

Cognitive-behavioral therapy for patients with chronic pain

Implications of gender differences in empathy

Jae-A Lim, MA^a, Soo-Hee Choi, MD, PhD^{a,b}, Won Joon Lee, MD^c, Joon Hwan Jang, MD, PhD^{a,d}, Jee Youn Moon, MD, PhD^e, Yong Chul Kim, MD, PhD^e, Do-Hyung Kang, MD, PhD^{a,b,*}

Abstract

Chronic pain is defined as persistent or recurrent pain lasting longer than 3 months; the severity of pain can be rated in terms of intensity, pain-related distress, and functional impairment. Researches have shown an association between psychosocial factors, such as empathic ability, and the severity of pain. Cognitive-behavioral therapy (CBT) is the most common psychologic intervention for individuals with chronic pain. The aim of this study was to investigate the effect of CBT on empathy in chronic pain patients, examining especially gender differences. In total, 89 patients with severe chronic pain (46 men and 43 women) underwent 8 sessions of CBT over the course of 4 weeks. Self-reported clinical symptoms were measured at the beginning and end of the CBT. Empathy was measured using the interpersonal reactivity index, and pain severity was assessed using the short-form McGill pain questionnaire. A comparison of male and female patients before CBT indicated that females showed higher levels of empathy in response to affective issues and reported greater affective pain than males. A mixed analysis of variance revealed that female patients showed higher levels of empathy than did male patients, both before and after CBT. We also found significant relationships between affective pain and empathy for others' personal distress in all patients. These results suggest that the effectiveness of CBT may be affected by chronic pain patients' level of empathy. Although the evident result was not shown in this study, the present findings imply that female patients may formulate excellent therapeutic alliance in CBT intervention that can lead to a clinical benefit.

Abbreviations: BAI = Beck Anxiety Inventory, BDI = Beck Depression Inventory, CBT = cognitive-behavioral therapy, CRPS = complex regional pain syndrome, EC = empathic concern, FS = fantasy scale, IRI = interpersonal reactivity index, PD = personal distress, PPI = present pain intensity, PRI = pain rating index, PT = perspective taking, SF-MPQ = short-form McGill pain questionnaire, VAS = visual analog scale, WHOQOL = World Health Organization quality of life abbreviated version.

Keywords: chronic pain, cognitive-behavioral therapy, empathy, gender differences

1. Introduction

Pain is a response to nociceptive stimuli and is often the driving force behind seeking treatment. Chronic pain tends to alter the psychological state of being (and of mind) of those who experience

it. Indeed, physical and emotional pain can be placed on the same continuum, but the evolution or transition to chronic pain is not obvious.^[1-4] Chronic pain can involve a reward deficit syndrome or anti-reward processes, which may relate to ongoing circuit dysfunction. Increasing evidence suggests that the plasticity of neural circuits is responsible for the subtle changes over time that contribute to the behavioral manifestations of altered affective processes, including blunting of pleasurable responses and/or enhancement of depressed ones that accompany chronic pain.^[1,3,5] One of phenotype of chronic severe pain is complex regional pain syndrome (CRPS). This chronic pain condition characterized by spontaneous pain, hyperalgesia, allodynia, and motor dysfunction, impairs the quality of life and social functioning of sufferers.^[6,7] Most studies have provided compelling evidence that CRPS patients are more anxious and depressed than are healthy controls.^[8] Additionally, disability and burden of cognitive impairments associated with depression pervasively impacts elementary and complex neurocognitive processes.^[9] Although the mechanism underpinning CRPS remains unknown, investigators have proposed various hypotheses, including that CRPS is a systemic disease involving the central nervous system, the peripheral nervous system (ie, neuropathic), and associated interactions between the immune system and sensitive nociceptive nervous system transmissions.^[10-12] Imaging studies in patients with CRPS have shown abnormalities in brain structure and functioning in regions associated with emotion, autonomic functioning, and pain perception.^[13-16] The experience of pain and observation of others' painful injuries activate the anterior cingulate cortex and

Editor: Chang-Bing Huang.

