



Anxiety Sensitivity and Comorbid Psychiatric Symptoms over the Course of Cognitive Behavioural Therapy for Panic Disorder

Sei Ogawa^{1*}, Masaki Kondo¹, Keiko Ino¹, Toshitaka Ii¹, Risa Imai¹,
Toshi A. Furukawa² and Tatsuo Akechi¹

¹Department of Psychiatry and Cognitive-Behavioral Medicine, Nagoya City University, Graduate School of Medical Sciences, Nagoya, Japan.

²Department of Health Promotion and Human Behavior, Kyoto University, Graduate School of Medicine / School of Public Health, Kyoto, Japan.

Authors' contributions

This work was carried out in collaboration between all authors. Author SO was the primary investigator of this study. Author TAF initiated and supervised the overall research project. All the authors took part in the clinical investigation (diagnosis, treatment, and assessment). All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMRR/2016/23979

Editor(s):

(1) Xin-an Liu, Neuroscience Department, the Scripps Research Institute, Scripps, Florida, USA.

Reviewers:

(1) Anonymous, Spain.

(2) Diana C. Tapia-Pancardo, National Autonomous University of Mexico, Mexico.

Complete Peer review History: <http://sciencedomain.org/review-history/13288>

Original Research Article

Received 30th December 2015
Accepted 30th January 2016
Published 14th February 2016

ABSTRACT

Aims: Anxiety sensitivity (AS) might be the core vulnerability in the pathogenesis of AXIS I diagnosis and might be the important transdiagnostic target for the interventions for comorbid psychiatric symptoms in panic disorder (PD). This study aimed to examine the relationship of changes in the three factors of AS and changes in comorbid psychiatric symptoms over the course of cognitive behavioural therapy (CBT) for PD.

Methodology: One hundred eighteen patients with PD were treated with manualized group CBT. Using multiple regression analysis, we examined the associations between the changes in subscales of Symptom Checklist-90 Revised (SCL-90-R) and the changes in factors of the Anxiety Sensitivity Index (ASI) involving Physical Concerns, Mental Incapacitation Concerns, and Social Concerns over the course CBT.

*Corresponding author: E-mail: seiogawa1964@nifty.com;

Results: Reductions in Mental Incapacitation Concerns of ASI were related to decreases in 8 SCL-90-R scales, including Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Hostility, Phobic Anxiety, Paranoid Ideation, Psychoticism, and GSI. Reductions in Physical Concerns were related to decreases in 5 SCL-90-R scales, including Somatization, Depression, Anxiety, Phobic Anxiety, and GSI.

Discussion: The present study suggests that reductions in AS, especially mental and physical dimensions, predict comorbid psychiatric symptoms reduction over the course of CBT for PD.

Keywords: Panic disorder; anxiety sensitivity; cognitive behavioural therapy; comorbid psychiatric symptoms.

1. INTRODUCTION

Panic disorder (PD) patients commonly have comorbid psychiatric symptoms. 50-80% of PD patients meet criteria for at least one other diagnosis, most typically other anxiety or mood disorders [1,2]. PD with comorbid psychiatric symptoms is thought to be a severe condition. For example, the comorbidity between PD and depressive disorder is thought to be a condition associated with greater symptom severity [3], poorer outcome [3], and poorer treatment response [4].

PD patients with comorbidity reported significantly higher anxiety sensitivity (AS) than those without comorbidity [5]. AS refers to the fear of anxiety-related sensations [6] and is a dispositional variable distinguishable from trait anxiety, which merely reflects a tendency to experience frequent episodes of state anxiety [7]. Higher levels of AS are observed in individuals with anxiety disorders compared to healthy individuals [8], and elevated levels of AS are prospectively associated with panic attacks [9], anxiety symptoms [10], anxiety disorders [11], and depressive symptoms [12]. AS might act as a vulnerability factor in the pathogenesis of AXIS I diagnosis [10] and appears to be a transdiagnostic construct of clinical relevance. AS has a multidimensional construct. Evidence for three facets has been found, the Physical facet, the Mental Incapacitation facet, and the Social facet (Zinbarg et al. [13]). The Mental Incapacitation facet and Physical facet are more strongly associated with cognitive vulnerabilities than the social facet (Riskind et al. [14]).

