact of catastrophic cognitions. In this study didn't address the positive cognitions. Further research will be needed to investigated how self efficacy changes.

In the present study, one of the exclusive criteria was that only patients with PD diagnosis were involved as participants. However, in clinical situations, many people who suffer from panic symptoms have comorbid with other behavioral mental health problems, especially depression, another anxiety disorder, substance abuse or suicidality (Nock, Hwang, Sampson, Kessler, 2010). Therefore, future studies should evaluate and compare the effectiveness of ICBT and GCBT in PD with comorbidity.

A replication of this study with a combination of individual and group cognitive behavioral intervention, preferably with the same therapist, may be particularly effective for many panic disorder patients. Thus the group would provide a laboratory where the patient can test out maladaptive beliefs about fear-evoking stimuli in relative safety.

Summary

There is an evidence to support the effectiveness and cost effectiveness of group cognitive behavioral therapy in the treatment of panic disorder. The main objective of the present study was to compare the effectiveness of individual and group formats of cognitive-behavioral therapy in panic disorder patients.

45 outpatients with panic disorder with or without agoraphobia were randomly assigned to three groups: Group Therapy, Individual Therapy or a waiting -list group. In the two treatment conditions, patients received 14 weekly sessions of treatment based upon Cognitive-Behavioral therapy. Assessments were carried out pre and post treatment and in the two treatment groups at a 4-month follow-up. Treatment effectiveness of individual and group CBT was compared with each other and the untreated wait-list control group with regard to Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI), Panic Disorder Severity Scale (PDSS), Agoraphobic Cognition Questionnaire (ACQ), Anxiety Sensitivity Index (ASI) and agoraphobic avoidance (FQ-AG).

Data analysis revealed that the three groups were not significantly different from each other at pre-treatment. Compared with the waiting list control group, the participants in both CBT formats showed significant improvement after treatment with reduction of panic disorder symptoms, while, two treatment formats were equally effective in the reduction of, depression (BDI), agoraphobic cognition (ACQ), sensitivity of anxiety (ASI) and agoraphobic avoidance (FQ-AG), but individual CBT led to greater improvement than group CBT in relation to the reduction of overall anxiety, and panic disorder severity in post treatment. Furthermore participants in both treatment groups is maintained their improvement at 4 months follow-up phase, while, individual CBT group led to greater improvement than group CBT in relation the reduction of overall anxiety (BAI), depression symptoms (BDI), panic disorder severity (PDSS) and sensitivity to anxiety (ASI) at 4 months follow-up.

Reference

- Abramowitz, J. S., Deacon, B. J., Whiteside, S. P. H. (2011). How well does Exposure Therapy work? Exposure therapy for anxiety: Principles and practice, (pp. 17-32). New York: Guilford Press.
- Addis, M. E., Hatgis, C. E., Cardemil, E., Jacob, K., Krasnow, A. D. & Mansfield, A. (2006). Effectiveness of cognitive behavioral treatment for panic disorder versus treatment as usual in a managed care setting: Two year follow-up. *Journal of Consulting and Clinical Psychology*, 74, 377-385.
- Agras, W. S. (1993). The diagnosis and treatment of panic disorder. *Annual Review of Medicine*, 44, 39-51.
- Ahmadvand, A., Sepehrmanesh, Z., Ghoreishi, F. S, Afshinmajd, S. (2012). Prevalence of psychiatric disorders in the general population of Kashan, Iran. *Archives of Iranian medicine*, 15, 205-509.
- Aina, Y., & Susman, J.L. (2006). Understanding comorbidity with depression and anxiety disorders. *Journal of the American Osteopathic Association*. 106, 9-14.
- Allen, L. B., White, K. S., Barlow, D. H., Shear, K. J., Gorman, J. M. and Woods, S. W. (2010). Cognitive-Behavior Therapy for Panic Disorder: Relationship of Anxiety and Depression Comorbidity with Treatment Outcome. *Journal of Psychopathology Behavior Assessment*, 32, 185-192.
- Alkin, T., Tural, U., Onur, E., Oztürk, V., Monkul, E. S. & Kürşad, K. (2007). Basilar artery blood flow velocity changes in patients with panic disorder following 35% carbon dioxide challenge. *Journal of Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 31, 115-122.
- American Psychiatric Association (2000). *Diagnostic and Statistical Manual of mental disorder (text revision)*. Washington, D. C: Author.
- American Psychiatric Association. (2007). *Practice Guideline for the treatment of patients with panic disorder*. Washington, DC: American Psychiatric Association.
- Anderson, G., & Carlbring, P. (2010). Panic disorder. In W. T. O'Donohue., C. Draper (Eds.), *Stepped Care and E-Health: Practical Applications to Behavioral disorder* (pp. 61-77). New York Dordrecht Heidelberg London: Springer.
- Antony, M. M. (2001). Measures for panic disorder and agoraphobia. In M. M. Antony, & S. M. Orsillo (Eds.), *Practitioner's guide to empirically based measures of anxiety*. AABT clinical assessment series (pp. 95-125). Dordrecht, Netherlands: Kluwer Academic Publishers
- Antony, M. M., Brown, T. A., & Barlow, D. H. (1992). Current perspective on panic and panic disorder (Current Direction) in psychological science. *Journal of the*

- American psychological society, 1, 79-82.
- Apfeldorf, W. J., Shear, M. K., Leon, A. C., & Portera, L. (1994). A brief screen for panic disorder. *Journal of Anxiety Disorders*, 8, 71-78.
- Arch, J. J., Eifert, G. H., Davies, C., Vilardaga, J. C. P., Rose, R. D., & Craske, M. G. (2012). Randomized clinical trial of cognitive behavioural therapy (CBT) versus acceptance and commitment therapy (ACT) for mixed anxiety disorders. *Journal of Consulting and Clinical Psychology*, 80, 750-765.
- Argyropoulos, S. V., Sandford, J. J., & Nutt, D. J. (2000). The psychobiology of anxiolytic drugs Part 2: pharmacological treatments of anxiety, *Journal of Pharmacology & Therapeutics*, 88, 213-227.
- Arntz, A. (2002). Cognitive therapy versus interoceptive exposure as treatment of panic disorder without agoraphobia. *Journal of Behavior Research Therapy*, 40, 325-341.
- Arntz, A. & van den Hout, M. (1996). Psychological treatments of panic disorder without agoraphobia: Cognitive therapy versus applied relaxation. *Journal of Behavior Research and Therapy*, 34, 113-121.
- Austin, D. W. & Richards J. C. (2001). The catastrophic misinterpretation model of panic disorder. *Journal of Behavior Research Therapy*, 39, 1277-1291.
- Baldwin, D. S., Anderson, I. M., & Nutt, D. J. (2005). Evidence-based guidelines for the pharmacological treatment of anxiety disorders: recommendations from the British Association of Psychopharmacology. *Journal of Psychopharmacology*, 19, 567-596.
- Bandelow, B., Seidler-Brandler, U., Becker, A., Wedekind, D., & Rütger, E. (2007). Meta-analysis of randomized controlled comparisons of psychopharmacological and psychological treatments for anxiety disorders. *World Journal of Biological Psychiatry*, 8, 175-187.
- Bandura, A. (1988). Self-efficacy conception of anxiety. *Journal of Anxiety Research*, 1, 77 - 98.
- Barker, R. (Ed), (1989). Introduction: Where does panic disorder come from? *Panic disorder: theory research and therapy* (pp. 1-16). New York: John Wiley and sons.
- Barlow, D. H. (1988). Diagnosis and assessment of panic disorder and agoraphobia. In *anxiety and its disorders: The nature and treatment of anxiety and panic*. New York: The Guilford press.
- Barlow, D. H. (1990). Long-term outcome for patients with panic disorder treated with cognitive-behavioral therapy. *Journal of Clinical Psychiatry*, 51, 17-24.
- Barlow, D. H. (1994). Effectiveness of behavior treatment for panic disorder with and

- without agoraphobia. In B. E. Wolfe & J. D. Maser (Eds.), *Treatment of panic disorder* (pp. 105-120). Washington, DC: American Psychiatric Press.
- Barlow, D. H. (2002). *Experience of anxiety. Anxiety and its disorders: The nature and treatment of anxiety and panic* (pp. 1-36) (2th ed.). New York: Guilford Press.
- Barlow, D. H. (2008). *Panic disorder and Agoraphobia. Clinical handbook of psychological disorders: A step by step treatment manual* (pp. 24-28) (4th ed). New York, NY: Guilford press.
- Barlow, D. H. (2011). The development and evaluation of psychological treatments for panic disorder. In M. Gernsbacher, D. Pew & L. Hough (Eds.), *Psychology and the real world: Essays illustrating fundamental contributors to society* (pp. 198-204). New York: Worth Publishers.
- Barlow, D. H., Brown, T. A., & Antony, M. M. (1995). Diagnostic Comorbidity in Panic Disorder: Effect on Treatment Outcome and Course of Comorbid Diagnoses Following Treatment. *Journal of Consulting and Clinical Psychology*, 63, 408-418.
- Barlow, D. H. & Cerny, J. A. (1988). The nature and consequences of panic, Psychological treatment of panic. *The psychological treatment of panic* (pp. 1-28). New York: Guilford Press.
- Barlow, D. H., Chorpita, B. F., & Turousky, J. (1996). Fear, panic, anxiety and disorders of emotion. In D. A. Hope, (Ed), *Annual Nebraska Symposium on motivation*, (pp. 251-328). Lincoln: Nebraska university press.
- Barlow, D. H. & Craske, M. G. (2007). *Master your anxiety and panic: Client workbook for anxiety and panic* (4th ed). New York: Oxford university press.
- Barlow, D. H., Craske, M. G., Cerny, J. A. & Klosko, J. S. (1989). Behavioral treatment of panic disorder. *Journal of Behavior Therapy*, 20, 261-282.
- Barlow, D. H., Gorman, J. M., Shear, M. K., & Woods, S. W. (2000). Cognitive-behavioral therapy, imipramine, or their combination for panic disorder: A randomized controlled trial. *Journal of American Medical Association*, 283, 2529-2536.
- Battaglia, M., Bernardeschi, L., Politi, E., Bertella, S., & Bellodi, L. (1995). Comorbidity of panic and somatization disorder: A genetic-epidemiological approach. *Journal of Comprehensive Psychiatry*, 36, 411-420.
- Beamish, P. M., Granello, P. E, Granello, D. H., McSteen, P. B., Bender, B. A., & Hermon, D. (1996). Outcome studies in the treatment of panic disorder: A review. *Journal of Counseling and Development*, 74, 460-467.
- Beamish, P. M., Granello, D. H., & Belcastro, A. L. (2002). Treatment of panic disorder: Practical guidelines. *Journal of Mental Health Counseling*, 24, 224-246.

- Beck, A. T., & Emery, G. (1985). *Anxiety disorders and phobias: A cognitive perspective*. New York: basic Books.
- Beck, J. G., & Shipherd, J. (1997). Repeated exposure to interoceptive cues: Does habituation of fear occur in panic disorder patients? *Journal of Behavior Research and Therapy*, 35, 551-557.
- Beck, A. T., Sokol, L., Clark, D. A., Berchick, B., & Wright, F. (1992). Focused cognitive therapy for panic disorder: a crossover design and one year follow-up. *American Journal of Psychiatry*, 147, 778-783.
- Beck, A. T., Epstein, N., Brown, G., & Steer, R. A. (1988a). An inventory for measuring clinical anxiety: psychometric properties. *Journal of Consulting and Clinical Psychology*, 56, 893-897.
- Beck, A. T., Steer, R. A., & Garbin, M. G. (1988b). Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation. *Journal of Clinical Psychology Review*, 8, 77-100.
- Beck, A. T., & Steer, R. A. (1990). *Manual for the Beck Anxiety Inventory*. San Antonio, TX: Psychological Corporation.
- Beck, A.T., Steer, R.A., & Brown, G.K. (1996). *Manual for the Beck Depression Inventory-II*. San Antonio, TX: Psychological Corporation.
- Beck, J. G., Stanley, M. A., Baldwin, L. E., Deagle, E. A., & Averill, P. M. (1994). Comparison of cognitive therapy and relaxation training for panic disorder. *Journal of Consulting and Clinical Psychology*, 62, 818-826.
- Bednar, R. L. & Kaul, T. J. (1994). Experiential group research: Can the cannon fire? In A. E. Bergin, & S. L. Garfield (Eds.), *Handbook of psychotherapy and behavior change* (pp. 631-663) (4th ed.). New York: Wiley.
- Bieling, P.J., McCabe, R.E., Antony, M.M. (2009). Group process in CBT. *Cognitive-Behavioral Therapy in Groups*, (pp. 22-45). New York: Gillford Press.
- Bennett, B. (2004). *Mental illness: A Guide to Recovery* (pp. 40-42). Trafford publishing.
- Berger, B. G. (2001). The treatment of panic disorder: A comparative study between breathing retraining and cognitive behavioral therapy: *Dissertation Abstracts International:-Section-B:-The Sciences-and-Engineering*. 61, 43-90.
- Bergström, J., Andersson, G., Ljótsson, B., Rück, C., Andréewitch, S., Karlsson, A., Carlbring, P., Andersson, E., & Lindefors, N. (2010). Internet-versus Group administered Cognitive Behavior Therapy for Panic Disorder in a Psychiatric Setting: A Randomized Trial. Unpublished manuscript. *BMC Psychiatry*, 10-54.
- Bernstein, D. A., & Borkovec, T. D. (1973). *Progressive relaxation training*.

Champaign, I. L: Research Press.

- Bernstein, A., Zvolensky, M. J., Sachs-Ericsson, N., Schmidt, N. B., & Bonn-Miller, M. O. (2006). Associations between age of onset and lifetime history of panic attacks Panic in the Military 60 and alcohol use, abuse, and dependence in a representative sample. *Journal of Comprehensive Psychiatry*, 47, 342-349.
- Berzak, E., Reznik, M., Narsia, O., Benjamin, J. (2004). Sensitivity to carbon dioxide in subjects with a single lifetime panic attack: possible clinical "bedside" predictive test for panic disorder after a first attack. *Journal of Depression and Anxiety*, 20, 48-50.
- Bloch, S., & Crouch, E. (1986). *Therapeutic Factors in Group Psychotherapy*. Oxford University Press.
- Bohni, M. K., Spindler, H., Arendt, M., Hougaard, E, & Rosenberg, N.K. (2009). A randomized study of massed three-week cognitive behavioral therapy schedule for panic disorder. *Journal Acta Psychiatrica Scandinavica*, 120, 187-95.
- Bonn, J. A., Readhead, C. P. A., & Timmons, B. H. (1984). Enhanced behavioral response in agoraphobic patients pretreated with breathing retraining. *Lancet*, 2, 665-669.
- Botella, C., García-Palacios, A., Villa, H., Banos, R.M., S, Alcaniz, M. (2007). Virtual Reality Exposure in the Treatment of Panic Disorder and Agoraphobia: A Controlled Study. *Journal of Clinical Psychology and Psychotherapy*, 14, 164-175.
- Bouchard, S., Gauthier, J., Laberge, B., & French, D. (1996). Exposure versus cognitive restructuring in the treatment of panic disorder with agoraphobia. *Journal of Behaviour Research and Therapy*, 34, 213 - 224.
- Bouton, M.E., Mineka, S., & Barlow, D.H. (2001). A modern learning theory perspective on the etiology of panic disorder. *Journal Psychological Review*, 108, 4-32.
- Brabender, V., Fallon, A.E., & Smolar, A.I. (2004). *Essentials of Group Therapy*. (p.36). John Wiley & Sons, Inc.
- Breier, A., Charney D.S., & Heninger, G.R. (1986). Agoraphobia with panic attacks. Development, diagnostic stability, and course of illness, *Arch General Psychiatry*, 43, 1029-1036.
- Bremner, J.D. (2004). Brain imaging in anxiety disorders. *Expert Review of Neurotherapeutics*, 4, 275-284.
- Breslau, N., & Davis, G.C. (1993). Migraine, Physical Health and Psychiatric Disorder: A Prospective Epidemiological Study in Young Adults. *Journal of Psychiatric Research*, 27, 211-221.