Jae-A Lim and Soo-Hee Choi contributed equally to this work.

This work was supported by Institute for Information & Communications Technology Promotion (IITP) grant funded by the Korean Government (MSIT) (No R-20150902-002176, Development of Military Life Management System based on Emotion Recognition).

The authors have no conflicts of interest to disclose.

^aDepartment of Psychiatry, Seoul National University Hospital, ^bDepartment of Psychiatry, Seoul National University College of Medicine, Seoul, ^cDepartment of Psychiatry, Armed Forces Capital Hospital, Seongnam, ^dDepartment of Medicine, Seoul National University College of Medicine, ^eDepartment of Anesthesiology and Pain Medicine, Seoul National University Hospital, Seoul, Republic of Korea.

*Correspondence: Do-Hyung Kang, Department of Psychiatry, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea (e-mail: basuare@hanmail.net).

Copyright © 2018 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

Medicine (2018) 97:23(e10867)

Received: 4 September 2017 / Accepted: 3 May 2018

<http://dx.doi.org/10.1097/MD.0000000000010867>

anterior insula, and these empathic responses are correlated with the intensity of pain.^[17–20]

“Empathy” is a sense that there is a similarity between one’s own feeling and the feeling expressed by others. It can be understood as an interaction between any 2 individuals, with one experiencing a feeling and the other sharing it.^[21,22] In view of the subjectivity of chronic pain, understanding how patients experience pain and communicate it to others is crucial for accurate evaluation and treatment planning in clinical practice.^[13] Given that empathy plays a key role in social interactions, the empathic ability of patients with chronic pain may influence their interactions with clinicians, the social support they receive from family or caregivers, their social functioning, and their quality of life in interpersonal contexts. In contrast to the abundant emphasis placed on others’ empathy (eg, clinicians, caregivers, and spouses) in the evaluation and management of patients with chronic pain,^[13,23–27] little attention has been devoted to the empathic abilities of the patients themselves.^[13] Recent studies have shown that chronic pain patients lack empathy^[13] and that the social emotions of patients with CRPS are impaired, providing evidence of defective socio-emotional perception in CRPS patients at the behavioral level.^[6] Pain-related empathy was shown to be mediated by brain regions that represent the affective dimension of pain, but not by those that represent the sensory dimension.^[6,20] Meanwhile, women typically have superior empathy compared with men, which seems to have a neurologic basis with sex differences in the structure and function of neural networks involved in empathy.^[28,29] Tracy and Giummarra^[28] has demonstrated a sex differences in empathy for pain are associated with divergent physiologic mechanisms using vagally mediated heart rate variability. Compared with men, women had superior trait empathy, especially empathic concern (EC) and affective distress when they imagine another person in pain from an injury.^[28]

Cognitive-behavioral therapy (CBT), a form of psychotherapy, has recently been applied to patients with chronic pain. Several studies have found that, whether administered alone or in combination with medical treatment, CBT improved pain and related problems. Pain is affected by individual cognitions as well as by tissue injury, and the core premise of CBT is that maladaptive cognitions contribute to the maintenance of emotional distress and behavioral problems.^[30] Previous studies have shown that CBT is effective for depression, anxiety, stress, and chronic pain.^[31–34] Additionally, CBT has been reported to improve quality of life and activities of daily living, chronic headache, facial pain, arthralgia, and fibromyalgia.^[35–40] CBT focuses on reducing pain and distress by modifying physical sensations, catastrophic thinking, and maladaptive behaviors.^[30] Pieh et al^[41] provided a evidence that women benefit more from multimodal pain therapy including CBT-oriented group program than men.

Given that men and women have shown different patterns of pain presentation and empathic abilities,^[29,42] the present study examined the clinical characteristics and effects of CBT in patients with chronic pain according to gender. In addition, we evaluated the association of symptom severity of pain and empathic ability in patients with chronic pain. We hypothesized that female patients with chronic pain would score higher on empathic ability and exhibit greater clinical improvement than would male patients before and after CBT. We also expected that affective component of pain would be specifically related to empathic ability in patients with chronic pain.