The efficacy of cognitive behavioural therapy (CBT) has been established for PD [15]. There is now evidence indicating that CBT for a targeted anxiety disorder yields positive benefits upon comorbid psychiatric symptoms [1,15,16]. CBT for PD is also efficacious in reducing AS [17]. AS is an important transdiagnostic target of CBT,

and its reduction represents an important process of change across the spectrum of “emotional disorders (anxiety and unipolar depressive disorders)” [18]. In CBT for PD, however, it is unclear whether changes in specific dimensions of AS are related to changes in comorbid psychiatric symptoms.

The purpose of the present study was to examine the relationship of changes in specific dimensions of AS and changes in comorbid psychiatric symptoms over the course of CBT for PD.

2. METHODOLOGY

2.1 Participants

One hundred thirty-two patients with PD who attended the group CBT program at Nagoya City University Hospital Department of Psychiatry, participated in the present study between September 2005 and May 2013. All of the patients met the following entry criteria: (i) principal Axis I diagnosis of PD according to the DSM-IV criteria, as assessed by the Structured Clinical Interview for DSM-IV(SCID) [19]; (ii) absence of current psychosis, bipolar disorder and substance-use disorder. The patients who had difficulty continuing their participation in the CBT program because of symptoms of other comorbid depressive disorders were medicated with antidepressants and were admitted to the CBT program after their depression symptoms had abated and they were able to attend the CBT sessions regularly. The patients provided their written informed consent after receiving full explanation of the study's purpose and procedures.

2.2 Measures

All subjects were assessed with the following instruments at pre- and post-treatment.

2.2.1 Symptom checklist-90 revised (Derogatis, 1992 [20])

The Symptom Checklist-90 Revised is a widely used assessment tool for general psychopathology [20]. It contains 90 items, subdivided into nine subscales of somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. As the summary score, the Global Severity Index (GSI) combines information on numbers of symptoms and intensity of perceived distress. The reliability and validity of the Japanese version has been reported [21]. Each item is scored between 0 (not at all) and 5 (extremely), and the average of the relevant items was taken to be the subscale score.

2.2.2 Anxiety sensitivity index [6]

The Anxiety Sensitivity Index (ASI) is commonly used to assess AS, which refers to beliefs about the dangerousness of anxious symptoms, as well as the resulting fear of these symptoms [6]. The ASI is a 16-item questionnaire in which respondents indicate on a 5-point Likert-type scale (0=very little to 4=very much). Higher scores represent greater anxiety sensitivity. We utilized the lower-order factors, involving Physical Concerns (Items 3, 4, 6, 8, 9, 10 and 14), Mental Incapacitation Concerns (Items 2, 12, 15 and 16), and Social Concerns (Items 1, 5, 7 and 13) [13]. Physical Concerns measures a fear that physical reactions can lead to catastrophic outcomes (eg. strokes, heart attacks). Mental Incapacitation Concerns captures concerns about insanity or going crazy, while Social Concerns measures fears of having anxiety noticed by others [14].

2.2.3 Panic disorder severity scale [22]

The Panic Disorder Severity Scale (PDSS) is an interview-based, seven-item scale for assessing PD severity in which the clinician rates the severity of seven features of PD on a scale ranging from 0 (none) to 4 (extreme) [22]. The seven areas covered by the scale include: the frequency of panic attacks, distress during the panic attacks, anticipatory anxiety, agoraphobic fear/avoidance, work impairment/distress, and impairment of social functioning. Adequate inter-rater reliability and validity have been reported for both the original and the Japanese versions [23].

2.3 Intervention

We followed the established CBT treatment manual for PD [24]. Treatments were conducted in groups of three to four patients led by one principal therapist and one co-therapist. The two therapists were psychiatrists or clinical psychologists with at least 2 years of clinical experience. The treatments consisted of ten sessions, each lasting approximately two hours. The 1st through 9th sessions were held weekly, and the 10th session was conducted 4 weeks after the 9th session. The first two sessions included psycho-education concerning the nature of anxiety, panic and agoraphobia and provided a rationale for training in breathing retraining. From the third session on, cognitive restructuring, in vivo exposure and interoceptive exposure were introduced, and the patients were asked to try to formulate rational thoughts and to perform self-exposure tasks to reproduce both external and interoceptive phobic cues during and between sessions.

2.4 Statistical Methods

All the data were examined using SPSS 18.0 for Windows [25]. First, we used χ^2 tests to compare the demographic and clinical data among the patients who completed the program and those who did not. Second, we used t-tests to compare the baseline and post-therapy scores. Third, to examine the predictors of change in comorbid psychiatric symptoms, we performed multiple linear regression analysis. We used the changes in subscales of SCL-90-R as dependent variables, and the change in total score of PDSS and the changes in lower-order factors of ASI, involving Physical Concerns, Mental Incapacitation Concerns, and Social Concerns, as independent variables. All the statistical tests were two-tailed, and an alpha value of less than 0.05 was considered statistically significant.