- Brown, G.K., Beck, A.T., Newman, C.F., Beck, J.S., & Tran, G.Q. (1998). A Comparison of Focused and Standard Cognitive Therapy for Panic Disorder. *Journal of Anxiety Disorders*, 11, 329-345.
- Brown, T.A., & Cash, T.F. (1989). The phenomenon of panic in nonclinical populations: Further evidence and methodological considerations: *Journal of Anxiety Disorders*, 3, 139-148.
- Burlingame, G.M., Fuhriman, A., & Mosier. (2003). The differential effectiveness of group psychotherapy : A meta-analytic perspective. *Group Dynamics: Theory, Research and practice*, 7, 3-12.
- Burlingame, G.M., MacKenzie, K.R., & Strauss, B. (2004). Small group treatment: Evidence for effectiveness and mechanism of change. In M.J. Lambert (5th ed.). *Bergin & Garfield's Handbooks of psychotherapy and behavior change* (pp. 647-696). New York: Wiley & Sons.
- Burns, L.E., Thorpe, G.L., & Cavallaro, L.A. (1986). Agoraphobia 8 years after behavioral treatment: A follow-up study with interview, self-report, and behavioral data. *Journal Behavioral Therapy*, 17, 580-591.
- Butler, A. C., Chapman, J. E., Forman, E. M., Beck, A. T. (2006). The empirical status of cognitive-behavioral therapy: a review of meta-analyses. *Journal of Clinical Psychology Review*, 26, 17-31.
- Bystritsky, A., Craske, M., Maidenberg, E., Vapnik, T., & Shapiro, D. (2000). Autonomic reactivity of panic patients during a CO2 inhalation procedure. *Journal Depression and Anxiety*, 11, 15-26.
- Cabill, S. P. & Foa, E. B. (2003). Anxiety disorders. In Nutt, D. J. & Ballenger, J. C, (Eds), *Exposure therapy in treatment of anxiety disorders*, pp. 445-463. Blackwell publishing company.
- Caldirola, D., Bellodi, L., Caumo, A., Giovanni, M., & Giampaolo, P. (2004). Approximate Entropy of Respiratory Patterns in Panic Disorder. *American Journal of Psychiatry*, 161, 79-87.
- Calloway, N. J. (2007). A comparative study of the effects of photostimulation and Autogenic training in reducing stress, Anxiety, and depression. A comparative study.
- Cameron, O.G. (2007). Understanding Comorbid Depression and Anxiety. *Psychiatric Times Magazine*, 14, 24.
- Carlbring P, Ekselius L, Andersson G. (2002). Treatment of panic disorder via the Internet: a randomized trial of CBT vs. applied relaxation. *Journal of behavior therapy and experimental Psychiatry*.
- Carlbring, P., Bohman, S., Brunt, S., Buhrman, M., Westling, B. E., Ekselius, L., &

- Anderson, G. (2006). Remote treatment of panic disorder: A randomized trial of Internet based cognitive behavior therapy supplemented with telephone calls. *American Journal of Psychiatry*, 163, 2119-2125.
- Carter, M. M., Sbrocco, T., Gore, K. L., Watt Marin, N. W., & Lewis, E. L. (2003). Cognitive-behavioral group therapy versus a wait-list control in the treatment of African-American women with panic disorder. *Journal of Cognitive Therapy and Research*, 27, 505-518.
- Cartner, M. M., & Barlow, D. H. (1995). Learned alarms: The origins of panic. In W. L. O'Donohue & L. Krasner. (Eds), *Theories of behavior therapy: Exploring behavior change*, (pp. 209-228). New York: Guilford press.
- Casey, L. M., Oei, T. P. S., Newcombe, P. A., & Kenardy, J. (2004a). The role of catastrophic misinterpretation of bodily sensations and panic self-efficacy in predicting panic severity. *Journal of Anxiety Disorders*, 18, 325-340.
- Casey, L. M., Oei, T. P. S., & Newcombe, P. A. (2004b). An integrative cognitive model of panic disorder: The role of positive and negative cognitions. *Journal of Clinical Psychology Review*, 24, 529-555.
- Chambless, D. L. (1985). The relationship of severity of agoraphobia to associated psychopathology. *Journal of Behavior Research Therapy*, 23, 305-310.
- Chambless, D. L., Caputo, G., Bright, P. & Gallagher, R. (1985). Assessment of fear among agoraphobics: The body sensation questionnaire and the Agoraphobic cognition questionnaire. *Journal of consulting and clinical psychology*, 6, 1090-1097.
- Chambless, D., & Gillis, M. (1993). Cognitive therapy of Anxiety disorders. *Journal of consulting and clinical psychology*, 61, 248-260.
- Choi, K.W., Woo, J. M., Kim, Y. R., Lee, S. H., Lee, S.Y., Kim, E. J., Chung, S. K., Kang, E. H., Lee, J. H., & Yu, B. H. (2012). Long-term escitalopram treatment in Korean patients with Panic Disorder: A Prospective, Naturalistic, Open-label, Multicenter Trial. *Journal Clinical Psychopharmacol Neuroscience*.10, 1-44.
- Choi, Y. H., Park, K. H. (2006). Therapeutic factors of cognitive behavioral group treatment for social phobia. *Journal of the Korean Medical Society*, 21, 333-336.
- Chouinard, G. (2004). Issues in the clinical use of benzodiazepines: potency, withdrawal, and rebound. *Journal of clinical psychiatry*, 65, 7-12.
- Choy, Y. (2008). Treatment Planning for Panic Disorder. *Psychiatric Times magazine*, Vol. 25 No. 2.
- Clark, D. M. (1986). A cognitive approach to panic. *Journal of Behavior Research and Therapy*, 24, 461-470.

- Clark, D. M. (1988). A cognitive model of panic attacks. In S. Rachman & J. D. Maser, (Eds), *Panic: Psychological perspectives* (pp. 71-90). New Jersey: Lawrence Erlbaum Associations.
- Clark, D. M. (1996). Panic disorder: From theory to therapy. In P. M. Salkovskis (Ed.), *Frontiers of cognitive therapy*, (pp. 318-344). New York: Guilford Press.
- Clark, D. A., & Beck, A. T. (2009). *Cognitive Therapy of Anxiety Disorders: Science and Practice*. *Cognitive therapy of panic disorder*, (pp. 275-332): Guilford Press.
- Clark, D. M., Salkovskis, P. M., & Challey, A. J. (1985). Respiratory control as a treatment for panic attacks. *Journal of Behavioral Therapy and Experimental Psychiatry*, 16, 23-30.
- Clark, D. M., Salkovskis, P. M., Hackman, A., Middleton, H., Anastasiades, P., & Gelder, M. (1994). A comparison of cognitive therapy, applied relaxation and imipramine in the treatment of panic disorder. *British Journal of Psychiatry*, 164, 759-769.
- Clark, D. M., Salkovskis, P. M., Hackmann, A., Wells, A., Ludgate, J., & Gelder, M. (1999). Brief cognitive therapy for panic disorder: A randomized controlled trial. *Journal of Consulting and Clinical Psychology*, 67, 583-589.
- Clark, D. M., Steer, R. A., & Beck, A. T. (1994). Common and specific dimensions of self-reported anxiety and depression: Implications for the cognitive and tripartite models. *Journal of Abnormal Psychology*, 103, 645-654.
- Clerkin, E.M., Teachman, B.A., Smith Janik, S.B. (2008). Sudden gains in group cognitive-behavioral therapy for panic disorder. *Journal of Behavior Research and Therapy*, 46, 1244-1250.
- Clum, G. A. (1989). Psychological interventions vs. drug in the treatment of panic. *Journal of Behavior therapy*, 20, 429-457.
- Clum, G. A. (1990). *Coping with panic: A drug free approach to dealing with anxiety attack*. California: Brooks/Cole Publishing Co.
- Compton, W., Thomas, Y., Stinson, F., & Grant, B. (2007). Prevalence, Correlates, Disability, and Comorbidity of DSM-IV Drug Abuse and Dependence in the United States: Results From the menbereich the National Epidemiological Survey on Alcohol and Related Conditions. *Archives of General Psychiatry* 64, 566-576.
- Conrad, A. & Roth W. T. (2007). Muscle relaxation therapy for anxiety disorders: It works but how? *Journal of Anxiety Disorders*, 21, 243-264.
- Corey, G. (2008). *Ethical and professional issues in group practice*, (8 th ed). *Theory and practice of group counseling*, (pp. 47-67). Belmont, CA: Brooks/Cole.
- Corey, G. (2009). *Existential Therapy*, (9 th ed.). *Theory and Practice of Counseling*

and Psychotherapy (pp. 136-157). Brooks/Cole.

- Coryell, W., Pine, D., Fyer, A., Klein, D. (2006). Anxiety responses to CO₂ inhalation in subjects at high-risk for panic disorder. *Journal Affective disorder* 92, 63-70.
- Cosci, F., Knuts, I. J., Abrams, K., Griez, E. J., Schruers, K. R. (2010). Cigarette smoking and panic: a critical review of the literature. *Journal of Clinical Psychiatry*, 71, 606-615.
- Courtney, R. D. O. (2011). *Dysfunctional Breathing and Relevance: Its parameters, measurement and relevance*, (pp. 31-32). RMIT University.
- Cox, B. J. 1999. The role of anxiety sensitivity in panic and other disorders. Program abstracts of the 19th National Conference of the Anxiety Disorders Association of America (ADAA) 24:86.
- Cox, B. J., Endler, N. S., & Swinson, R. P. (1995). An examination of levels of agoraphobic severity in panic disorder. *Journal of Behavior Research & Therapy*, 33, 57-62.
- Cox, B. J., Swinson, R. P., & Shaw, B. F. (1991). Value of the Fear Questionnaire in differentiating agoraphobia and social phobia. *The British Journal of Psychiatry*, 159, 842-845.
- Cramer, V., Torgersen, S., & Kringlen, E. (2005). Quality of life and anxiety disorders: a population study. *Journal of Nervous and Mental Disease*, 193, 196-202.
- Craske, M. G. (1999). *Anxiety disorder: psychological approaches to theory and treatment*. Boulder, Co: West view press.
- Craske, M. G., DeCola J. P., Sachs A. D., & Pontillo, D. C. (2003). Panic control treatment for agoraphobia. *Journal Anxiety Disorder*, 17, 321-333.
- Craske, M.G., Farchione, T.J., Allen, L.B., (2007). Cognitive behavioural therapy for panic disorder and comorbidity: More of the same or less of more? *Journal of Behavior Research Therapy*, 45, 1095-109.
- Craske, M. G., Barlow, D. H., & Meadows, E. A. (1994). *Therapist guide for the mastery of your anxiety and panic II and agoraphobia supplement*. Albany, New York: Graywind Publications Incorporated.
- Craske, M. G., & Barlow, D. H. (2008). Panic disorder and agoraphobia. In D. H. Barlow (Ed). *Clinical handbook of psychological disorders* (pp. 1-64) (4th ed.). New York: Guilford Press.
- Craske, M. G., Brown, T. A., & Barlow, D. H. (1991). Behavioral treatment of panic disorder: A two-year follow-up. *Journal Behavior Therapy*, 22, 289-304.
- Craske, M. G., Maidenberg, E. & Bystritsky, A. (1995). Brief cognitive behavioral

- versus nondirective therapy for panic disorder. *Journal of behavior therapy and experimental psychology*, 26, 113-120.
- Craske, M. G., Miller, P. P., Rotunda, R., & Barlow, D. H. (1990). A descriptive report of features of initial unexpected panic attacks in minimal and extensive avoiders. *Journal of Behavior Research and therapy*, 28, 395-400.
- Craske, M. G., Rowe, M., Lewin, M., & Noriega-Dimitri, R. (1997). Interoceptive exposure versus breathing retraining within cognitive-behavioural therapy for panic disorder with agoraphobia. *British Journal of Clinical psychology* 36, 85-99.
- Crowe, R. R. (1985). The genetics of panic disorder and agoraphobia. *Journal of Psychiatric Development*, 2, 171-186.
- Crowe, R. R., Noyes R., Pauls, D. L., & Slymen, D. (1983). A family study of panic disorder. *Archive General Psychiatry*, 40, 1065-1069.
- Cuijpers, P., van Straten, A., & Warmerdam, L. (2008). Are individual and group treatments equally effective in the treatment of depression in adults? A meta-analysis. *Journal of European Psychiatry*, 22, 38-51.
- Dannon, P. N., Gon-Usishkin, M., Gelbert, A., Lowengrub, K., & Grunhaus, L. (2004). Cognitive behavioral group therapy in panic disorder patients: the efficacy of CBGT versus drug treatment. *Annals of Clinical Psychiatry*, 16, 41-46.
- Dannon, P. N., Iancu I., & Grunhaus, L. (2002). Psychoeducation in panic disorder patients: effect of a self-information booklet in a randomized, masked-rater study. *Journal of Depression and Anxiety*, 16, 71-76.
- Deacon, B., Lickel, J., Possis, E., Abramowitz, B. M., & Taylor. K. W. (2012). Do Cognitive Reappraisal and Diaphragmatic Breathing Augment Interoceptive Exposure for Anxiety Sensitivity? *Journal of Cognitive Psychotherapy: An International Quarterly*, 26, 257-269.
- Deacon, B., & Abramowitz, J. (2006). A pilot study of two-day cognitive-behavioral therapy for panic disorder. *Journal of Behavior Research and Therapy*, 44, 807-817.
- Deacon, B., & Abramowitz, (2004). Cognitive and behavioural treatments for Anxiety Disorders: A review of meta-analytic findings. *Journal of Clinical Psychology*, 60, 429-441.
- DeGuire, S., Gevirtz, R., Hawkinson, D., & Dixon, K. (1996). Breathing retraining: a three-year follow-up study of treatment for hyperventilation syndrome and associated functional cardiac symptoms. *Journal of biofeedback and self-regulation*, 21, 191-198.
- DeGuire, S., Gevirtz, R., Kawahara, Y., & Maguire, W. (1992). Hyperventilation syndrome and the assessment of treatment for functional cardiac symptoms.

American Journal of Cardiology 70, 673-677.

De Ruiter, C., Rijken, H., Garssen, B., & Kraaimatt, F. (1989). Breathing retraining, exposure and a combination of both, in the treatment of panic disorder with agoraphobia. *Journal of Behavior Research and Therapy*, 27, 647-655.

DiNardo, P. A., & Barlow, D. H. (1988). *Anxiety Disorders Interview Schedule-Revised (ADIS-R)*. Albany, NY: Graywind Publications.

Dixon, L. J., Sy, J.T., Kemp, J. J., & Deacon, B. J. (2013). Does Anxiety Sensitivity Cause Panic Symptoms? An Experimental Investigation, *Journal of Experimental Psychopathology*, 4, 208-223.

Donnel, C. D., & McNally, R. J. (1990). Anxiety sensitivity and panic attacks in a nonclinical population. *Journal of Behavior Research and Therapy*, 28, 83-85.

Dorland's pocket medical Dictionary (1982). (23 th ed). WB Saunders Co Philadelphia.

Eaton, W. W., Kessler, R. C., Wittchen, H. U., & Magee, W. J. (1994). Panic and panic disorder in the United States. *American Journal Psychiatry* 151, 413 - 420.

Ehlers, A. (1993). Somatic symptoms and panic attacks: A retrospective study of learning experiences. *Journal of Behavior Research and Therapy*, 31, 269-278.

Ehlers, A. (1995). A one-year prospective study of panic attacks: Clinical course and factors associated with maintenance. *Journal of Abnormal psychology*, 104, 164-172.

Eidelson, J. I. (1985). Cognitive group therapy for depression: Why and What. *International journal of Mental Health*, 13, 54-66.

Eifert, G. H., & Forsyth, J. P. (2005). *Acceptance and commitment therapy for anxiety disorders: A practitioner's guide to using mindfulness, acceptance, and value-based behavior change strategies*. Oakland, CA: New Harbinger.

Emmrich, A., Beesdo-Baum, K., Gloster, A. T., Knappe, S., Höfler, M., Arolt, V., Deckert, J., Gerlach, A. L., Hamm, A. O., Kircher, T., Lang, T., Richter, J., Ströhle, A., Zwanzger, P., & Wittchen, H. U. (2012). Depression does not affect the treatment outcome of CBT for panic and agoraphobia: results from a multicenter randomized trial. *Journal of Psychotherapy and Psychosomatics*, 8, 161-172.

Erickson, D. H., Janeck, A. S., & Tallman, K. (2007). A cognitive-behavioral group for patients with various anxiety disorders. *Journal of Psychiatry Service*, 58, 1205-1211.

Evans, L., Holt, C., & Oei, T.P. (1991). Long term follow-up of agoraphobics treated by brief intensive group cognitive behavioural therapy. *Australian and New Zealand Journal of Psychiatry* 25, 343-349.

- Fava, G. A., Rafanelli, C., & Grandi, S. (2001). Long-term outcome of panic disorder with agoraphobia treated by exposure. *Journal of Psychological Medicine*, 5, 891-898.
- Foa, E., & Kozak, M. J. (1986). Emotional processing of fear: Exposure to correcting information. *Psychological Bulletin*, 99, 20-35.
- Forsyth, J. P., & Eiferta, J. H. (1996). Systemic alarms in fear conditioning I: A reappraisal of what is being conditioned. *Journal of Behavior Therapy*, 27, 441-462.
- Forsyth, J. P., Acheson, D. A., & Fusé, T. M. (2009). General principles and empirically supported. In W. O'Donohue., J. Fisher & S. C. Hayes (Eds), *Interoceptive exposure for panic disorder*. John Willey & Sons.
- Frankel, B. (2002). Existential issues in group psychotherapy. *International Journal of Group Psychotherapy*, 52, 115-131.
- Franklin, J. A. (1989). A 6-years follow-up of the effectiveness of respiratory retraining in-situ isometric relaxation and cognitive modification in the treatment of agoraphobia. *Journal of Behavior modification* 13, 139-167.
- Franklin, J. A., & Andrews, G. (1989). Stress and the onset of agoraphobia. *Australian psychologist journal*, 24, 203-219.
- Fuhriman, A., & Burlingame, G. M. (1994). Group psychotherapy: Research and practice. In A. Fuhriman & G. M. Burlingame (Eds.). *Handbook of group psychotherapy* (pp. 3-40). New York: Wiley.
- Furer, P., Walker, J. R., Chartier, M. J., Stein, M. B. (1997). Hypochondriacal concerns and somatization in panic disorder. *Journal of Depression & Anxiety*. 6, 78-85.
- Furukawa, T. A., Watanabe, N., & Churchill, R. (2006). Psychotherapy plus antidepressant for panic disorder with or without agoraphobia: systematic review. *British Journal of Psychiatry*, 188, 305-312.
- Fydrich, T., Dowdall, D., & Chambless, D. L. (1992). Reliability and validity of the Beck Anxiety Inventory. *Journal of Anxiety Disorders*, 6, 55-61.
- Fyer, M. R., Uy, J., Martinez, J., Goetz, R., Klein, D. F., Fyer, A., Liebowitz, M. R., & Gorman, J. (1987). CO₂ challenge of patients with panic disorder. *American Journal of psychiatry*, 144, 1080-1082.
- Fyer, A. J., Mannuzza, S., Chapman, T. F., Lipsitz, J., Martin, L. Y., & Klein, D. F. (1996). Panic disorder and social phobia: effects of comorbidity on familial transmission. *Journal of Anxiety* 2, 173-178.
- Gabbard, G. O. (2004). Panic Disorder. *Gabbard's treatments of psychiatric disorders* (pp. 485-487) (4 th ed). American Psychiatric Publishing.