2. Methods

2.1. Participants

We recruited 89 patients with severe chronic pain from the Seoul National University Hospital Psychiatric Pain Clinic: 12 patients were diagnosed with CRPS, 4 were diagnosed with only fibromyalgia alone, and 73 patients were diagnosed with multiple symptoms (19 CRPS, 20 fibromyalgia, 39 back pain, and 41 headache). Forty-five patients were also diagnosed with somatic symptom disorder, 2 patients were diagnosed with visceral pain, and 6 patients were diagnosed with neuropathic pain. Additionally, 3 patients were diagnosed with post-traumatic stress disorder, and 1 patient was diagnosed with panic disorder. Severe pain was defined as a score greater than 7 on a 1- to 10-point visual analog scale (VAS). All participants were 18 to 70 years of age and suffered from chronic pain lasting at least 3 months. None of the participants had an acute illness that could have affected their pain or psychiatric symptoms during 1 month prior to CBT. Demographic information on educational level, occupation, and marital status were obtained. Following completion of CBT, 39 of the 89 patients completed the self-report questionnaire (20 men and 19 women; 10 CRPS, 11 fibromyalgia, 22 back pain, 21 headache). The patients received routine care throughout the CBT. The study protocol was approved by the Seoul National University Hospital Institutional Review Board (Seoul, South Korea).

2.2. CBT for chronic pain

The patients participated in group CBT twice per week for a total of 8 sessions over a 4-week period. Groups were usually composed of up of 5 or 6 patients, and interventions were delivered by an experienced psychiatrist. We used mindfulness-based CBT, which has been found to reduce self-reported pain and pain-related behaviors in patients with chronic pain.^[43] The format of the sessions included a review of the previous session, an introduction of new principles, a review of the new content, and assignment of homework. The foci of the 8 sessions were as follows: Session 1: introduction to CBT, training in abdominal breathing, and training in the use of the daily pain, mood, and activity charts; Session 2: identification of automatic thoughts (recording automatic thoughts) and the first part of progressive muscle relaxation; Session 3: evaluation of automatic thoughts (identification of thinking errors) and the second part of progressive muscle relaxation; Session 4: correction of automatic thoughts (alternative thoughts) and the third part of progressive muscle relaxation; Session 5: understanding the core beliefs related to pain and the first part of mindfulness meditation; Session 6: problem-solving strategies and the second part of mindfulness meditation; Session 7: assertiveness skills training, coping with stress-related pain, and the third part of mindfulness meditation; and Session 8: final remarks and strategies for preventing relapse.

2.3. Clinical measures

2.3.1. Interpersonal reactivity index. The Korean version of the Interpersonal reactivity index (IRI)^[44,45] was used to measure multiple dimensions of empathy. The IRI is a 28-item self-report multidimensional scale that measures the cognitive and emotional dimensions of empathy. The scale consists of four 7-item subscales, each of which addresses an aspect of the global concept of empathy; the perspective taking (PT) subscale and the fantasy subscale (FS) are used to measure the cognitive dimension, and

the EC and personal distress (PD) subscales are used to measure the emotional dimension. The total score for each subscale ranges from 0 to 28. The PT subscale assesses the tendency to employ a psychologic perspective in interaction with others. The FS measures the tendency to get involved in fictional stories and imagine the feelings and actions of fictitious characters in books, movies, and plays. The EC subscale assesses sympathy and concern for others, and the PD subscale measures feelings of personal anxiety and unease in tense interpersonal settings.^[44] As the IRI is not intended to measure overall empathy, each subscale should be used separately. This instrument is intended to provide continuous measures of empathy-related dimensions rather than a categorical measure that stratifies study participants into groups such as “high empathy” and “low empathy.”^[46]