3. RESULTS

3.1 Patients Characteristics

Seven patients (5.3%) out of the 132 who started the treatment dropped out prematurely from the CBT program. Because of missing data, 118 patients were included in the current analysis (Fig. 1). Table 1 shows their baseline demographic and clinical characteristics. No statistically significant differences were seen among the subgroups.

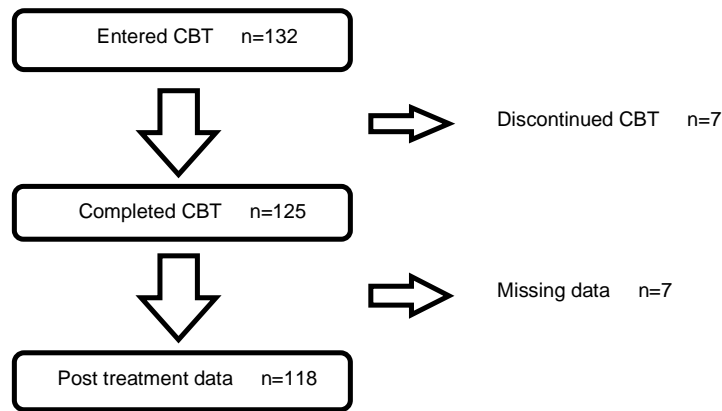


Fig. 1. Subject enrolment

Table 1. Baseline characteristics

Characteristics	Completer (n=118)	Completer with missing data (n=7)	Dropout (n=7)	P value
Female, no. (%)	88(75.6)	6(85.7)	4(57.1)	0.47
Mean age (SD)	36.8(11.4)	37.7(14.9)	33.0(11.9)	0.68
Onset (SD)	29.5(10.5)	28.1(13.4)	32.4(15.1)	0.74
Duration (SD)	7.3(6.3)	5.3(3.3)	4.9(5.2)	0.44
PDSS (SD)	13.0(4.9)	14.7(5.2)	13.9(6.3)	0.62
Agoraphobia (%)	94.0	85.7	100	0.53

Table 2. Pre-treatment and post-treatment rating scale scores (n=118)

	Pre-treatment	Post-treatment	P value
PDSS (SD)	12.97(4.89)	6.04(3.83)	<0.01
ASI			
Total (SD)	28.03(14.02)	17.09(13.62)	<0.01
Physical concerns (SD)	16.67(7.70)	10.34(7.91)	<0.01
Mental incapacitation concerns (SD)	4.96(4.47)	2.70(3.82)	<0.01
Social concerns (SD)	6.31(4.15)	4.03(3.71)	<0.01
SCL-90-R			
Somatization (SD)	1.17(0.83)	0.87(0.79)	<0.01
Obsessive-compulsive (SD)	1.20(0.82)	0.93(0.78)	<0.01
Interpersonal sensitivity (SD)	1.09(0.79)	0.80(0.70)	<0.01
Depression (SD)	1.18(0.82)	0.86(0.75)	<0.01
Anxiety (SD)	1.23(0.86)	0.90(0.81)	<0.01
Hostility (SD)	0.71(0.66)	0.53(0.59)	<0.01
Phobic anxiety (SD)	1.40(0.95)	0.83(0.83)	<0.01
Paranoid ideation (SD)	0.64(0.69)	0.45(0.56)	<0.01
Psychoticism (SD)	0.60(0.56)	0.38(0.45)	<0.01
GSI (SD)	1.06(0.66)	0.76(0.61)	<0.01

3.2 Pre-treatment and Post-treatment Rating Scale Scores

Table 2 above shows all scale scores at pre-and post –treatment. All the post-treatment scores were significantly lower than the pre-treatment scores (p<0.01).

3.3 Predictors of the Comorbid Psychiatric Symptoms

In regression analysis (Table 3), reduction in Mental Incapacitation Concerns of ASI predicted

decreases in 8 SCL-90-R scales, including Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Hostility, Phobic Anxiety, Paranoid Ideation, Psychoticism, and GSI. Reduction in Physical Concerns of ASI predicted decreases in 5 SCL-90-R scales, including Somatization, Depression, Anxiety, Phobic Anxiety, and GSI. Reduction in PDSS and Social Concerns of ASI predicted nothing significantly.