- Galassi, F., Quercioli, S., Charismas, D., Niccolai, V., & Barciulli, E. (2007). Cognitive-behavioral group treatment for panic disorder with agoraphobia. *Journal Clinical Psychology, 63*, 409-416.
- Gallo K. P., Chan P. T., Buzzella, B. A., Whitton, S. W., & Pincus, D. B. (2012). The impact of an 8-day intensive treatment for adolescent panic disorder and agoraphobia on comorbid diagnoses. *Journal of Behavior therapy, 43*, 153-159.
- Garakani, A., Mathew, S. J., & Charney, D. S. (2006). Neurobiology of anxiety disorders and implications for treatment. *Mount Sinai Journal Medicine, 73*, 941-949.
- García-Cabeza, I., Ducajú, M., Chapela, E., & González de Chávez, M (2011). Group Analysis. *American psychological association (APA), 44*, 421-438.
- Garsen, B., De Ruiter, C., & Van Dyck, R. (1992). Breathing retraining: A rational placebo? *Clinical Psychology Review, 12*, 141-153.
- Gibbs, D. M. (1992). Hyperventilation-Induced Cerebral Ischemia in Panic Disorder and Effect of Nimodipine. *American Journal of Psychiatry, 49*, 1589-1591.
- Gloster, A. T., Wittchen, H. U., Einsle, F., Lang, T., Helbig-Lang, S., Fydrich, T., Fehm, L., Hamm, A. O., Richter, J., Alpers, G. W., Gerlach, A. L., Ströhle, A., Kircher, T., Deckert, J., Zwanzger, P., Höfler, M., & Arolt, V. (2011). Psychological Treatment for Panic Disorder with Agoraphobia: A Randomized Controlled Trial to Examine the Role of Therapist-Guided Exposure in-situ in CBT. *Journal of Consulting and Clinical Psychology, 79*, 406-420.
- Goldstein, A. J., & Chambless, D. L. (1978). A reanalysis of agoraphobia. *Journal of Behavior Therapy, 9*, 47-59.
- Goldstein, R. B., Wickramaratne, P. J., Horwath, E., & Weissman, M. (1997). Familial aggregation and phenomenology of 'early'-onset (at or before age 20 years) panic disorder. *Archives of General Psychiatry, 54*, 271-278.
- Goldstein, R. B., Weissman, M. M., Adams, P. B., Howath, E., Lish, J.D., Charney, D., Woods, S.W., Sobin, C., & Wickramaratne, P.j. (1994). Psychiatric disorders in relatives of probands with panic disorders and or major depression. *Archive genetic psychiatry, 51*, 383-394.
- Goodwin, R. D. (2002). Self-report hay fever and panic attacks in the community. *Annals of Allergy, Asthma, and Immunology, 88*, 556-559.
- Goodwin, R. D., Pine, D. S., & Hoven, C. W. (2003). Asthma and panic attacks among youth in the community. *Journal of Asthma, 40*, 139-145.
- Goodwin, R. D., & Roy-Birne, P. (2006). Panic and suicidal ideation and suicide Attempt: Result from the National Comorbidity Survey. *Journal of Depression and Anxiety, 23*, 124-132.

- Gorman, J. M., Askanazi, J., Liebowitz, M. R., Fyer, A. J., Stein, J., Kinney, J. M., & Klein, D. F. (1984). Response to hyperventilation in a group of patients with panic disorder. *American Journal of Psychiatry*, 141, 857-861.
- Gorman, J. M., Fyer, M. R., Goetz, R., Askanazi, J., Liebowitz, M. R., Fyer, A. J., Kenny, J., & Klein, D. F. (1988). Ventilatory physiology of patients with panic disorder. *Archives of General Psychiatry*, 45, 31-39.
- Gorman, J. M., Kent, J. M., Sullivan, G. M., & Coplan, J. D. (2000). Neuroanatomical hypothesis of panic disorder, revised. *American Journal of Psychiatry*, 157, 493-505.
- Gorman, J. M., Martinez, J., Browne, S., Coplan, J., & Papp, L. A. (2001). Physiological Changes during Carbon Dioxide Inhalation in Patients with Panic Disorder, Major Depression, and Premenstrual Dysphoric Disorder: Evidence for a Central Fear Mechanism. *Journal of General Psychiatry*, 58, 125-131.
- Gorman, J. M., Papp, L. A., Coplan, J. D., Martinez, J. M., Lennon, S., Goetz, R. R., Ross, D., & Klein, D. (1994). Anxiogenic Effects of CO₂ and Hyperventilation in patients with Panic Disorder. *American Journal of Psychiatry*, 151, 547-553.
- Gould, R. A., Otto, M. W., & Pollack, M. H. (1995). A meta-analysis of treatment outcome for panic disorder. *Clinical Psychology Review*, 15, 819-844.
- Grant, B. F., Hasin, D. S., Stinson, F. S., Dawson, D. A., Goldstein, R. B., Smith, S., Huang, B., & Saha, T. D. (2006). The epidemiology of DSM-IV panic disorder and agoraphobia in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *The journal of clinical psychiatry*, 67, 363-374.
- Gratacòs, M., Sahún, I., Gallego, X., Amador-Arjona, A., & Dierssen, M. (2007). Candidate genes for panic disorder: insight from human and mouse genetic studies. *Journal of Genes, Brain and Behavior*, 6, 2-23.
- Greenberg, P. E., Sisitsky, T., Kessler, R. C., Finkelstein, S. N., Berndt, E. R., Davidson, J. R., Ballenger, J. C., & Fyer, A. J. (1999). The economic burden of anxiety disorders in the 1990s. *Journal of Clinical Psychiatry* 60, 427-435.
- Gregor, K. L., Zvolensky, M. J., & Yartz, A. R. (2005). Perceived health among individuals with panic disorder: associations with affective vulnerability and psychiatric disability. *The journal of nervous and mental disease*, 193, 697-699.
- Griez, E., de Loof, C, Pols, H., Zandbergen J., & Lousberg, H. (1990a). Specific sensitivity of patients with panic attacks to carbon dioxide inhalation. *Psychiatry Research*, 31, 193-199.
- Griez, E., Zandbergen, J., Pols, H., & de Loof, C. (1990b). Responses to 35% CO₂ as a marker of panic in severe anxiety. *American Journal of Psychiatry*, 145, 796-797.

- Grillon, C. H., Lissek, S., Rabin, S., McDowell, D., Dvir, S., & Pine, D. S. (2008). Increased Anxiety During Anticipation of Unpredictable But Not Predictable Aversive Stimuli as a Psychophysiologic Marker of Panic Disorder. *American Journal of Psychiatry*, 165, 898-904.
- Guy, J. D., Stark, M. J., & Polestra, P. L. (1988). Personal therapy for psychotherapists before and after entering professional practice. *Professional Psychology: Research and Practice*, 19, 474-476.
- Hafner, R. J., & Milton, F. (1977). The influence of propranolol on the exposure in vivo of agoraphobics. *Journal of Psychological Medicine*, 7, 419-425.
- Hayward, C., Killen, J. D., Kraemer, H. C., & Taylor, C. B. (2000). Prospective predictors of panic in adolescents. *Journal of the Academy of Child Psychiatry*, 39, 1-8.
- Hazlett-Stevens, H., & Craske, M. G. (2004). Brief Cognitive-Behavioral Therapy: Definition and Scientific Foundations. In F. W. Bond & W. Dryden (Eds.), *Handbook of Brief Cognitive Behavior Therapy* (pp. 1-21). John Wiley & Sons Ltd.
- Hazlett-Stevens, H. & Craske, M. G. (2009). Breathing retraining and diaphragmatic breathing techniques. In W. T. O'Donohue & J. E. Fisher (Eds.). *General Principles and Empirically Supported Techniques of Cognitive behavior therapy* (pp. 166-172). John Wiley & Sons, Inc., Hoboken, New Jersey.
- Hecker, J. E., Losee, M. C., Roxann, R. N., & Maki, K. (2004). Mastery of your anxiety and panic and brief therapies. *Journal of anxiety disorders*, 18, 111-126.
- Heimberg, R. G., & Becker, R. E. (2002). *Cognitive behavioral group therapy for social phobia: A treatment manual. Cognitive-behavioral group therapy for social phobia: Basic mechanisms and clinical strategies* (pp. 129-132). New York: Guilford Press.
- Heldt, E., Blava, C., Isolan, L., Kipper, L., Teruchkin, B., Otto, M. W., Fleck, M., & Manfro, G. G. (2006). Quality of life and treatment outcome in panic disorder: cognitive behavior group therapy effects in patients refractory to medication treatment. *Journal of Psychotherapy Psychosomatics*, 75, 183-186.
- Heldt, E., Kipper, L., Blava, C., Salum, G. A., Hirakata, V. N., Otto, M. W., & et al. (2010). Predictors of relapse in the second follow-up year post cognitive-behavior therapy for panic disorder. *Revista Brasileira de Psiquiatria*, 33, 23-29.
- Hendriks, G. J., Keijsers, G. P. J., Kampman, M., Oufroshaar, R. C., Verbraak, M. J. P. M., Broekman, T. G., & Hoogduin, C. A. L. (2010). A randomized controlled study of paroxetine and cognitive-behavioral therapy for late-life panic disorder. *ACTA Psychiatrica Scandinavica*, 122, 11-19.

- Hibbert, G. A., & Chan, M. (1989). Respiratory control: its contribution to the treatment of panic attacks. A controlled study. *Journal of Psychiatry*, 6, 154-232.
- Hiller, W., Leibbrand, R., Rief, W., & Fichter, M. M. (2005). Differentiating hypochondriasis from panic disorder. *Journal of Anxiety Disorders*, 19, 29-49.
- Hocaoglu, C., Gulec, M. Y., & Durmus, I. (2008). Psychiatric comorbidity in patients with chest pain without a cardiac etiology. *Israel Journal of Psychiatry & Related Sciences*, 45, 49-54.
- Hoffart, A., Sexton, H., Hedley, L. M., & Martinsen, E.W. (2008). Therapy Mechanisms of change in cognitive therapy for panic disorder with agoraphobia. *Journal of Behavior Therapy and Experimental Psychiatry*, 39, 262-272.
- Hofmann, S. G., Barlow, D. H., Papp, L. A., Detweiler, M. F., Ray, S. E., Shear, M. K., Woods, S. W., & Gorman, J. M. (1998). Pretreatment attrition in a comparative treatment outcome study on panic disorder. *American Journal of Psychiatry*, 155, 43-47.
- Hofmann, S. G., Meuret, A. E., Rosenfield, D., Suvak, M. K., Barlow, D. H., Gorman, J. M., Shear, M. K., & Woods, S. W. (2007). Preliminary evidence for cognitive mediation during cognitive behavioral therapy for panic disorder. *Journal of Consulting and Clinical Psychology*, 75, 374-379.
- Hofmann, S. G., & Smits, J. A. (2008). Cognitive-behavioral therapy for adult anxiety disorders: a meta-analysis of randomized placebo-controlled trials. *Journal of Clinical Psychiatry*, 69, 621-632.
- Hofmann, S. G., & Spiegel, D. A. (1999). Panic Control Treatment and its Applications. *Journal of Psychotherapy Practice and Research*, 8, 3-11.
- Hollander, E., Liebowitz, M. R., & Gorman, J. M. (1988). Anxiety. In J. A. Talbott, R. E. Hale & S. C. Yudofsky (Eds.). *The American Psychiatric press textbook of psychiatry*. Washington DC: American Psychiatric.
- Hollander, E., & Simeon, D. (2010). Anxiety disorders. In R. E. Hales., S. C. Yudofsky, G. O. Gabbard (Eds). *Essentials of Psychiatry*, (pp. 185-229) (3th ed). American Psychiatric Publishing, Inc.
- Holmes, S. E., & Kivlighan D. M. (2000). Comparison of Therapeutic factors in Group and individual treatments processes. *Journal of counseling psychology*, 47, 478-484.
- Hopper, J. L., Judd, F. K., Derrick, P. L., & Burrows, G. D (1987). A family study of panic disorder, "Genetic epidemiology, 4, 33-41.
- Horvath, A. O., Del Re, A. C., Flückiger, C., & Symonds, D. (2011). Alliance in individual psychotherapy. *Psychotherapy: Theory, Research, Practice, Training*, 48, 9-16.

- Houghton, S., & Saxon, D. (2007). An evaluation of large group CBT psycho-education for anxiety disorders delivered in routine practice. *Patient Education and Counseling journal*, 68, 107-110.
- Hoyer, J., Becker, E. S., Neumer, S., Soeder, U., & Margraf, J. (2002). Screening for anxiety in an epidemiological sample: Predictive accuracy of questionnaires. *Journal of Anxiety Disorders*, 16, 113-134.
- Huh, Y. J., Choi, Y. H., & Park, K. H. (2003). Therapeutic factors of group cognitive behavioral therapy for panic disorder. *Journal of Cognitive Behavior Therapy in Korea*, 3, 57-67.
- Iketani, T., Nagao, K., Minamikawa, N., Shidao, A., et al. (2002). Anxiety sensitivity and catastrophic cognition in panic disorder: Association with agoraphobia. *Journal Clinical Psychiatry*, 44, 977-983.
- Ito, L. M., de Araujo, L. A., Tess, V. L., de Barros-Neto, T. P., Asbahr, F. R., & Marks, I. (2001). Self-exposure therapy for panic disorder with agoraphobia: randomized controlled study of external v. interoceptive self-exposure. *British Journal of Psychiatry*, 178, 331-336.
- Jacob, R. G., & Rapport, M. D. (1984). Panic disorder: Medical and Psychological Parameters. In S. M. Turner (Ed), *Behavioral theories and treatment of anxiety* (pp. 321-365). New York: Plenum Press.
- Jacobson, E. (1938). *Progressive relaxation*. Chicago: University of Chicago Press.
- Jette, N., Patten, S., Williams, J., Becker, W., Wiebe, S. (2008). Comorbidity of migraine and psychiatric disorders – a national population-based study. *Headache*. 48, 501-516.
- Kajander, R., & Peper, E. (1998). Teaching diaphragmatic breathing to children. *Biofeedback*, 26, 14-17.
- Jang, K. L. (2005). *The behavioral genetics of psychopathology: a clinical guide*, Lawrence Erlbaum Associations., publishers.
- Jansson. L., Jerremalm. A., & Öst, L. G. (1986). Follow-up of agoraphobic patients treated with exposure in vivo or applied relaxation. *British Journal of Psychiatry*, 149, 486-490.
- Kashdan, T. B., Zvolensky, M. J., & McLeish, A. C. (2008). Anxiety sensitivity and affect regulatory strategies: Individual and interactive risk factors for anxiety-related symptoms. *Journal of Anxiety Disorders*, 22, 429-440.
- Katerndahl, D. A. (1988). The sequence of panic symptoms. *Journal of family practice*, 26, 49-52.
- Katerndahl, D. A., & Realini, J. P. (1997). Quality of life and panic-related work

disability in subjects with infrequent panic and panic disorder. *Journal of Clinical Psychiatry*, 58, 153-158.

Katon, W. (1986). Panic disorder; Epidemiology, diagnostic, and treatment in primary care. *Journal of clinical psychology*, 47, 21-27.

Katon, W. (1994). *Panic disorder in the medical setting*. Washington, DC: National Institute of Mental Health.

Katon, W., Hollified, M., Chapman, T., Mannuzza, S., Ballenger, J., & Fyer, A. (1995). In frequent panic attack: Psychiatric comorbidity, personality characteristic and functional disability. *Journal of psychiatric research*, 29, 121-131.

Katon, W., Lin, E., Von Korff, M., Russo, J., Lipscomb, P., & Bush, T. (1991). Somatization: a spectrum of severity. *American Journal of Psychiatry*, 148, 34-40.

Kaviani, H., & Mousavi, A. (2008). Psychometric properties of the Persian version of Beck Anxiety Inventory (BAI). *Tehran University Medical Journal*, 2, 136-140.

Kenardy, J. A., Dow, M. G., Johnston, D. W., Newman, D. G., Thomson, A., & Taylor, C. B. (2003). A multicenter comparison of delivery methods of cognitive-behavioral therapy for panic disorder: an international multicenter trial. *Journal of Consulting and Clinical Psychology*, 71, 1068-1075.

Kenardy, J., Oei, T. P. S., & Evans, L. (1990). Hyperventilation and Panic Attack. *Australian and New Zealand Journal of Psychiatry*, 24, 261-267.

Kenardy, J., & Taylor, C. B. (1999). Expected versus unexpected panic attacks: a naturalistic prospective study. *Journal Anxiety Disorder*, 13, 435-45.

Kendall, P. C., & Watson, D. (Eds.) (1989). *Anxiety and depression: Distinctive and overlapping features*. Academic Press, San Diego, CA.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005a). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of general psychiatry*, 62, 593-602.

Kessler, R. C., Chiu, W. T., Demler, O., Merikangas, K. R., & Walters, E. E. (2005b). Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry*, 62, 617-27.

Kessler, R. C., Chiu, W. T., Jin, R., Ruscio, A. M., Shear, K., & Walters, E. E. (2006). The epidemiology of panic attacks, panic disorder, and agoraphobia in the National Comorbidity Survey Replication. *Archives of general psychiatry*, 63, 415-424.