2.3.2. Short-form McGill pain questionnaire. Pain intensity was assessed using the short-form McGill pain questionnaire (SF-MPQ), a widely used short version of the MPQ.^[47] The main component of the SF-MPQ consists of 15 pain rating index (PRI) descriptors (11 sensory and 4 affective) that are rated on an intensity scale from 0 (none) to 3 (severe). The SF-MPQ includes a VAS and the present pain intensity (PPI) index drawn from the standard MPQ.^[48] Scores on the PPI range from 1 (mild) to 5 (excruciating). The Korean version of the SF-MPQ has been shown to be cross-culturally equivalent to the original questionnaire, with demonstrated reliability and validity.^[49]

2.3.3. Beck depression inventory. Depression was measured using the 21-item Beck depression inventory (BDI).^[50] Each item consists of 4 statements reflecting different levels of severity of a particular symptom experienced during the past week. Total scores from 0 to 13 are classified as reflecting minimal depression, those from 14 to 19 as reflecting mild depression, those from 20 to 28 as reflecting moderate depression, and those from 29 to 63 are classified as reflecting severe depression.^[50] We used the Korean version of the BDI, which has demonstrated reliability and validity.^[51]

2.3.4. Beck anxiety inventory. The Korean version of the Beck anxiety inventory (BAI)^[52,53], which consists of 21 items rated on a 4-point scale, measures the severity of anxiety experienced during the past week. Total scores from 0 to 7 indicate a minimal level of anxiety, those from 8 to 15 indicate mild anxiety, those from 16 to 25 indicate moderate anxiety, and those from 26 to 63 indicate severe anxiety.^[54]

2.3.5. World Health Organization quality of life-abbreviated version. Quality of life was assessed using the 26-item Korean version of the World Health Organization quality of life-abbreviated version (WHOQOL-BREF).^[55,56] This instrument is a self-report multidimensional measure that addresses the important aspects of life, thereby allowing for a comprehensive assessment of quality of life. It investigates the following 4 domains: the domain of physical health, the psychologic domain, the domain of social relationships, and the environmental domain. WHOQOL has been shown to assess adequately domains relevant to quality of life.^[56]

2.4. Statistical analysis

The Statistical Package for the Social Sciences version 21.0 (IBM Corp, Armonk, NY) was used to analyze demographic and clinical characteristics. We conducted data cleaning prior to the analysis. The demographic characteristics and baseline clinical

features of participants were compared according to gender using chi-square and independent *t* tests. A repeated-measures analysis of variance (rmANOVA) was used to compare the self-reported clinical data of male and female patients who completed questionnaires both pre- and post-CBT (male, *n*=20; female, *n*=19). Furthermore, a Pearson's correlation analysis was used to assess the pre-CBT associations between empathic ability and subjective pain severity scores. *P*-values <.05 were considered significant.

3. Results

3.1. Demographic and clinical characteristics

The mean age was 44.32 ± 10.75 years (males= 43.27 ± 10.37 years; females= 45.45 ± 11.17 years). We found no significant differences between males and females in age, educational level, marital status, and cohabiting status. Diagnostic distribution between males and females were somewhat different. CRPS were prominent than fibromyalgia in male patients; however, female patients were diagnosed more with fibromyalgia than CRPS ($\chi^2 = 9.670$, *P*=.046). Males were more likely to have jobs than females ($\chi^2 = 3.986$, *P*=.046).

Females had higher level of affective score on the SF-MPQ PRI than males ($t(80) = -2.384$, *P*=.020), while sensory score and overall pain severity on the SF-MPQ were comparable in females and males. Also, female patients showed higher scores on emotional dimension of IRI-EC ($t(86) = -2.760$, *P*=.007) and IRI-PD ($t(87) = -2.761$, *P*=.007) than males. For the WHOQOL, only environmental subscore was higher in females than that of males ($t(87) = -2.078$, *P*=.041). These results are presented in Table 1.