Table 3. Unique predictors of change in comorbid psychiatric symptoms (n=118)

	Δ Somati- zation	Δ Obsessive- compulsive	ΔInter- personal	ΔDepression	ΔAnxiety	ΔHostility	ΔPhobic anxiety	ΔParanoid ideation	ΔPsycho- ticism	ΔGSI
Δ PDSS total	0.05	-0.06	-0.06	-0.13	-0.06	-0.11	0.03	-0.02	-0.10	-0.07
Δ ASI-physical	0.32**	0.15	0.02	0.21*	0.22*	0.03	0.25*	-0.00	0.08	0.20*
Δ ASI-mental	0.13	0.42**	0.34**	0.39**	0.21	0.44**	0.27*	0.51**	0.31**	0.39**
Δ ASI-social	0.07	0.07	0.13	-0.02	0.10	0.08	0.00	-0.01	0.08	0.06
Adjusted R ²	0.20	0.29	0.15	0.25	0.17	0.23	0.19	0.22	0.14	0.30

The table shows the standardized Beta coefficients.

**P<0.05; **P<0.0*

4. DISCUSSION

The present study demonstrates that reductions in AS, especially mental and physical dimensions, predict decreases in comorbid psychiatric symptoms over the course of CBT. Our results supported that AS may be an important transdiagnostic target of treatment [18]. While reduction in PDSS was not related to changes in comorbid psychiatric symptoms, reduction in AS may represent an important process of change across the comorbid psychiatric symptoms in CBT for PD. These results were also consistent with the finding that mental and physical dimensions of AS have significant links to anxiety, depression, and general distress [14]. The Mental Incapacitation facet and the Physical facet may capture the fears of catastrophic and irrevocable outcomes compared to the Social facet [14]. In CBT for PD, the Mental Incapacitation facet and the Physical facet may also center on fears of catastrophic and irrevocable consequences of anxiety in comparison to the Social facet. For the purpose of improving comorbid psychiatric symptoms with PD patients, we need to pay more attention to AS, especially mental and physical dimensions, during CBT.

The present study has several limitations. First, the study did not include a control group, and it relied on within-group changes to examine the effects of CBT. Second, the rules regarding medication in this study were not precise. We deem this unavailable in naturalistic clinical settings. Third, we lacked follow-up data and could not refer to long-term effect of CBT for comorbid psychiatric symptoms. Fourth, this study was done in between 2005 and 2013, using the DSM-IV. Although DSM-5 has been included to use since 2013, its Japanese version was published in 2014. We therefore could not use DSM-5.

5. CONCLUSION

The present study demonstrated that our CBT program for PD was effective for psychiatric comorbid symptoms and that no major differences in the baseline characteristics were observed between completers and dropouts. Our study suggests that reductions in AS, especially mental and physical dimensions, predict decreases in comorbid psychiatric symptoms over the course of CBT.

ETHICAL APPROVAL

The study was performed in accordance with the Declaration of Helsinki and the study's protocol was approved by the Ethics Committee of Nagoya City University Graduate School of Medical Sciences.

ACKNOWLEDGEMENTS

This study was supported by a Grant-in-Aid from the Ministry of Education, Culture, Sports, Science, and Technology (23530910).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Tsao JC, Lewin MR, Craske MG. The effects of cognitive-behavior therapy for panic disorder on comorbid conditions. *J Anxiety Disord.* 1998;12:357-71.
2. Brown TA, Antony MM, Barlow DH. Diagnostic comorbidity in panic disorder: Effect on treatment outcome and course of comorbid diagnoses following treatment. *J Consult Clin Psychol.* 1995;63:408-18.
3. Noyes R. Jr., Reich J, Christiansen J, Suelzer M, Pfohl B, Coryell WA. Outcome of panic disorder. Relationship to diagnostic subtypes and comorbidity. *Arch Gen Psychiatry.* 1990;47:809-18.
4. Keller MB, Lavori PW, Goldenberg IM, Baker LA, Pollack MH, Sachs GS, et al. Influence of depression on the treatment of panic disorder with imipramine, alprazolam and placebo. *J Affect Disord.* 1993;28:27-38.
5. Tsao JC, Mystkowski JL, Zucker BG, Craske MG. Effects of cognitive-behavioral therapy for panic disorder on comorbid conditions: Replication and extension. *Behavior Therapy.* 2002;49:3-509.
6. Reiss S, Peterson RA, Gursky DM, McNally RJ. Anxiety sensitivity, anxiety frequency and the prediction of fearfulness. *Behav Res Ther.* 1986;24:1-8.
7. McNally RJ. Anxiety sensitivity and panic disorder. *Biol Psychiatry.* 2002;52:938-46.
8. Taylor S, Cox BJ. An expanded anxiety sensitivity index: Evidence for a hierarchic structure in a clinical sample. *J Anxiety Disord.* 1998;12:463-83.
9. Schmidt NB, Lerew DR, Jackson RJ. The role of anxiety sensitivity in the