Kessler, R.C., Stang, P.E., Wittchen, H.U., Ustun, T.B., Roy-Burne, P.P., & Walters,

- E.E. (1998). Lifetime panic-depression comorbidity in the National Comorbidity Survey. *Arch General Psychiatry*, 55, 801-808.
- Khawaja, N. G., & Oei, T. P. S. (1998). Catastrophic cognitions in panic disorder with and without agoraphobia. *Clinical Psychology Review*, 18, 341-365.
- Khoshbooi, R. (2012). Comparison Group and Individual Cognitive Behavioral Therapy in Treatment of Depression among Iranian Women around Menopause. *International Journal of Psychological Studies*, 4, 174-181.
- Kiliç, C., Noshirvani, H., Basoglu, M., & Marks, I. (1997). Agoraphobia and panic disorder: 3. 5 years after alprazolam and/or exposure treatment. *Journal of Psychotherapy Psychosomatic*, 66, 175-178.
- Kim, B., Lee, S. H., Kim, Y. W., Choi, T. K., Yook, K., Suh, S. Y., Cho, S. J., & Yook, K. H. (2010). Effectiveness of a mindfulness-based cognitive therapy program as an adjunct to pharmacotherapy in patients with panic disorder. *Journal Anxiety Disorder*, 24, 590-595.
- King, A. L. S., Valença, A. M., de Melo-Neto, V. L., Freire, R. C. H., Mezzasalma, M. A., de Oliveira e Silva, A. C., & Nardi, A. E. (2011). Efficacy of a specific model for cognitive-behavioral therapy among panic disorder patients with agoraphobia: a randomized clinical trial. *Sao Paulo Medical Journal*, 129, 325-334.
- Kinley, D. J., Cox, B. J., Clara, I., Goodwin, R. D., & Sareen, J. (2009). Panic attacks and their relationship to psychological and physical functioning in Canadians: results from a nationally representative sample. *Canadian Journal of Psychiatry*, 54, 113-122.
- Kivlighan, D. M., & Holmes, S. E. (2004). The importance of therapeutic factors: A typology of therapeutic factors studies. In J. L. DeLucia-Waack, D. A. Gerrity, C. R. Kalonder, & M. T. Riva (Eds.) *Handbook of group counseling and psychotherapy* (pp. 23-36). Sage Publications, Inc., Thousand Oaks, CA.
- Klein D. F. (1984). Introduction to the Anxiety Disorders Program. In: L. Grinspoon, (Ed). *Psychiatry Update American Psychiatric Association Annual Review*, Washington, DC: American Psychiatric Press, Inc., 3, 390-392.
- Klein, D. F. (1993). False suffocation alarms, spontaneous panics, and related conditions: an integrative hypothesis. *Archives of General Psychiatry*, 50, 306-317.
- Klerman, G. L., Weissman, M. M., Ouellette, R., Johnson, J., & Greenwald, S. (1991). Panic attacks in the community. Social morbidity and health care utilization. *Journal of the American Medical Association (JAMA)*, 265, 742-74.
- Klerman, G. L., Hirschfeld, R. M. A., & Weissman, M. M. (1993). Panic Anxiety and its treatments: Report of the World Psychiatric Association Presidential Educational Program Task Force, (pp. 44). American Psychiatric Association.

- Klosko, J. S., Barlow, D. H., Tassinari, R., & Cerny, J. A. (1990). A comparison of alprazolam and behavior therapy in the treatment of panic disorder. *Journal of Consulting Clinical Psychology, 58*, 77-84.
- Kösters, M., Burlingame, G., Nachtigall, C., & Strauss, B. (2006). A meta-analytic review of the effectiveness of inpatient group psychotherapy. *Group Dynamics: Theory, Research & Practice, 10*, 143-163.
- Kühner, C., Burger, C., Keller, F., & Hautzinger, M. (2007). Reliability and validity of the Revised Beck Depression Inventory (BDI-II): Results from German samples. *Journal of Nervenarzt, 78*, 651-656.
- Lau, J. J., Calamari, J. E., & Waraczynski M. (1996). Panic attack symptomatology and anxiety sensitivity in adolescents. *Journal of Anxiety Disorders, 10*, 355-364.
- Lazarus, A. A. (1971). *Behavior therapy and beyond*. New York:Mc Craw-Hill.
- Lazarus, A. A. (2006). The Utility and Futility of Combining Treatments in Psychotherapy. *Clinical Psychology: Science and Practice, 3*, 59-68.
- Leahy, R. L., Holland, S. J. F., & McGinn. L. K. (2011). *Treatment Plans and Interventions for Depression and Anxiety Disorders*, (2 th ed).
- Lepöla, U., Koponen, H., Leinonen, E. (1996). A naturalistic 6-year follow-up study of patients with panic disorder. *Journal of Acta Psychiatrica Scandinavica, 93*, 181-183.
- Leszcz, M. (2008). The interpersonal approach to group psychotherapy. In G. M. Saiger., S. Rubenfeld & M. D, Dluhy. (Eds.), *Windows into today's group therapy* (pp. 129-149). New York: Rutledge.
- Leszcz, M., & Kobos, J. C. (2008). Evidence-based group psychotherapy: Using AGPA's practice guidelines to enhance clinical effectiveness. *Journal of Clinical Psychology, 64*, 1238-1260.
- Levitt, J. T., & Karekl. M. (2005). Acceptance and mindfulness-based approaches to anxiety conceptualization and treatment. In S. M, Orsillo (Ed.), *Integrating Acceptance and Mindfulness with Cognitive Behavioral Treatment for Panic Disorder*, (pp. 165-173). Springer Link.
- Leyfer, O.T., Ruberg J.L, Woodruff-Borden, J. (2006). Examination of the utility of the Beck Anxiety Inventory and its factors as a screener for anxiety disorders. *Journal of Anxiety Disorder, 20*, 444-458.
- Ley, R. (1987). Panic disorder: A hyperventilation interpretation, In L. Michelson & I. M, Ascher (Eds.). *Anxiety and stress disorders: Cognitive-behavior assessment and treatment*; (pp. 191-212). New York. Guilford press.
- Lidren, D. M., Watkins, P. L., Gould, R. A., Clum, G. A., Asterino, M., & Tulloch, H.

- L. (1994). A comparison of bibliotherapy and group therapy in the treatment of panic disorder. *Journal of Consulting & Clinical Psychology*, 62, 865-869.
- Li, X., Sundquist, J., & Sundquist, K. (2011). Sibling risk of anxiety disorders based on hospitalizations in Sweden. *Journal of Psychiatry and Clinical Neuroscience*, 65, 233-238.
- Lilienfeld, S. O. (1997). The relation of anxiety sensitivity to higher and lower order personality dimensions: Implications for the etiology of panic attacks. *Journal of Abnormal Psychology*, 106, 539-544.
- Lim, S. H., Anantharaman, V., Teo, W. S., Goh, P. P., & Tan, A. T. (1998). Comparison of treatment of supra ventricular tachycardia by Valsalva maneuver and carotid sinus massage. *Annals of Emergency Medicine*, 31, 30-35.
- Loughlin, K., & Generali, J. (2006). The guide to off-label prescription drugs: new uses for FDA-approved. *Mental health* (pp. 402-411). New York: free press.
- Lousberg, H., Griez, E., & Van den Hout, M. A. (1988). Carbon dioxide chemosensitivity in panic disorder. *Journal of Acta Psychiatrica Scandinavica*, 77, 214-218.
- Luby, j. L. (1995). Group therapy. In Glick, I. D. (Ed.): *Treating depression* (pp. 123-151). San Francisco: Jossey-Bass.
- Luster, E. A., Baumgartner, N., Adams, W. C., & Convertino, V. A. (1996). Effects of hypovolemia and posture on responses to the Valsalva maneuver. *Aviation, space, and environmental medicine*, 67, 308-13.
- Lydiard, R. B., Otto, M. W., & Milrod, B. (2001). Panic disorder. In Go. Gabbard (Ed). *Treatments of psychiatric Disorders*, (pp. 247-282) (3th ed). American psychiatric press: Washington, D. C.
- MacKenzie K. R. (1983). The clinical application of a group climate measure. In: Dies, R. R, MacKenzie K. R, (Eds), *Advances in group psychotherapy: Integrating research and practice*, (pp. 159-170). Madison, CT: International Universities Press.
- Maier, W., Lichtermann, D., Meyer, A., et al. (1993). A controlled family study in panic disorder. *Journal of psychiatric research*, 27, 79-87.
- Mailer, R. G., & Reiss, S. (1992). Anxiety sensitivity in 1984 and panic attacks in 1987. *Journal of Anxiety Disorders*, 6, 241-247.
- Manjula, M., Kumariah, V., Prasadarao, P. S. D. V., & Raguram, R. (2009). Cognitive behavior therapy in the treatment of panic disorder. *Indian Journal Psychiatry*, 51, 108-116.
- Mantar, A., Yemez, B., & Alkin, T. (2010). The validity and reliability of the Turkish

- version of the anxiety sensitivity. *Turkish Journal of Psychiatry*, 21, 225-234.
- Manzoni, G. M., Pagnini, F., Castelnuovo, G., & Molinari, E. (2008). Relaxation training for anxiety: a ten-year systematic review with meta-analysis. *Journal BMC Psychiatry*, 2, 8- 41.
- Marchand, A., Coutu, M. F., Dupuis, G., Fleet, R., Borgeat, F., Todorov, C., & Mainguy, N. (2008). Treatment of panic disorder with agoraphobia: randomized placebo-controlled trial of four psychosocial treatments combined with imipramine or placebo. *Journal of Cognitive Behavior Therapy*, 37, 146-159.
- Marchand, A., Germain, V., Reinharz D, Mainguy, N., & Landry, P. (2004). Analysis of the cost and the effectiveness of a psychotherapy for panic disorder with agoraphobia (PDA) versus a treatment combining pharmacotherapy and psychotherapy. *Journal mental health Quebec*, 29, 201-220.
- Marchand, A., Roberge, P., Primiano, S., & Germain, V. (2009). A randomized, controlled clinical trial of standard, group and brief cognitive-behavioral therapy for panic disorder with agoraphobia: A two-year follow-up. *Journal of anxiety disorders*, 23, 1139-1147.
- Marcus, S. M., Gorman, J., Shear, M. K., Lewin, D., Martinez, J., Ray, S., Goetz, R., Mosovich, S., Gorman, L., Barlow, D., & Woods, S. (2007). A Comparison of Medication Side Effect Reports by Panic Disorder Patients with and without Concomitant Cognitive Behavior Therapy. *American Journal Psychiatry*, 164, 273-275.
- Margraf, J., Barlow, D. H., Clark, D. M., & Telch, M. J. (1993). Psychological treatment of panic: Work in Progress on outcome, active ingredients, and follow-up. *Journal of Behavior Research and Therapy*, 31, 1-8.
- Margraf, J., & Schneider, S. (1991). Outcome and active ingredients of cognitive behavioral treatment for panic disorder. Paper presented at the 25th Annual meeting of the association for the Advancement behavior therapy, New York.
- Margraf, J., Taylor, B., Ehlers, A., Roth, W. T., & Agras, W. S. (1987). Panic attacks in the natural environment. *Journal of nervous and mental disease*, 175, 558-565.
- Markowitz, J.S., Weissman, M. M., Ouellette, R., Lish, J., & Klerman, G.L. (1989). Quality of life in panic disorder. *Archives of General Psychiafry*, 46, 984-992.
- Marks, I. M., Grey, S., Cohen, S. D., Hill, R., Mawson, D., Ramm, E. M., & Stern, R.S. (1983). Imipramine and brief therapist aided exposure in agoraphobics having self exposure homework: A controlled trial. *Archives of General psychiatry*, 40, 153-162.
- Marks, I. M., & Mathews, A. M. (1979). Brief standard self-rating for phobic patients. *Journal of Behavior Research and Therapy*, 17, 263-267.

- Marks, I. M., Swinson, R. P., Basoglu, M., Kuch, K., Noshirvani, H., O'Sullivan, G., Lelliott, P. T., Kirby, M., McNamee, G., & Sengun S. (1993). Alprazolam and exposure alone and combined in panic disorder with agoraphobia. A controlled study in London and Toronto. *British Journal of Psychiatry*, 162, 776-787.
- Maron, E., Hettema J. M., & Shlik. (2010). Advances in molecular genetics of panic disorder. *Molecular Psychiatry*, 15, 681-701.
- Marshall, E. C., Zvolensky, M. J., Sachs-Ericsson, N., Schmidt, N. B., & Bernstein, A. (2008). Panic attacks and physical health problems in a representative sample: singular and interactive associations with psychological problems, and interpersonal and physical disability. *Journal of Anxiety Disorders*, 22, 78-87.
- Martinsen, E. W., Olsen, T., Tønset, E., Nyland, K. E., & Aarre, T. F. (1998). Cognitive-behavioral group therapy for panic disorder in the general clinical setting: a naturalistic study with 1-year follow-up. *Journal Clinical Psychiatry*, 59, 437-442.
- Mavissakalian, M. R., & Guo, S. (2002). Predictors of entering a long-term drug treatment study of panic disorder. *Journal of Comprehensive Psychiatry*, 43, 88-94.
- Mavissakalian, M. R., & Michelson, L. (1986). Agoraphobia: Relative and combined effectiveness of therapist-assisted in vivo exposure and imipramine. *Journal of psychiatry*, 47, 117-122.
- McCabe, R. E., Chudzik, S. M., Antony, M. M., Young, L., Swinson, R. P., & Zvolensky, M. J. (2004). Smoking behaviors across anxiety disorders. *Journal of Anxiety Disorders*, 18, 7-18.
- McCabe, R. E., & Gifford, S. M. (2009). Handbook of anxiety and related disorders. In M. M, Antony, and M. B, Stein (Eds.). *Psychological treatment of panic disorder and agoraphobia* (pp. 308-320). Oxford University Press.
- McCarter, R. H. G. (1996). Panic disorder: Cognitive-behavioral treatment integration with pharmacotherapy. In Ellison, J. M (Ed.), *Integrative treatment of anxiety disorders* (pp. 77-112). Washington, DC: American Psychiatric Press.
- McCrone, P., Weeramanthri, T., Knapp, M., Rushton. A., Trowell, J., Miles, G., & Kolvin, I. (2005). Cost-effectiveness of individual versus group psychotherapy for sexually abused girls. *Journal of Child and Adolescent Mental Health*, 10, 26-31.
- McDermut, W., Miller, I., & Brown, R. A. (2001). The efficacy of group psychotherapy for depression : A meta analysis and review of the empirical research. *Clinical psychology: Science and practice* 8, 98-116.
- McNally, R. J., & Foa, E. B. (1996). The limitations of self efficacy theory in explaining therapeutic changes in phobic behavior. In R. M Rapee (Ed.), *Current controversies in the anxiety disorders* (pp. 369-372). New York: Guilford Press.

- McNally, R. J., & Lorenz, M. (1987). Anxiety sensitivity in agoraphobics. *Journal of Behavior Therapy and Experimental Psychiatry*, 18, 3-11.
- Mc Nally, R. J. (1990). Psychological approaches to panic disorder: A review. *Psychological Bulletin*, 34, 403-419.
- Mc Nally, R. J. (2002). Anxiety Sensitivity and panic disorder. *Journal of Biological psychiatry*, 52, 938-946.
- McNally, R. J. (1989). Is anxiety sensitivity distinguishable from trait anxiety? Reply to Lilienfield, Jacob and Turner. *Journal of Abnormal Psychology*, 98, 193-194.
- McNally, R. J. (1994). Panic disorder: A critical analysis. Psychological aspects (pp. 139-151). NewYork: Guilford Press.
- McRoberts, C., Burlingame, G. M., & Hoag, M. J. (1998). Comparative efficacy of individual and group psychotherapy: A meta-analytic perspective. *Group Dynamic: Theory, Research, and practice*, 2, 101-117.
- Malbos, E., Rapee, R. M., & Kavakli, M. (2013). A controlled study of agoraphobia and the independent effect of virtual reality exposure therapy. *Australian & New Zealand Journal of Psychiatry*, 47, 160-168.
- Merikangas, K. R., Angst, J., Eaton, W., Canino, G., Rubio-Stipeck, M. Walker, H., Wittchen, H. U., Andrade, L., Essau, C., Whitaker, A., Kraemer, H., Robins, L. N., & Kupfer, D. J. (1996). Comorbidity and boundaries of affective disorders with anxiety disorders and substance misuse: results of an international task force. *British Journal of Psychiatry*, 168, 58-67.
- Meulenbeek, P., Willemsse, G., Smit, F., van Balkom, A., Spinhoven, P., & Cuijpers P. (2008). Early intervention in panic: randomized controlled trial and cost-effectiveness analysis. *British Journal of Psychiatry*, 196, 326-331.
- Meuret, A. E, Rosenfield, D., & Seidel A. (2010a). Respiratory and cognitive mediators of treatment change in panic disorder: evidence for intervention specificity. *Journal Consult Clinical Psychology*, 78, 691-704.
- Meuret, A. E., Hofmann, S. G., & Rosenfield, D. (2010b). Catastrophic appraisal and perceived control as moderators of treatment response in panic disorder. *International Journal of Cognitive Therapy*, 3, 262-277.
- Meuret, A. E., Rosenfield, D., Hoffman, S. G., Roth, W. T., & Suvak, M. K. (2009). Changes in respiration mediate changes in fear of body sensations in panic disorder. *Journal of Psychiatric Research*, 43, 634-641.
- Meuret, A. E., Wilhelm, F. H., & Roth, W. T. (2001). Respiratory Biofeedback-Assisted Therapy in Panic Disorder. *Journal of Behavior Modification*, 25, 584-605.