3.2. Clinical characteristics before and after CBT according to gender

Table 2 shows the clinical changes after mindfulness-based CBT among male and female patients. There was no significant main effect of time and group \times time interaction effect for any clinical variables. However, we found significant group effects for gender in IRI-FS ($F(1, 36) = 8.904$, *P*=.005, $\eta_p^2 = 0.198$) and IRI-EC ($F(1, 37) = 6.869$, *P*=.013, $\eta_p^2 = 0.157$) scores. Female patients had higher pre- and post-CBT IRI-FS and IRI-EC subscale scores compared with male patients (Fig. 1). Both before and after CBT, female patients scored higher in all 4 domains of empathic ability than did male patients, although the statistical significance of these differences varied.

3.3. Correlation between pre-CBT empathy and pain severity

We also examined the correlations between each subscale of the IRI and the pain and clinical measures in participants. Table 3 shows the correlations between the pre-CBT clinical scales. SF-MPQ PRI affective scores were positively correlated with IRI-PD ($r = 0.390$, *P*<.001, Fig. 2), BDI ($r = 0.538$, *P*<.001), and BAI ($r = 0.584$, *P*<.001) scores. SF-MPQ PRI affective scores were negatively correlated with all aspects of the WHOQOL subscales (physical health: $r = -0.460$, *P*<.001; psychological: $r = -0.466$, *P*<.001; social relationships: $r = -0.356$, *P*=.001; environmental: $r = -0.331$, *P*=.002). There were no significant associations between SF-MPQ PRI sensory scores and IRI subscales. However, SF-MPQ PRI sensory scores were also positively

Table 1**Baseline demographic and clinical characteristics of patients with chronic pain.**

	Male (n = 46)	Female (n = 43)	χ^2 or <i>t</i>	<i>P</i>
Demographics				
Age (y)	43.27 ± 10.37	45.45 ± 11.17	−0.900	.371
Diagnosis (%)				
CRPS	25.5	12.7	9.670*	.046
Fibromyalgia	6.4	17.6		
Back pain	20.2	20.6		
Headache	19.1	22.5		
Others	28.7	26.5		
Level of education (%)				
Elementary school	4.4	2.3	3.165	.531
Middle school	11.1	7.0		
High school	40.0	46.5		
Undergraduate	42.2	34.9		
Graduate	2.2	9.3		
Marital status (%)				
Single	44.4	32.5	4.229	.238
Married	48.9	52.5		
Divorced	6.7	7.5		
Bereavement	0.0	7.5		
Cohabitant (%)				
Yes/no	78.9/21.1	89.5/10.5	1.583	.208
Job (%)				
Yes/no	35.6/64.4	16.7/83.3	3.986*	.046
Clinical variable				
IRI-PT	20.46 ± 4.92	22.28 ± 5.07	−1.722	.089
IRI-FS	19.04 ± 5.99	21.47 ± 6.46	−1.824	.072
IRI-EC	23.22 ± 6.32	26.50 ± 4.65	−2.760*	.007
IRI-PD	22.26 ± 4.83	25.38 ± 5.82	−2.761*	.007
SF-MPQ PRI sensory	20.34 ± 7.92	21.73 ± 8.35	−0.767	.445
SF-MPQ PRI affective	6.66 ± 3.50	8.37 ± 2.90	−2.384*	.020
SF-MPQ PPI	3.33 ± 0.95	3.18 ± 0.99	0.673	.503
SF-MPQ VAS	7.04 ± 1.99	6.36 ± 3.16	1.065	.292
BDI	31.67 ± 13.42	31.51 ± 12.26	0.059	.953
BAI	33.01 ± 13.61	35.94 ± 15.65	−0.944	.348
WHOQOL physical health	6.86 ± 2.18	6.72 ± 2.36	0.275	.784
WHOQOL psychological	8.01 ± 2.57	7.52 ± 3.02	0.825	.412
WHOQOL social relationships	9.62 ± 2.71	10.47 ± 3.09	−1.370	.174
WHOQOL environmental	9.16 ± 2.39	10.33 ± 2.88	−2.078*	.041

Continuous variables are presented as mean ± standard deviation.