- pathogenesis of panic: Prospective evaluation of spontaneous panic attacks during acute stress. *J Abnorm Psychol.* 1997;106:355-64.
10. Schmidt NB, Mitchell MA, Richey JA. Anxiety sensitivity as an incremental predictor of later anxiety symptoms and syndromes. *Compr Psychiatry.* 2008;49: 407-12.
 11. Schmidt NB, Zvolensky MJ, Maner JK. Anxiety sensitivity: Prospective prediction of panic attacks and Axis I pathology. *J Psychiatr Res.* 2006;40:691-9.
 12. Cox BJ, Fuentes K, Borger SC, Taylor S. Psychopathological correlates of anxiety sensitivity: Evidence from clinical interviews and self-report measures. *J Anxiety Disord.* 2001;15:317-32.
 13. Zinbarg RE, Brown TA, Barlow DH. Hierarchical structure and general factor structure saturation of the Anxiety Sensitivity Index: Evidence and implication. *Psychological Assessment.* 1997;9:277-84.
 14. Riskind JH, Kleiman EM, Weingarden H, Danvers AF. Cognitive vulnerability to anxiety in the stress generation process: further investigation of the interaction effect between the looming cognitive style and anxiety sensitivity. *J Behav Ther Exp Psychiatry.* 2013;44:381-7.
 15. Craske MG, Farchione TJ, Allen LB, Barrios V, Stoyanova M, Rose R. Cognitive behavioral therapy for panic disorder and comorbidity: More of the same or less of more? *Behav Res Ther.* 2007;45: 1095-109.
 16. Brown TA, Barlow DH. Long-term outcome in cognitive-behavioral treatment of panic disorder: Clinical predictors and alternative strategies for assessment. *J Consult Clin Psychol.* 1995;63:754-65.
 17. Smits JA, Berry AC, Tart CD, Powers MB. The efficacy of cognitive-behavioral sensitivity: A meta-analytic review. *Behav Res Ther.* 2008;46:1047-54.
 18. Boswell JF, Farchione TJ, Sauer-Zavala S, Murray HW, Fortune MR, Barlow DH. Anxiety sensitivity and interoceptive exposure: A transdiagnostic construct and change strategy. *Behav Ther.* 2013;44: 417-31.
 19. First MB. Structured clinical interview for DSM-IV axis I disorders: SCID - I: Clinician version: Administration booklet. Washington, D.C.: American Psychiatric Press; 1997.
 20. Derogatis LR. SCL-90-R: Administration, scoring & procedures manual -II, for the R (revised) version and other instruments of the psychopathology rating scale series. 2nd ed. Towson, Md.: Clinical Psychometric Research; 1992.
 21. Furukawa TA, Nakanishi M, Sakurai A, Suzuki A, Suzuki-Moor A, Hamanaka T. Effects of rhyt loflazepate in mood and neurosis-related disorders (ICD-10 JCM); Changes in SCL-90-R subscale scores. *Rinsho Seisninigaku (Clinical Psychiatry).* 1996;25:233-40.
 22. Shear MK, Brown TA, Barlow DH, Money R, Sholomskas DE, Woods SW, et al. Multicenter collaborative panic disorder severity scale. *Am J Psychiatry.* 1997; 154:1571-5.
 23. Yamamoto I, Nakano Y, Watanabe N, Noda Y, Furukawa TA, Kanai T, et al. Cross-cultural evaluation of the Panic Disorder Severity Scale in Japan. *Depress Anxiety.* 2004;20:17-22.
 24. Andrews G, Creamer M, Crino R, Hunt C, Lampe L, Page A. The treatment of anxiety disorders: Clinician guides and patient manuals (2nd ed.). Cambridge, UK; New York, NY. Cambridge University Press.; 2003.
 25. SPSS. SPSS for Windows (Version 18.0); 2009.

© 2016 Ogawa et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

*The peer review history for this paper can be accessed here:
<http://sciedomain.org/review-history/13288>*