- Meuret, A. E., Wilhelm, F. H., & Roth, W. T. (2006). Effect of capnometry assisted breathing therapy on symptoms and respiration in panic disorder. *Archieve of General Psychiatry*. In revision.
- Meuret, A. E., Wilhelm, F. H., Ritz, T., & Roth, W. T. (2008). Feedback of end-tidal pCO₂ as a therapeutic approach for panic disorder. *Journal of Psychiatric Research*, 42, 560-568.
- Michelson, L., Marchione, K., Greenwald, M., Glanz, L., Testa, S., & Marchione, N. (1990). Panic disorder: Cognitive-behavior treatment. *Journal of Behavior Research and Therapy*, 28, 141-151.
- Miller, R. C., & Berman, J. S. (1983). The efficacy of cognitive behavior therapies: a quantitative review of the research evidence. *Psychological Bulletin*, 94, 39-53.
- Mitchell, C. G. (1999). Treating anxiety in a manged care setting: A controlled comparison of medication alone versus medication plus. *Research on social work practice*, 9, 188-200.
- Mitte, K. (2005). A meta-analysis of the efficacy of psycho and pharmachotherapy in panic disorder with and without agoraphobia. *Journal of Affective Disorders*, 66, 27-45.
- Mohammadi, M. R., Davidian, H., Noorbala, A. A., Malekafzali, H., Naghavi, H. R., Pouretamad, H. R., Bagheri Yazdi, S. A., Rahgozar, M., Alaghebandrad, J., Amini, H., Razzaghi, E. M., Mesgarpour, B., Soori, H., Mohammadi, M., & Ghanizadeh, A. (2005). An epidemiological survey of psychiatric disorders in Iran. *Clinical Practice and Epidemiology in Mental Health*. Published online.
- Mohammadi, M. R., Rahgozar, M., Bagheri Yazdi, S. A., Mesgarpour, B., Zandi, A., & Vosough, F. (2001). Epidemiology of psychiatric disorders in Hormozgan province.
- Moller T, Hegna EA. (2001). Group therapy of anxiety benefits and profits, *Abstact, Pubmed*.
- Morrison, N. (2001). Group cognitive therapy: treatment of choice or suboptimal option? *Journal of Behavioral and Cognitive Psychotherapy*, 29, 311-332.
- Moscovitch, D. A., Antony, M. M., & Swinson, R. P. (2009). Exposure based treatments for anxiety disorders: Theory and process. In M. M. Antony. & M. B. Stein (Eds.), *Handbook of anxiety and anxiety disorders* (pp. 461-475). New York: Oxford University Press.
- Nakano, Y., Lee, K., Noda, Y., Ogawa, S., Kinoshita, Y., Funayama, T., Watanabe, N., Chen J., Noguchi, Y., & Furukawa, T. A. (2008). Cognitive-behavior therapy for Japanese patients with panic disorder: acute phase and one-year follow-up results. *Journal of Psychiatry and Clinical Neuroscience*, 62, 313-321.

- Nardi, A. E. (2006). Some notes on a historical perspective of panic disorder. *Brazilian Journal of Psychiatry*, 55, 154-160.
- Nardi, A. E., Nascimento, I., Valença, A. M., Lopes, F. L., Mezzasalma, M. A., & Zin, W. A. (2003). Panic disorder in a breath-holding challenge test: A simple tool for a better diagnosis. *Archives of Nerero Psychiatry*, 61, 718-722.
- Nardi, A. E., Valença, A. M., Nascimento, I., Mezzasalma, M. A., & Zin, W. (1999). Panic disorder and hyperventilation. *Archives of Nerero Psychiatry*, 57, 932-936.
- National Institute of Mental Health. (2007). "Panic Disorder <http://www.pueblo.gsa.gov/cictext/health/panic/panfly.htm>.
- Nauert, R. (2011). Twin Studies Suggest Genetic Risk for Panic Disorder. *Journal of Psych Central*. Retrieved on October.
- Nazemi, H., Ronald A. Kleinknecht, Dale L. Dinnel, Walter J. Lonner Nazemi, S., Shamlo, S., & Sobhan, A. (2003a). A Study of Panic Attacks in University Students of Iran. *Journal of Psychopathology and Behavioral Assessment*, 25, 191-201.
- Nazemi, H., & Dager, S. R. (2003b). Coping strategies of panic and control subjects undergoing lactate infusion during MRI confinement. *Comprehensive Psychiatry*, 44, 190-197.
- Neimeyer, R. A. (1985). Group psychotherapies for depression: An overview: *international journal of mental helth*, 13, 3-7.
- Neron, S., Lacroix, D., & Chaput, Y. (1995). Group vs. individual cognitive behavior therapy in panic disorder: An open clinical trial with a six month follow-up. *Canadian Journal of Behavioral Science*, 27, 379-392.
- Nezu, A. M., Nezu, C. M., & Lombardo, E. (2004). *Cognitive behavioral case formulation and treatment Design*. Springer publishing company.
- Ninan, P. T., & Dunlop, B. W. (2005). Neurobiology and etiology of panic disorder. *Journal of Clinical Psychiatry*, 66, 3-7.
- Nixon, P. G. (1993). The grey area of effort syndrome and hyperventilation from Thomas Lewis to today. *Journal of the Royal College of Physicians of London*, 27, 377-383.
- Nock, M. K., Hwang, I., Sampson, N., & Kessler, R. C. (2010). Mental disorders, comorbidity and suicidal behaviors: results from the national comorbidity survey replication. *Journal of Molecular Psychiatry*, 15, 868-876.
- Noda, Y., Nakano, K., Lee, S. Ogawa, Y. Kinoshita, T. Funayama, N. Watanabe, J. Chen, Y., Noguchi, M., Kataoka, M., Suzuki, & Furukawa, T. A. (2007). Sensitization of catastrophic cognition in cognitive-behavioral therapy for panic disorder. *Journal of BMC Psychiatry*, 10, 7- 70.

- Norcross, J. C., Strausser, D., & Missar, C. D. (1988). The process and outcomes of psychotherapists' personal treatment experiences. *Journal of Psychotherapy, 25*, 36-43.
- Norton, G. R., Cox, B. J., & Malan, J. (1992). Nonclinical panickers: A critical review. *Clinical Psychology Review, 12*, 121-139.
- Norton, G. R., Harrison, B., Hauch, J., & Rhodes, L. (1985). Characteristics of people with infrequent attacks. *Abnormal psychiatry, 94*, 216-221.
- Noyes, R. Jr., Anderson, D. J. Clancy, J., Crowe, R. R., Slymen, D. J., Choneilm, M. M., & Hinrichs, J. V. (1984). Diazepam and propranolol in panic disorder and agoraphobia. *Archives of General Psychiatry, 41*, 287-292.
- Noyes, R. Jr., Crowe, R. R., Harris, E. L, Hamra, B. J., McChesney, C. M., & Chaudhry, D. R. (1986). Relationship between panic disorder and agoraphobia. A family study. *Archive of Genetic Psychiatry, 43*, 227-232.
- Nutt, D., & Ballenger, J. (2003). Generalized anxiety disorder, obsessive-compulsive disorder and post-traumatic stress disorder. In *Anxiety disorders* (pp, 39-51). Oxford, Blackwell Publishing.
- Oei, T. P. S., Llamas, M., & Devilly, G. J. (1999). The efficacy and cognitive processes of cognitive behavior in the treatment of panic disorder with agoraphobia. *Journal of Behavioral & Cognitive Psychotherapy, 27*, 63-88.
- Olatunji, B. O., Cisler, J. M., & Deacon, B. J. (2010). Efficacy of cognitive behavioral therapy for anxiety disorders: a review of meta-analytic findings. *Psychiatric Clinics of North America, 33*, 557-577.
- Olatunji, B.O., & Wolitzky-Taylor, K.B. (2009). Anxiety sensitivity and the anxiety disorders: a meta-analytic review and synthesis. *Psychological Bulletin, 135*, 974-999.
- Öst, L. G. (1987). Applied relaxation: Description of a coping technique and review of controlled studies. *Journal of Behavior Research and therapy, 25*, 397-409.
- Öst, L. G. (1988). Applied relaxation vs. progressive relaxation in the treatment of panic disorder. *Journal of Behavior Research and Therapy, 26*, 13-22.
- Öst, L. G. (2008). Cognitive behavior therapy for anxiety disorders: 40 years of progress. *Nord Journal Psychiatry, 62*, 5-10.
- Öst, L. G., & Hugdahl, K. (1983). Acquisition of agoraphobia, mode of onset and anxiety response patterns. *Journal of Behavior Research and Therapy, 21*, 623-631.
- Öst, L. G., Thulin, U., & Ramnerö, J. (2004). Cognitive behavior therapy vs. exposure in vivo in the treatment of panic disorder with agoraphobia (corrected from

- agoraphobia). *Journal Behavior Research Therapy*, 42, 1105-1127.
- Öst, L. G., & Westling, B. E., & Hellstrom, K. (1993). Applied relaxation, exposure in vivo and cognitive methods in the treatment of panic disorder with agoraphobia. *Journal of Behavior Research and therapy*, 31, 383-394.
- Öst, L. G., & Westling, B. E. (1995). Applied relaxation vs. cognitive behavior therapy in the treatment of panic disorder. *Journal of Behavior Research Therapy*, 33, 145-158.
- Otto, M., Deveney, D. (2005). Cognitive-behavioral therapy and the treatment of panic: Efficacy and strategies. *Journal of Clinical Psychiatry*, 66, 28-32.
- Otto, M. W., Pollack, M. H., Penava, S. J., & Zucker, B. G. (1999). Group cognitive-behavior therapy for patients failing to respond to pharmacotherapy for panic disorder: a clinical case series. *Journal of Behavior Research Therapy*, 37, 763-770.
- Otto, M. W., Pollack, M. H., & Maki, K. M. (2000). Empirically-supported treatment for panic disorder: Costs, benefits, and stepped care. *Journal of Consulting and Clinical Psychology*, 68, 556-563.
- Otte, C.H. (2011). Cognitive behavioral therapy in anxiety disorders: current state of the evidence. *Journal of Dialogues Clinical Neuroscience*, 13, 413-421.
- Özkan, M. A., & Altindag. (2005). Comorbid personality disorders in subjects with panic disorder: do personality disorders increase clinical severity? *Comprehensive Psychiatry journal*, 46, 20-26.
- Papp, L. A., Goetz, R., Cole, R., Klein, D. F., Jordan, F. F., Liebowitz, M. R., Fyer, A. L., Hollander, E., & Gorman, J. (1989). Hypersensitivity to carbon dioxide in panic disorder: *American Journal of psychiatry*, 146, 779-781.
- Papp, L. A., Klein, D. F., & Gorman, J. M. (1993). Carbon Dioxide Hypersensitivity, hyperventilation, and panic disorder. *American Journal of Psychiatry*, 150, 1149-1157.
- Payne, K. T., & Marcus, D. K. (2008). The efficacy of group psychotherapy for older adult clients: A meta-analysis. *Group Dynamics: Theory, Research, and Practice*, 12, 268-278.
- Pelissolo, A., Zaoui, M., Aguayo, G., Sai Nan Yao, Roche, S., Ecochard, R., Gueyffier, F., Pull, CH., Berthoz, A., Jouvent, A., & Cottraux, J. (2012). Virtual reality exposure therapy versus cognitive behavior therapy for panic disorder with agoraphobia: A randomized comparison study. *Journal of Cybertherapy & Rehabilitation*, 5, 35-43.
- Pérez-Ara, M. A., Quero, S., Botella, C., Baños, R., Andreu-Mateu, S., García-Palacios, A., & Bretón-López, J. (2010). Virtual reality interoceptive exposure for the treatment of panic disorder and agoraphobia. *Study Health Technology*

Information, 154, 77-81.

Peterson, R. A., & Reiss, S. (1993). *Anxiety Sensitivity Index*. Worthington, OH: International Diagnostic Services Publishing Corporation.

Peter, H., Bruckner, E., Hand, I., Rohr, W., & Rufer, M. (2008). Treatment outcome of female agoraphobics 3-9 years after exposure in vivo: A comparison with healthy controls. *Journal of Behavior Therapy Experimental Psychiatry*, 39, 3-10.

Perna, G., Barbini, B., Cocchi, S., Bertani, A., & Gasperini, M. (1995). 35% CO₂ challenge in panic and mood disorders. *Journal Affective Disorder* 33, 189-194.

Perna, G., Caldirola, D., Arancio, C., & Bellodi, L. (1997). panic attacks: a twin study. *Journal of Psychiatry research*, 66, 69-71.

Perna, G., Casolari, A., Bussi, R., Cucchi, M., Arancio, C., & Bellodi L. (2004). Comparison of 35% carbon dioxide reactivity between panic disorder and eating disorder. *Journal of Psychiatry research*, 125, 277-283.

Peterson, R. A., & Heilbronner, R. L. (1987). The Anxiety Sensitivity Index: Construct validity and factor analytic Structure. *Journal of Anxiety Disorders*, 3, 25-32.

Petrocelli, J., (2002). Effectiveness of Group Cognitive Behavioral Therapy for General Symptomatology: A Meta-Analysis journal for specialists in group work. *American Counseling Association (ACA)*, 27, 92-115.

Pincus, D. B., Ehrenreich- May, J., Whitton, S. W., Mattis, S. G., & Barlow, D. H. (2010). Cognitive-behavioral treatment of panic disorder in adolescence. *Journal Clinical Child Adolescent Psychology*. 39, 638-649.

Plehn, K., & Peterson, R. A. (2002). Anxiety sensitivity as a predictor of the development of panic, symptoms, panic attacks, and panic disorder: A prospective study. *Journal of Anxiety Disorders*, 16, 455-474.

Pollack, M. H. J. (2005). The pharmacotherapy of panic disorder. *Journal of Clinical Psychiatry*, 66, 23-27.

Pollock, R., & Kuo, I. (2004). New research in Anxiety Disorders. Poster presented at the International Congress of Biological Psychiatry.

Pollack, M. H., Lepöla, U., & Koponen, H., Simon, N.M, Worthington, J.J, Emilien, G., Tzanis, E., Salinas, E., Whitaker, T., & Gao, B. (2006). A double-blind study of the efficacy of venlafaxine extended-release, paroxetine, and placebo in the treatment of panic disorder. *Journal of Depression and Anxiety*, 24, 1-14.

Pollack, M. H., Rapaport, M. H., & Clary, C. M. (2000). Sertraline treatment of panic disorder: response in patients at risk for poor outcome. *Journal Clinical Psychiatry*, 61, 922-927.

- Power, K. G., Sharp, D. M., Swanson, V., & Simpson, R. J. (2000). Therapist contact in cognitive behavior therapy for panic disorder and agoraphobia in primary care. *Journal of Clinical Psychology and Psychotherapy*, 7, 37-46.
- Rachman, S., & Levitt, K. (1985). Panics and their consequences. *Journal of Behavior Research Therapy*, 23, 585-600.
- Rachman, S., Levitt, K., & Lopatka, C. (1987). The links between cognitions and bodily symptoms. *Journal Behavior Research and Therapy*, 5, 411-423.
- Rachman, S., Lopatka, C., & Levitt, K. (1988). Experimental analysis of panic: Panic patients. *Journal of Behavior Research and Therapy*, 26, 33-40.
- Ramage-Morin, P. L. (2004). Panic disorder and coping. *Health Reports (Statistics Canada, Catalogue)*, 15, 31-43.
- Rapee, R. M. (1985). A case of panic disorder treated with breathing retraining. *Journal of Behavior therapy and experimental psychiatry*, 16, 63-65.
- Rapee, R. M., & Barlow, D. H. (1991). The cognitive-behavioral treatment of panic attacks and agoraphobic avoidance. In Walker, J. R., Norton, G. R. & Ross; C. A. (Eds.), *Panic disorder and agoraphobia: A comprehensive guide for the practitioner*, (pp. 252-305). Brooks/Cole Publishing Company.
- Rapee, R. M., Craske, M. G., Brown, T. A., & Barlow, D. H. (1996). Measurement of perceived control over anxiety-related events. *Journal of Behavior Therapy*, 27, 279-293.
- Rauch, S. L., Shin L. M., & Wright, C. (2003). Neuroimaging studies of amygdala function in anxiety disorders. *Annual New York Academy of Science*, 985, 389-410.
- Rayburn, N. R., & Otto, M. W. (2003). Cognitive-behavioral therapy for panic disorder: a review of treatment elements, strategies, and outcomes, 5, 356-362.
- Razran, G. (1961). The observable unconscious and the in ferable conscious in current soviet psychophysiology: Interoceptive conditioning, semantic conditioning, and the orienting reflex, *psychological Review* 68, 81-147.
- Rector, N. A., Szacun-Shimizu, K., & Leybman, M. (2007). Anxiety sensitivity within the anxiety disorder: disorder-specific sensitivities and depression comorbidity: *Behavior Research and Therapy*, 45, 1967-1975.
- Reiss, S., Peterson, R. A., Gursky, D. M., & McNally, R. J. (1986). Anxiety sensitivity, anxiety frequency and the prediction of fearfulness. *Journal of Behavior Research & Therapy*, 24, 1-8.
- Reiss, S. (1997). Trait anxiety: It's not what you think it is. *Journal of Anxiety Disorders*, 11, 201-214.

- Riskind, J. H., Beck, A. T., Brown, G., & Steer, R. A. (1987). Taking the measure of anxiety and depression. Validity of the reconstructed Hamilton scales. *The Journal of Nervous and Mental Disease*, 175, 474-9.
- Robinson, L. A., Berman, J. S., & Neimeyer, R. A. (1990). Psychotherapy for the treatment of depression : A comprehensive review of controlled outcome research. *Psychological Bulletin*, 108, 30-49.
- Ronen, T., & Freeman, A. (2007). Cognitive behavior therapy for anxiety disorders. In *Cognitive Behavior Therapy in Clinical Social Work Practice* (pp. 375-395). Springer publishing.
- Ross, C.J.M., Davis, T.M.A., Macdonald, G.F. (2005). Cognitive-Behavioral Treatment combined with Asthma education for adults with Asthma and coexisting Panic Disorder. *Clinical Nursing Research*, 14, 131-157.
- Rosenberg, N. K., & Hougaard, E. (2005). Cognitive-behavioral group treatment of panic disorder and agoraphobia in a psychiatric setting: A naturalistic study of effectiveness. *Nord Journal Psychiatry*, 59, 198-204.
- Roth, A., & Fonagy, P. (2005). *What Works for Whom?* (2th ed). Anxiety disorder: specific phobia, social phobia, generalized anxiety disorder, and panic disorder with or without agoraphobia, (pp. 150-198). New York: Guilford press.
- Roy-Byrne, P. P., Wagner, A. W., & Schraufnagel, T. J. (2005a). Understanding and treating panic disorder in the primary care setting. *Journal Clinical Psychiatry*, 66, 16-22.
- Roy-Byrne, P. P., Craske, M. G., Stein, M. B., Sullivan, G., Bystritsky, A., Katon, W., Golinelli, D., & Sherbourne, C. (2005b). A randomized effectiveness trial of cognitive-behavioral therapy and medication for primary care panic disorder. *Archives of General Psychiatry*, 62, 290-298.
- Roy-Byrne, P. P., Craske, M. G., & Stein, M. B. (2006). Panic Disorder. *Lancet* 368, 1023-1032.
- Roy-Byrne, P. P., Stang, P., Wittchen, H. U., Ustun, B., Walters, E. E., & Kessler, R. C. (2000). Lifetime panic-depression comorbidity in the National Comorbidity Survey. Association with symptoms, impairment, course and help-seeking. *The British Journal of Psychiatry*, 176, 229-235.
- Rubenstein, A. (2003). Effects of emotional engagement and habituation on exposure therapy for PTSD. Yeshiva University.
- Rubin, H. C., Rapaport, M. H., Levine, B., Gladsjo, J. K., Rabin, A., Auerbach, M., Judd, L. L., & Kaplan, R. (2000). Quality of well-being in panic disorder: the assessment of psychiatric and general disability. *Journal of Affective Disorders*, 57, 217-221.