CRPS = complex regional pain syndrome, IRI = interpersonal reactivity index, PT = perspective taking, FS = fantasy scale, EC = empathic concern, PD = personal distress, SF-MPQ = short-form McGill pain questionnaire, PRI = pain rating index, PPI = present pain intensity, VAS = visual analog scale, BDI = Beck Depression Inventory, BAI = Beck Anxiety Inventory, WHOQOL = World Health Organization quality of life abbreviated version. Others on diagnosis include somatic symptom disorder, visceral pain, neuropathic pain, post-traumatic stress disorder, and panic disorder.

* *P* < .05.

correlated with the BDI and BAI, and negatively correlated with all of the WHOQOL subscale scores.

4. Discussion

As hypothesized, female patients with chronic pain showed greater empathic abilities than those of male patients, while they had comparable overall pain severity. Additionally, affective component of pain was associated with empathic ability in all patients and especially higher in females than males. However, there were no significant differences in the effects of CBT between males and females. Also, we could not find significant clinical improvement on CBT, neither in men, nor in women.

Few studies have addressed impaired empathic abilities in patients with severe pain.^[13] We found that women showed higher levels of empathic abilities both pre- and post-CBT than did men. Indeed, gender differences have been reported that indicate a tendency for women to score higher than men on all

subscales.^[13,44] The gender differences in empathy have been most evident when a specific behavior or trait was being assessed by having individuals rate themselves on behaviors or reactions clearly related to the concept of empathy. In such cases, females have scored higher on empathy than have males.^[42] A number of acute and chronic pain treatments that may target psychologic phenomena have been examined in terms of their effects on brain activity; these treatments have included cognitive and operant behavioral interventions, meditation and hypnosis, neuro- and biofeedback, discrimination training, and imagery and mirror treatment. These treatments affect both ascending and descending aspects of pain processing and act through brain mechanisms that involve sensorimotor areas as well as those involved in affective-motivational and cognitive-evaluative phenomena.^[57] Mindfulness focuses on the awareness and acceptance of pain, and mindfulness training teaches patients to be aware of pain and observe it calmly and closely. The acceptance of pain weakens its effect, and patients realize that they can control their pain

Table 2
Changes in the clinical features at pre- and post-treatment with cognitive-behavioral therapy by gender.

	Group	Pre-CBT (n=39)	Post-CBT (n=39)	F (group)	F (scale)	F (Scale × group)	Effect size (partial η ²)
IRI-PT	Male	19.80 ± 4.81	19.15 ± 4.48	2.039	0.232	0.275	0.054
	Female	21.67 ± 5.89	21.69 ± 5.43				
IRI-FS	Male	19.10 ± 7.29	17.85 ± 5.72	8.904*	0.927	1.108	0.198
	Female	23.83 ± 5.19	23.89 ± 4.81				
IRI-EC	Male	21.90 ± 7.27	22.60 ± 5.75	6.869*	0.327	0.700	0.157
	Female	26.97 ± 4.77	26.84 ± 4.79				
IRI-PD	Male	23.75 ± 4.99	23.05 ± 5.01	1.112	3.806	0.678	0.030
	Female	25.97 ± 5.62	24.25 ± 5.80				
SF-MPQ PRI sensory	Male	20.10 ± 8.73	19.38 ± 8.56	1.337	2.146	0.233	0.038
	Female	23.56 ± 8.64	22.13 ± 6.98				
SF-MPQ PRI affective	Male	6.50 ± 3.85	6.15 ± 3.73	3.674	2.116	0.389	0.098
	Female	8.94 ± 3.19	8.06 ± 3.53				
SF-MPQ PPI	Male	3.25 ± 1.16	3.48 ± 0.94	0.193	1.688	0.116	0.005
	Female	3.16 ± 1.07	3.29 ± 1.12				
SF-MPQ VAS	Male	7.07 ± 2.21	7.45 ± 2.09	0.140	0.220	2.034	0.005
	Female	7.90 ± 2.23	7.14 ± 2.14				
BDI	Male	31.55 ± 16.29	30.85 ± 17.01	0.151	0.725	0.220	0.004
	Female	30.61 ± 14.67	28.18 ± 14.07				
BAI	Male	31.70 ± 16.24	30.75 ± 15.04	0.749	0.646	0.035	0.020
	Female	36.21 ± 16.26	34.68 ± 16.35				
WHOQOL physical health	Male	6.43 ± 2.32	6.26 ± 2.03	0.971	0.509	0.014	0.026
	Female	7.13 ± 2.37	6.89 ± 2.45				
WHOQOL psychological	Male	7.30 ± 2.51	7.83 ± 2.45	0.013	0.403	0.523	0.000
	Female	7.68 ± 3.67	7.65 ± 3.25				
WHOQOL social relationships	Male	9.73 ± 2.60	9.33 ± 2.41	0.155	0.005	1.057	0.004
	Female	9.68 ± 3.26	10.04 ± 3.03				
WHOQOL environmental	Male	8.90 ± 2.09	9.18 ± 2.52	1.767	0.848	0.022	0.046
	Female	9.76 ± 2.35	10.14 ± 2.70				