- Rufer, M., Alberecht, R., Schmidt, O., Zaum, J., Schnyder, U., Hand, I., & Mueller-Pfeiffer, C. (2010). Changes in quality of life following cognitive behavioral group therapy for panic disorder. *Journal of European Psychiatry* 25, 8-14.
- Ruhmland, M. & Margraf, J. (2001). Efficacy of psychological treatments for panic and agoraphobia. *Journal of behavior therapy*, 11, 41-53.
- Rupert, P. A., Dobbins, K., & Mathew, R. J. (1981). EMG biofeedback and relaxation instructions in the treatment of chronic anxiety. *American journal of clinical biofeedback*, 4, 52-61.
- Rutan, S. J., Stone, N. W., & Shay, J. (2007). Beginning to group Psychodynamic Group Psychotherapy, (pp. 190-212). The Guilford press.
- Ruwaard, J., Broeksteeg, J., Schrieken, B., Emmelkamp, P., & Lange, A. (2010). Web-based therapist-assisted cognitive behavioral treatment of panic symptoms: A randomized controlled trial with a three-year follow-up. *Journal of Anxiety Disorders*, 24, 387-396.
- Sadock, B. J., & Sadock, V. A. (2008). Physical illness and psychiatric disorder. *Concise textbook of clinical psychiatry* (pp, 10-15) (3th ed.). Lippincott Williams & Wilkins.
- Salkovkis, P. M., Clark, D. M., & Hackmann, A. (1991). Treatment of panic attacks using cognitive therapy without exposure or breathing retraining. *Journal of Behavior research and therapy*, 29, 161-166.
- Salkovskis, P. M., & Clark, D. M. (1990). Affective responses to hyperventilation: a test of the cognitive model of panic. *Journal of Behavior Research and Therapy*, 28, 51-61.
- Salkovskis, P. M., Jones, D. R., & Clark, D. M. (1986). Respiratory control in the treatment of panic attacks: Replication and extension with concurrent measurement of behavior and pCO₂. *British Journal of Psychiatry*, 148, 526-532.
- Salkovskis, P. M., Hackmann, A., Wells, A., Gelder, M., & Clark, D. M. (2006). Belief disconfirmation versus habituation approaches to situational exposure in panic disorder with agoraphobia: A pilot study. *Journal of Behavior Research and Therapy*, 45, 877-885.
- Sánchez-Meca, J., Rosa-Alcázar, A. I., Marín-Martínez, F., & Gómez-Conesa, A. (2010). Psychological treatment of panic disorder with or without agoraphobia: a meta-analysis. *Journal of Clinical Psychology Review*, 30, 37-50.
- Sanderson, W. C., & Rego, S. A. (2002). Empirically supported treatment for panic disorder: research, theory, and application of cognitive behavioral therapy. In R. L. Leahy & E. T. Dowd (Eds), *Clinical advance in cognitive psychotherapy. Theory and Application* (pp. 213-216). Springer publishing company.

- Sanderson, W. C., & Wetzler, S. (1995). Cognitive behavioral treatment of panic disorder. In G. M. Asnis & H. M. van Praag (Eds.). *Panic disorder: Clinical, biological, and treatment aspects*, (pp. 314-335). New York: Wiley & Sons.
- Sargent, M. (1990). NIMH report: Panic disorder. *Journal of Hospital and community psychiatry*, 41, 621-623.
- Sarp A., Arık, A. C., Guz, H., Şahin, A. R., & Abanoz, Z. (2010). Possible subtypes of panic disorders. *Turkish Journal of Psychiatry*, 21, 269-279.
- Sartory, G., & Olajide, D. (1988). Case histories and shorter communications. Vagal innervation techniques in the treatment of panic disorder. *Journal Behavior Research Therapy*, 26, 431-434.
- Schmidt, N. B., Lerew, D. R., & Jackson, R. J. (1997). The role of anxiety sensitivity in the pathogenesis of panic: Prospective evaluation of spontaneous panic attacks during acute stress. *Journal of Abnormal Psychology*, 106, 355-364.
- Schmidt, N. B., Telch, M. J., & Joiner, T. E. (1996). Factors influencing health perceptions in patients with panic disorder. *Journal of Comprehensive Psychiatry*, 37, 253-260.
- Schmidt, N. B., Trakowski, J. H., & Staab, J. P. (1997). Extinction of panicogenic effects of a 35% CO₂ challenge in patients with panic disorder. *Journal of Abnormal Psychology*, 106, 630-638.
- Schmidt, N. B., Woolaway-Bickel, K., Trakowski, J., Santiago, H., Storey, J., Koselka, M., & Cook, J. (2000). Dismantling cognitive-behavioral treatment for panic disorder: questioning the utility of breathing retraining. *Journal of consulting clinical psychology*, 68, 417-24.
- Schmidt, N. B., Zvolensky, M. J., & Maner, J. K. (2006). Anxiety sensitivity: prospective prediction of panic attacks and Axis I pathology. *Journal of Psychiatric Research*, 40, 691-699.
- Schneider, R., & Schulte, D. (2008). Catastrophic associations predict level of change in anxiety sensitivity in response to cognitive-behavioral treatment for panic. *Journal of Behavior Research and Therapy* 46, 557-572.
- Seddon, K., & Nutt, D. (2007). Pharmacological treatment of panic disorder. *Psychiatry journal*, 6, 198-203.
- Schwartz, D., & Lellouch, J. (1967). Explanatory and pragmatic attitudes in therapeutic trials. *Journal of Chronic Disorders*, 20, 637-648.
- Segal, Z. V., & Shaw, B. F. (1996). Cognitive Therapy. In L. J. Dickstein., M. B, Riba & J. M. Oldham (Eds), *American Psychiatry Press Review of psychiatry*. American Psychiatric Press, Inc. Washington DC.

- Senge, P. (1990). *The fifth discipline. The art and practice of learning organization*, New York: Doubleday.
- Sharp, D. M., Power, K. G., & Swanson, V. (2004). A comparison of the efficacy and acceptability of group versus individual cognitive behavior therapy in the treatment of panic disorder and agoraphobia in primary care. *Journal of Clinical Psychology and Psychotherapy*, 11, 73-82.
- Shear, M. K., Barlow, D. H., Brown, T., Money, R., Sholomskas, D., Woods, S., Gorman, J., & Papp, L. (1997). The Multicenter Collaborative Panic Disorder Severity Scale (PDSS). *American Journal of Psychiatry*, 11, 1571-1575.
- Shear, M. K., Houck, P., Greeno, C., & Masters, S. (2001a). Emotion-focused psychotherapy for patients with panic disorder. *American Journal of Psychiatry*, 158, 1993-1998.
- Shear, M. K., Ricci, P., Williams, J., Frank, E., Grochocinski, V., Vander Bilt, J., Houck, P., & Wang, T. (2001b). Reliability and validity of the Panic Disorder Severity Scale: Replication and extension. *Journal of Psychiatric Research*, 35, 293-296.
- Shear, M. K., & Masser, J. M. (1994). Standardized assessment for panic disorder research. A conference report. *Archives of General Psychiatry*, 51, 346-354.
- Shear, M. K., Meuret, A. E., Rosenfield, D., Gorman, J. M., & Woods, S. W. (2007). Preliminary Evidence for Cognitive Mediation During Cognitive-Behavioral Therapy of Panic Disorder. *Journal Consult Clin Psychol.* 75, 374-379.
- Sheehan, D. V., Ballenger, J., & Jacobsen, G. (1980). Treatment of endogenous anxiety with phobic, hysterical, and hypochondriacal symptoms. *Archive General Psychiatry*, 37, 51-59.
- Sheehan, D. V., & Sheehan, K. H. (1982). The classification of anxiety and hysterical states: historical review and empirical delineation. *Journal of Clinical Psychopharmacology*, 2, 235-244.
- Sheikh, J. I., Leskin, G. A., & Klein, D. F. (2002). Gender differences in panic disorder: findings from the National Comorbidity Survey. *American Journal Psychiatry*, 159, 55-58.
- Shoenberger, D., & Hazlett-Stevens, H. (in press). Interpersonal problems linked to panic disorder with agoraphobia. To appear in *advances in psychology research* volume 50. New York: Nova Science Publishers, Inc.
- Skre, I., Onstad, S., Torgersen, S., Lygren, S., & Kringlen, E. (1993). A twin study of DSM-III-R anxiety disorders. *Acta Psychiatr Scand Journal*, 88, 85-92.
- Sokol, L., Beck, A. T., Greenberg, R. L., Wright, F. D., & Berchick, R. J. (1989). Cognitive therapy of panic disorder. A nonpharmacological alternative. *Journal of Nervous and Mental disease* 177, 711-716.

- Smits, J. A., Berry, A. C., Rosenfield, D., Powers, M. B., Behar E., & Otto M. W. (2008a). Reducing anxiety sensitivity with exercise. *Depression and Anxiety, 25*, 689-699.
- Smits, J. A., Berry, A. C., Tart, C. D., & Powers, M. B. (2008b). The efficacy of cognitive-behavioral interventions for reducing anxiety sensitivity: A meta-analytic review. *Journal of Behavior Research and Therapy, 46*, 1047-1054.
- Smits, J. A., Powers, M. B., Cho, Y., & Telch, M. J. (2004). Mechanism of change in cognitive-behavioral treatment of panic disorder: Evidence for the fear of fear mediational hypothesis. *Journal of Consulting and Clinical Psychology, 72*, 646-652.
- Spitzer, R. L., Williams, J. B. W., Gibbon, M., & First, M. (1997). Structured clinical interview for DSM-IV personality disorders, (SCID-II). Washington, D. C: American Psychiatric Press.
- Steer, R. A., Ranieri, W. F., Beck, A. T., & Clark, D. A. (1993). Further evidence for the validity of the Beck Anxiety Inventory with psychiatric outpatients. *Journal of Anxiety Disorders, 7*, 195-205.
- Stein, M. B., Goin, M. K., Pollack, M. H., Roy-Byrne, P., Sareen, J., Simon, N. M., & Campbell-Sills, L. (2009). Practice guideline for the treatment of patients with panic disorder, (pp 24-29). Arlington, VA: American Psychiatric Association.
- Stein, M. B., Steckler, T., Lightfoot, J. D., Hay, E., & Goddard, A. W. (2010). Pharmacological Treatment of Panic Disorder, *Journal of curr top behavioral neuroscience, 2*, 469-485.
- Stevens, J. C., & Pollack, M. H. (2005). Benzodiazepines in clinical practice: consideration of their long-term use and alternative agents. *Journal of Clinical Psychiatry 66*, 21-27.
- Stewart, W., Breslau, N., & Keck, P. E. (1994). Comorbidity of migraine and panic disorder. *Journal of Neurology, 44*, 23-27.
- Stewart, R. E., & Chambless, D.L. (2009). Cognitive-behavioral therapy for adult anxiety disorders in clinical practice: a meta-analysis of effectiveness studies. *Journal of Consulting Clinical Psychology, 77*, 595-606.
- Sturges, L. V., Goetsch, V. L., Ridley, J., & Whittal, M. (1998). Anxiety sensitivity and response to hyperventilation challenge: Physiologic arousal, interoceptive acuity and subjective distress. *Journal of Anxiety Disorders, 12*, 103-115.
- Struzik, L., Vermani, M., Duffin, J., & Katzman, M. A. (2004). Anxiety sensitivity as a predictor of panic attacks. *Journal of Psychiatry Research, 129*, 273-278.
- Subich, L. M., & Coursol, D. H. (1985). Counseling expectations of nonclients for group and individual treatment modes. *Journal of Counseling psychology, 32*,

245-251.

- Sullivan, G. M., Kent, J. M., Kleber, M., Martinez, J.M., Yeragani, V. K., & Gorman, J.M. (2004). Effects of hyperventilation on heart rate and QT variability in panic disorder pre-and post-treatment. *Psychiatry Research*, 125, 29-39.
- Swinson, R. P., Soulios, C., Cox, B. J & Kuch, K. (1992). Brief treatment of emergency room patients with panic attacks. *American Journal Psychiatry*, 149, 944-946.
- Taylor, S. (1999). *Anxiety sensitivity: theory, research, and treatment of the fear of anxiety*. Mahwah, New Jersey: Lawrence Erlbaum.
- Taylor, S. (2000). *Understanding and treating panic disorder, cognitive-behavioral approaches*. Chichester, UK: John Wiley and Sons.
- Taylor, S. (2001). Breathing Retraining in the Treatment of Panic Disorder: Efficacy, Caveats and Indications. *Scandinavian Journal of Behavior Therapy*, 30, 49-56.
- Taylor, S., & Cox, B. J. (1998). An expanded Anxiety Sensitivity Index: evidence for a hierarchic structure in a clinical sample. *Journal of Anxiety Disorders*, 12, 463-483.
- Taylor, S., Koch, W. J., & McNally, R. J. (1992). How does anxiety sensitivity vary across the anxiety disorders? *Journal of Anxiety Disorders*, 6, 249-259.
- Taylor, S., Zvolensky, M. J., Cox, B. J., Deacon, B., Heimberg, R. G., Ledley, D. R., & Cardenas, S. J. (2007). Robust dimensions of anxiety sensitivity: Development and initial validation of the Anxiety Sensitivity Index-3. *Journal Psychological Assessment*, 19, 176-188.
- Teachman, B. A., Marker, C. D., & Clerkin, E. M. (2010). Catastrophic misinterpretations as a predictor of symptom change during treatment for panic disorder. *Journal of Consulting and Clinical Psychology*, 78, 964-973.
- Teachman, B. A., Marker, C. D., & Smith-Janik, S. B. (2008). Automatic associations and panic disorder: Trajectories of change over the course of treatment. *Journal of Consulting and Clinical Psychology*, 76, 988-1002.
- Telch, M. J., Brouillard, M., Telch, C. F., Agras, W. S., & Taylor, C. B. (1989a). Role of cognitive appraisal in panic related avoidance. *Journal of Behavior Research and therapy*, 27, 373-383.
- Telch, M. J, Lucas, J. A., & Nelson, P. (1989b). Nonclinical panic in college students: an investigation of prevalence and symptomatology. *Journal of Abnormal Psychology*, 98, 300-306.
- Telch, M. J., Shermis, M. D., & Lucas, J. A. (1989c). Anxiety sensitivity: Unitary personality trait or domain-specific appraisal? *Journal of anxiety Disorder*, 3, 25-32.

- Telch, M. J., Lucas, J. A., Schmidt, N. B., Hanna, H. H., LaNae, Jaimez, T. l., & Lucas R. A. (1993). Group cognitive-behavioral treatment of panic disorder. *Journal of Behavior Research and Therapy* 31, 279-287.
- Telch, M. J., Schmidt, N. B., Jaimez, T. L., Jacquin, K. M., & Harrington, P. J. (1995). Impact of cognitive-behavioral treatment on quality of life in panic disorder patients. *Journal of Consulting and Clinical Psychology*, 63, 823-830.
- Tillitski, L. (1990). A meta-analysis of estimated effect sizes for group versus individual versus control treatments. *International Journal of Group Psychotherapy*, 40, 215-224.
- Tilli, V., Suominen, K., & Karlsson, H. (2012). Panic disorder in primary care: Comorbid psychiatric disorders and their persistence. *Scandinavian journal of primary health care* 30, 247-253.
- Tompking, M. A. (2002). Anxiety and panic disorder. In Patterson (Eds.). *Comprehensive Handbook of Psychotherapy: Cognitive-behavioral approaches*, 2, 273-295.
- Torgersen, S. (1983). Genetic factors in anxiety disorders. *Archives of General psychiatry*, 40, 1085-1089.
- Toseland, R. W., & Siporin, M. (1986). When to recommend group treatment: A review of the clinical and the research literature. *International journal of group psychotherapy*, 36, 43-61.
- Tsao, J. C., Mystkowski, J. L., Zucker, B. G., & Craske, M. G. (2002). Effects of cognitive-behavioral therapy for panic disorder on comorbid conditions: Replication and extension. *Journal of Behavior Therapy*, 33, 493-509.
- Turner, S., Beidel, D., & Costello, A. (1987). Psychopathology in the offspring of anxiety disorder patients. *Journal of consulting and clinical psychology*, 55, 229-235.
- Tweeddale, P. M., Rowbottom, I., & McHardy, G. J. (1994). Breathing retraining: effect on anxiety and depression scores in behavioral breathlessness. *Journal Psychosomatic Research*, 38, 11-21.
- Uhle, S. (2006). Short-and long-term effectiveness of high density exposure for panic disorder with agoraphobia in an inpatient setting: A 7 years follow-up.
- Uhlenhuth, E. H., Warner, T. D., & Matuzas, W. (2002). Interactive model of therapeutic response in panic disorder: moclobemide, a case in point. *Journal Clinical Psychopharmacology*, 22, 275-284.
- Van Beek, N., & Griez, E. (2000). Reactivity to a 35% CO₂ challenge in healthy first-degree relatives of patients with panic disorder. *Journal of Biological Psychiatry* 47, 830-835.

- Van Dam-Baggen, R., & Kraaimaat, F. (2000). Group social skills training or cognitive group therapy as the clinical treatment of choice for generalized social phobia? *Journal of Anxiety Disorders*, 14, 437-451.
- Van der Molen, G. M., van den Hout, M. A., Vroemen, J., Lousberg, H., & Griez, E. (1986). Cognitive determinants of lactate-induced anxiety. *Journal of Behavior Research and Therapy*, 24, 677-680.
- Vincelli, F., Anolli, L., Bouchard, S., Wiederhold, B. K., Zurloni, V., & Riva, G. (2003). Experiential cognitive therapy in the treatment of panic disorders with agoraphobia: A controlled study. *Journal of Cyberpsychology and Behavior*, 6, 321-328.
- Vos, T., Corry, J., Haby, M. M., Carter, R., & Andrews, G. (2005). Cost-effectiveness of CBT and drug interventions for major depression. *Australian and New Zealand Journal of Psychiatry*, 39, 683-692.
- Warren, R., & Zgourides, G. (1988). Panic attacks in high school students: Implications for prevention and intervention. *Phobia Practice and Research Journal*, 1, 97-113.
- Washton, A. (2011). Group therapy. In P. Ruiz & E. C. Strain. *Substance Abuse: A Comprehensive Textbook*. (pp. 575-584) (4th ed). Lippincott Williams & Wilkins.
- Watkins, P. L., Sturgis, E. T., & Clum, G. A. (1988). Guided imaginal coping: an integrative treatment for panic disorder. *Journal Behavior Therapy and Experimental Psychiatry*. 19, 147-155.
- W. B. Saunders Group. *Dorland's Pocket Medical Dictionary*, (26th ed.), US: W. B. Saunders Company, 2001.
- Weiner, H. (2008). The Concept of Psychosomatic Medicine. In R. Edwin., I. V. Wallace & J. Gach (Eds.). *History of psychiatry and medical psychology* (pp. 485-516). Springer Science.
- Weissman, M. M. (1993). Family genetic studies of panic disorder. *Journal of psychiatric research*, 27, 69-78.
- Weissman, M. M., Bland, R. C., Canino, G. J., Faravelli, C., Greenwald, S., Hwu, H. G., Joyce, P. R., Karam, E. G., Lee, C. K., Lellouch, J., Lepine, J. P., Newman, S. C., Oakley-Browne, M. A., Rubio-Stipec, M., Wells, J. E., Wickramaratne, P. J., Wittchen, H. U., & Yeh, E. K. (1997). The Gross national epidemiology of panic disorder. *Archive General Psychiatry*, 54, 305-309.
- Weissman, M. M., Klerman, G., Markowitz, J., & Ouellette, R. (1990). Suicidal ideation and suicide attempts in panic disorder and attacks. *The New England Journal of Medicine*, 321, 1209-1214.
- Wells, A. (1997). *Cognitive Therapy of Anxiety Disorders. A Practice Manual and*

Conceptual Guide. Chichester: John Wiley.

- Wenzel, A., Sharp, I.R., Brown, G.K., Greenberg, R.K., Beck, A.T. (2006). Dysfunctional beliefs in panic attacks: the Panic Belief Inventory. *Journal of Behavior Research Therapy*. In press.
- Westen, D., & Morrison, K. (2001). A multi-dimensional meta-analysis of treatments for depression, panic and generalized anxiety disorder: an empirical examination of the status of empirically supported therapies. *Journal of counseling and clinical psychology*, 69, 875-899.
- Westling, B. E., & Öst, L. B. (1993). Relationship between panic attacks symptoms and cognition in panic disorder patients. *Journal of anxiety Disorders*, 7, 181-194.
- Whalen, P. J., Rauch S. L., Etcoff, N. L., McInerney, S. C., Lee, M. B., & Jenike, M. A. (1998). Masked presentations of emotional facial expressions modulate amygdala activity without explicit knowledge. *Journal of Neuroscience*, 18, 411-418.
- White, K. S., & Barlow, D. H. (2002). Panic disorder and agoraphobia. *Anxiety and its Disorder: The nature and treatment of anxiety and panic*, (pp. 328-379) (2nd ed). New York: The Guilford press.
- White, J. R., & Freeman, A. S. (2000). Cognitive behavioral group therapy for specific problems and populations. (pp. 29-61). Washington, DC: American psychological Association.
- White, J. R. (2000). Introduction. In J. R. White & A. S. Freeman (Eds.). *Cognitive behavioral group therapy for specific problems and populations*, (pp. 3-25). Washington, DC: American Psychological Association.
- Wilhelm, F. H., Gevirtz, R., & Roth, W. T. (2001). Respiratory dysregulation in anxiety, functional cardiac, and pain disorders: Assessment, phenomenology, and treatment. *Journal of Behavior Modification*, 25, 513-545.
- Williams, S. L., & Falbo, J. (1996). Cognitive and performance-based treatments for panic attacks in people with varying degrees of agoraphobic disability. *Journal of Behavior Research and Therapy* 34, 253-64.
- Williams, S. L., Kinney, p., & Falbo, J. (1989). Generalization of therapeutic changes in agoraphobia: The role of perceived self-efficacy. *Journal of consulting and clinical psychology* 53, 436-442.
- Wilson, C. H. (2009). Examining the roles of acceptance, suppression and other therapeutic strategies in anxiety and relaxation. National University of Ireland Maynooth.
- Wittchen, H. U., & Essau, C. A. (1993). Comorbidity and mixed anxiety-depressive disorders: Is there epidemiological evidence? *Journal of Clinical Psychiatry*, 54, 9-15.

- Wittchen, H. U., & Essau, C. A. (1991). The epidemiology of panic attacks, panic disorder, and agoraphobia. In Walker, J. R., Norton, G. R. & Ross, C. A. (Eds.). *Panic Disorder and Agoraphobia. A Comprehensive guide for the Practitioner*. Belmont: Brooks/Cole.
- Wollburg, E. (2007). *Psychophysiological Effects of Respiratory Challenges before and after Breathing Training in Panic Disorder and Patients suffering from Episodic Anxiety Attacks*. University of Dresden.
- Wolpe, J. (1958). *Psychotherapy by Reciprocal Inhibition*. Stanford, CA: Stanford University Press.
- Wolpe, J. (1990). *The practice of behavior therapy (4th ed.)*. New York: Pergamon.
- Woods, S. W., Charney, D. S., Loke, J., Goodman, W. K., Redmond, D. E Jr., & Heninger, G. R. (1986). Carbon dioxide sensitivity in panic anxiety. Ventilatory and anxiogenic response to carbon dioxide in healthy subjects and patients with panic anxiety before and after alprazolam treatment. *Archives General Psychiatry*, 43, 900-909.
- World Health Organization. (2003). *Investing in mental health*. Geneva: World Health Organization, also available from: URL: <http://www.emro.who.int/mnh>.
- Yalom, I. D. (1995). *The Theory and Practice of Group Psychotherapy*. New York: Basic Books.
- Yalom, I. D., Cox, P. D., & Vinogradov, S. (2008). Group therapy. In R. E. Hales., S. C. Yudofsky & G. O Gabbard. (Eds), *Textbook of psychiatry*, (pp. 1329-1377). Washington, DC: American psychiatric publishing.
- Yalom, I. D., & Leszcz, M. (2005). *The theory and practice of group psychotherapy (pp. 3-105)*. New York: Basic Books.
- Yalom, I. D. Tinklenberg, j., & Gilula, M (1968) curative factors in group therapy. Unpublished manuscript.
- Yamada, K., Moriwaki, K., Oiso, H., & Ishigooka, J. (2011). High prevalence of comorbidity of migraine in outpatients with panic disorder and effectiveness of psycho pharmacotherapy for both disorders: a retrospective open label study. *Journal of Psychiatry Research* 185, 145-148.
- Yasamy, M. T., Shahmohammadi, D., Bagheri Yazdi, S. A., Layeghi, H. J, Bolhari, J., Razzaghi, E. M; Bina, M., & Mohit, A. (2002). Mental health in the Islamic Republic of Iran: achievements and areas of need. *Eastern Mediterranean Health Journal*, 7, 381-391.
- Yates, W. R. (2009). Phenomenology and epidemiology phenomenology and epidemiology of panic disorder f panic disorder. *Annals of clinical psychiatry* 21,

95-102.

Yonkers, K., Zlotnick, C., Warshaw, M., Allsworth, J., Shea, M. T, & Keller, M. B. (1998). Is the course of panic disorder the same in women and men. *American Journal of Psychiatry*, 5, 596-602.

Zal, H. M. (2001). *Panic disorder* (pp. 168-172). New York: Preseus publishing.

Zeitlin, S. B., & McNally, R. J. (1993). Alexithymia and anxiety sensitivity in panic disorder and obsessive-compulsive disorder. 25th Annual Meeting of the Association for Advancement of Behavior Therapy. *American Journal of Psychiatry*, 150, 658-660.

Appendix A

Criteria for Panic Attacks

(American Psychiatric Association, DSM-IV-TR, 2000)

A discrete period of intense fear or discomfort, in which four or more of the following symptoms developed abruptly and reached a peak within 10 minutes:

1. palpitations, 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. derealisation (feeling of unreality)
10. fear of losing control
11. fear of dying
12. paresthesias (numbness or tingling sensations)
13. chills or hot flushes

Appendix B

1) **The Structured Clinical Interview for DSM-IV (SCID) Axis I disorders clinical version (SCID-CV), (Spitzer, Willimas, Gibban & First, 1997):** The SCID-CV is a clinically administered interview with which to ascertain (DSM-IV). Approximate time of administration is one hour. After noting demographic information and questions, the interview begins with questions regarding the chief complaint, history of present and past psychiatric disorders, treatment history, and current functioning. The SCID has a diagnostic module which begins with closed-ended questions that invite a "yes" or "no" response. The interviewer then seeks elaboration by asking questions such as "tell me about that", or "what was that like"? If the interviewer suspects that a particular symptom is present, the participant can be further prompted. The reliability and validity of the SCID is comparable to other major diagnostic instruments and depends largely on the skills and knowledge of the interviewer, when the focus is on one or two disorders, reliability is likely to be higher. Spitzer, Williams, Gibbon, First, (1992) obtained high reliability rates for a current diagnosis of panic disorder. In this panic disorder study, there were 13 international sites and test-retest interviews of 72 patients which yielded a correlation of $r=.87$. More recently, the SCID has also been used successfully in diagnosing panic disorder in a dissertation regarding treatment effects (Rabin, 1996), and diagnosing individuals with panic disorder with and without Agoraphobia.

2) **Daily panic record Questionnaire (Clark, 1999):** For recording and reporting the number of panic attacks and their severity Clark's record daily panic (1999) was used. Clients are noting day and time and the situation when panic attacks occurred. They also identify either negative thoughts and physical signs or rational responses instead of negative thoughts. Severity of attack is determining between 0 to 100.

Appendix C

The results of mean scores in figures in a 3 (Status: ICBT, GCBT, WL) x 2 (Time: pretest vs. posttest) and a (Status: ICBT, GCBT) x 3 (Time: pretest, posttest, Follow-up) for BAI, BDI, PDSS, ACQ, ASI, FQ-AG are presented in Figures C1 to C12.

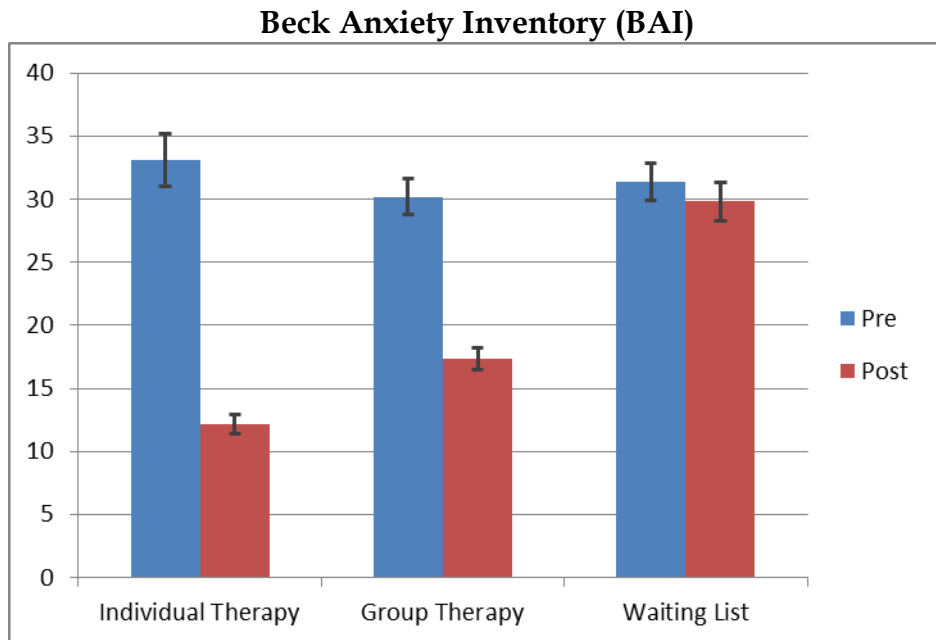


Figure C1: Beck Anxiety means scores of ICBT, GCBT and WL in pretest, posttest (bars represent standard errors)

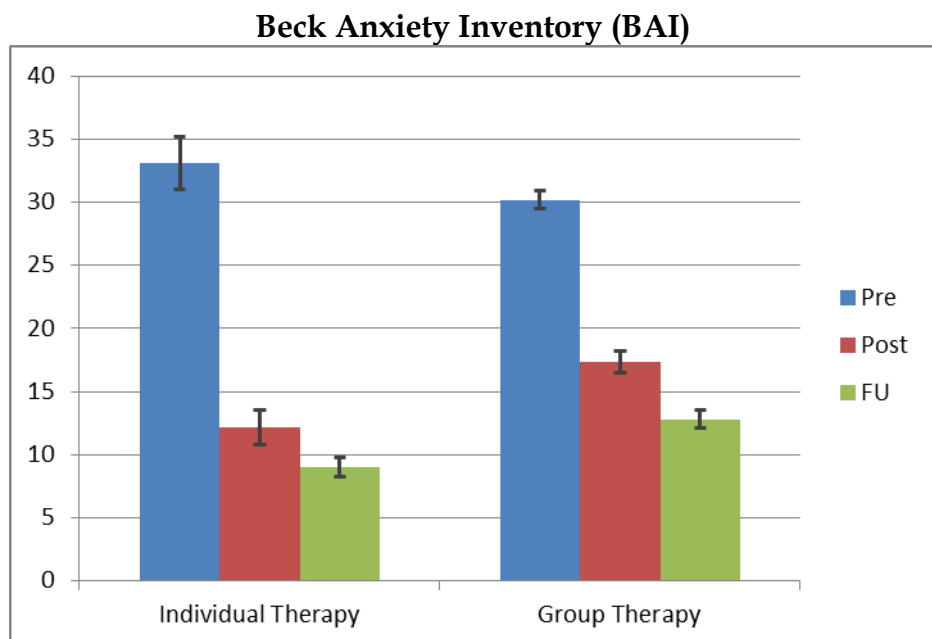


Figure C2: Beck Anxiety means scores of ICBT, GCBT (bars represent standard errors) in Pretest, Posttest, Follow-up

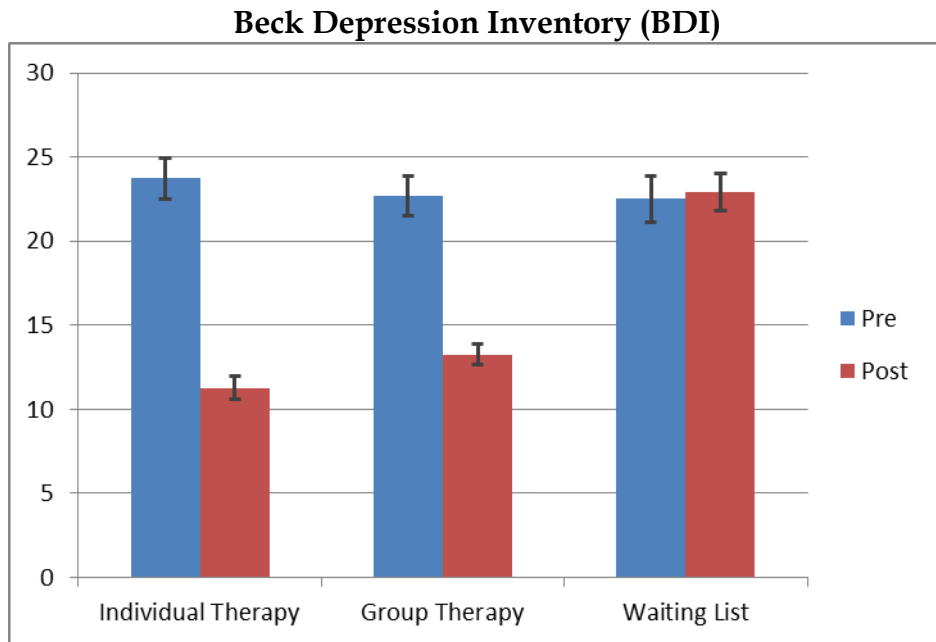


Figure C3: Beck Depression means scores of ICBT, GCBT and WL in Pretest, Posttest (bars represent standard errors)

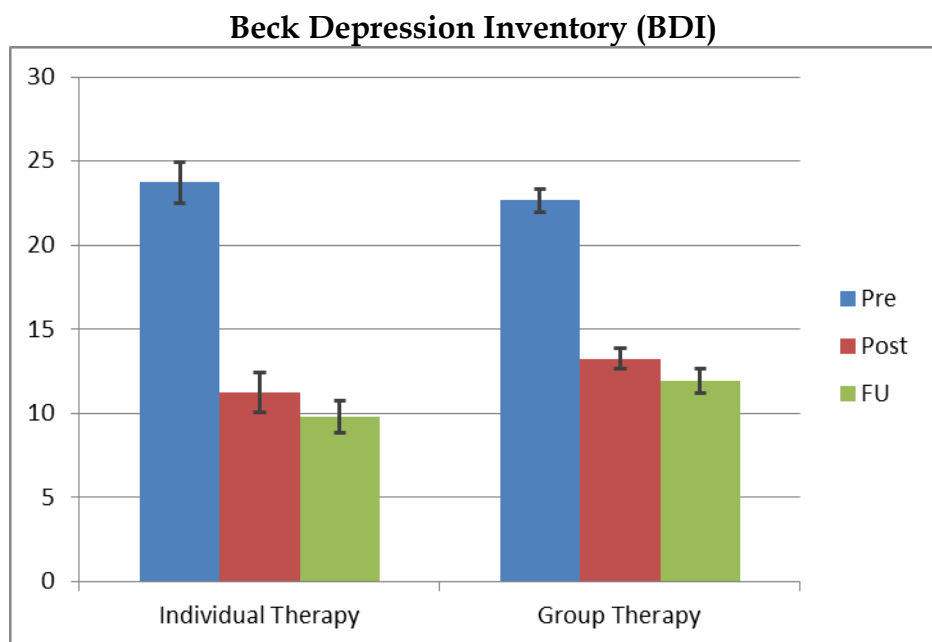


Figure C4: Beck Depression means scores of ICBT, GCBT in Pretest, Posttest and Follow-up (bars represent standard errors)

Panic Disorder Severity Scale (PDSS)

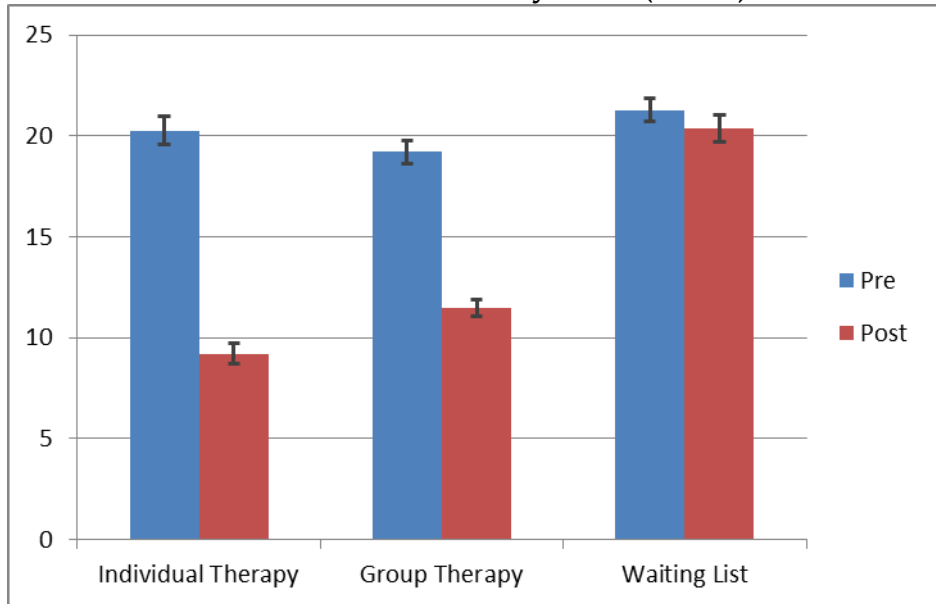


Figure C5: Panic Disorder Severity means scores of ICBT, GCBT and WL (bars represent standard errors) in Pretest, Posttest

Panic Disorder Severity Scale (PDSS)

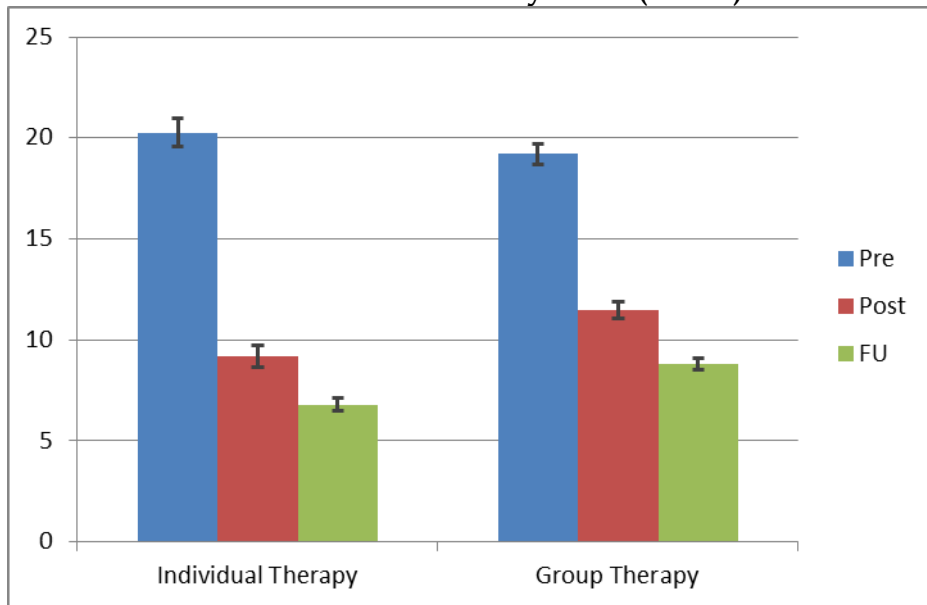


Figure C6: Panic Disorder Severity means scores of ICBT, GCBT (bars represent standard errors) in Pretest, Posttest, and Follow-up

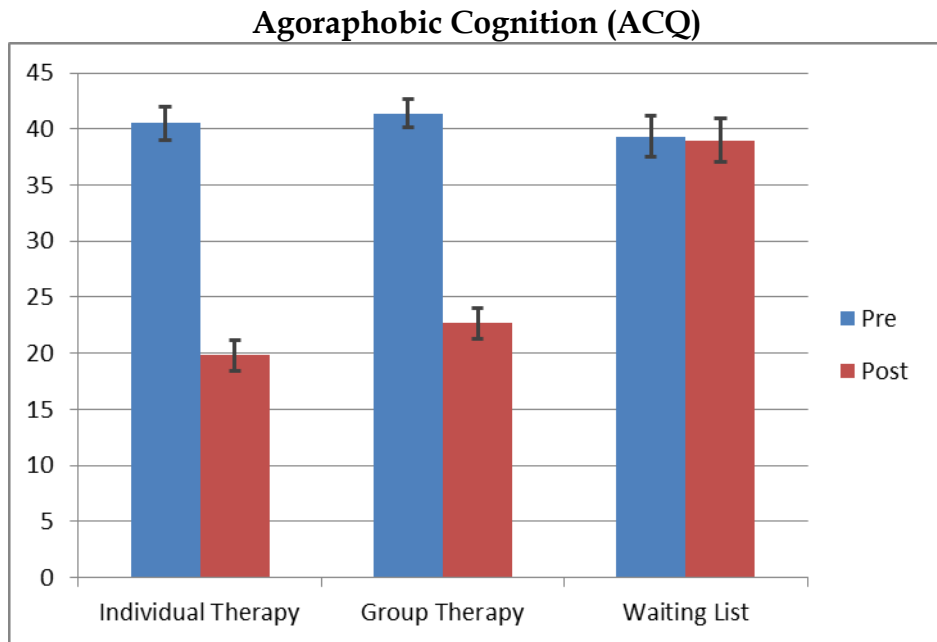


Figure C7: Agoraphobic Cognition (ACQ) means scores of ICBT, GCBT, WL (bars represent standard errors) in Pretest, Posttest

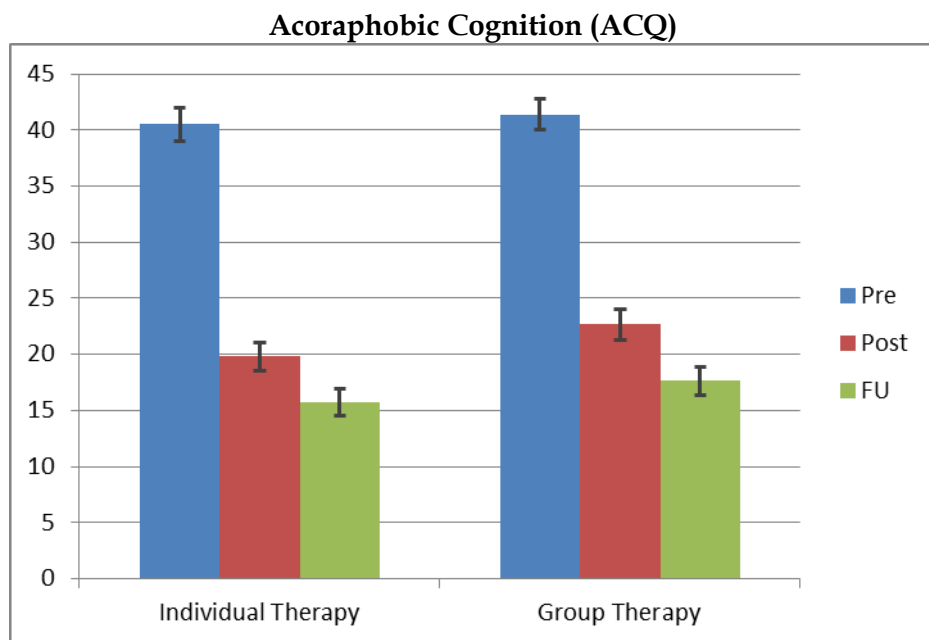


Figure C8: Agoraphobic Cognition (ACQ) means scores of ICBT, GCBT (bars represent standard errors) in Pretest, Posttest, and Follow-up

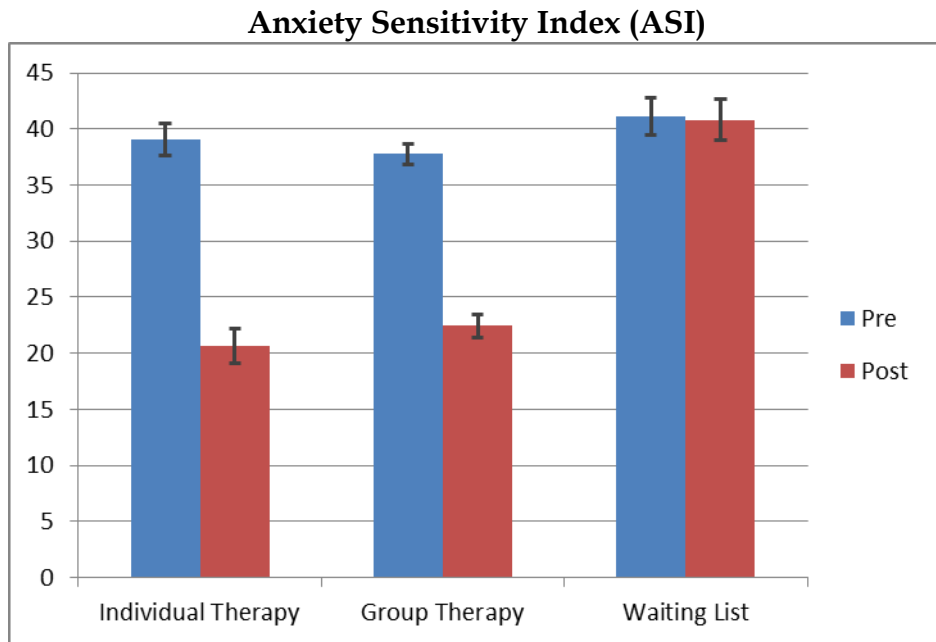


Figure C9: Anxiety Sensitivity mean scores of ICBT, GCBT and WL (bars represent standard errors) in Pretest, Posttest

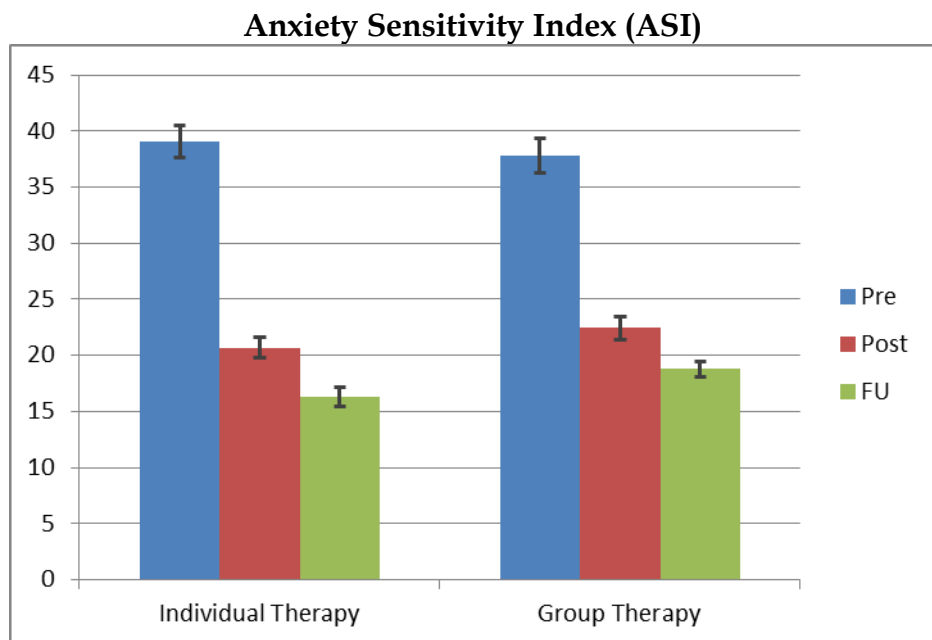


Figure C10: Anxiety Sensitivity means scores of ICBT, GCBT (bars represent standard errors) in Pretest, Posttest, and Follow-up

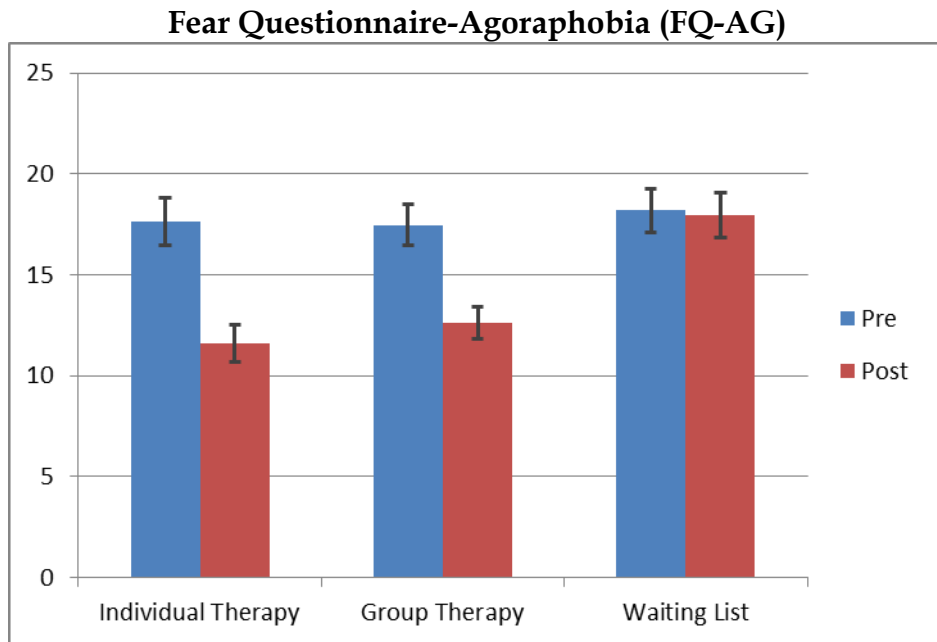


Figure C11: Fear-Agoraphobia means scores of ICBT, GCBT, WL (bars represent standard errors) in Pretest, Posttest

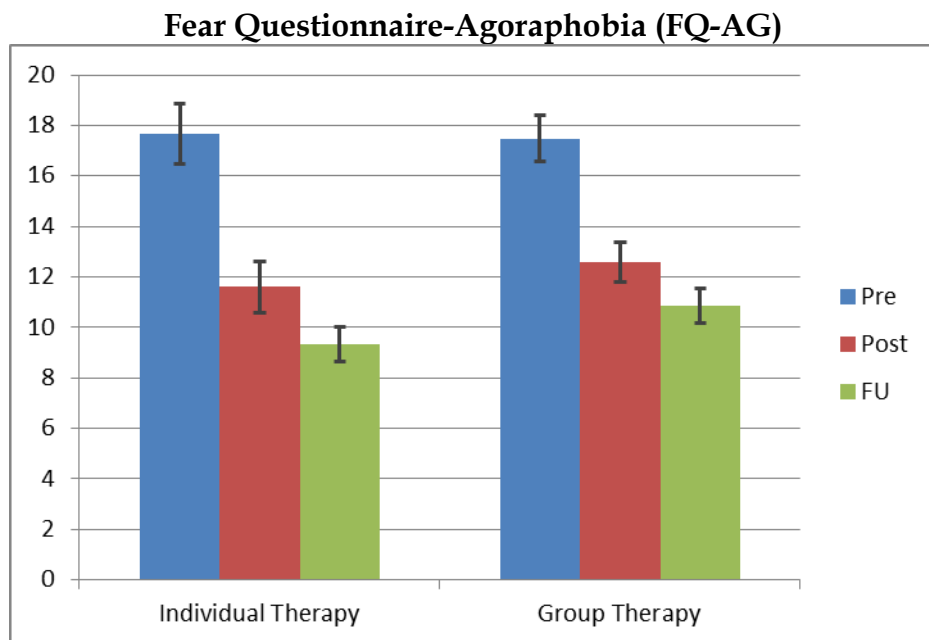


Figure C12: Fear-Agoraphobia means scores of ICBT, GCBT (bars represent standard errors) in Pretest, Posttest, and Follow-up