Continuous variables are presented as Mean ± standard deviation.

CBT = cognitive-behavioral therapy, IRI = interpersonal reactivity index, PT = perspective taking, FS = fantasy scale, EC = empathic concern, PD = personal distress, SF-MPQ = short-form McGill pain questionnaire, PRI = pain rating index, PPI = present pain intensity, VAS = visual analog scale, BDI = Beck Depression Inventory, BAI = Beck Anxiety Inventory, WHOQOL = World Health Organization quality of life abbreviated version.

* P < .05.

themselves. Our data showed that female patients scored higher than male patients did on the IRI-EC and IRI-PD measures. IRI-EC scores reflect feelings of warmth and sympathy, which are strongly related to other-oriented measures of sensitivity to and concern for others. IRI-PD scores are expected to be clearly and

negatively related to measures of social functioning. Additionally, female patients who completed CBT had higher IRI-FS and IRI-EC scores than did male patients who did so. The IRI-FS scale is expected to be significantly associated with measures of emotionality, as individuals who score high on this scale tend to

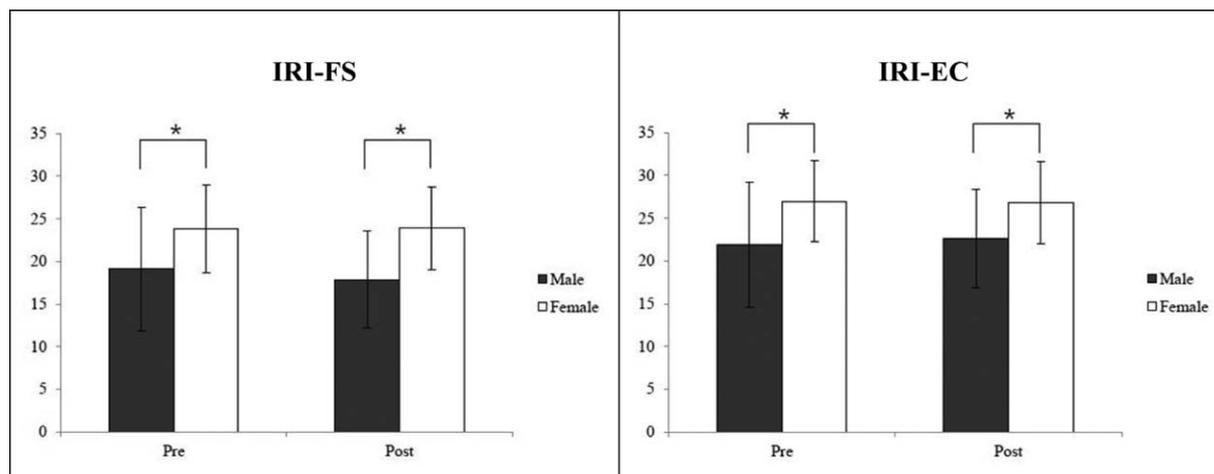


Figure 1. Gender differences in empathic abilities before and after cognitive-behavioral therapy. IRI=interpersonal reactivity index, FS=fantasy scale, EC=empathic concern. * P < .05.

Table 3

Correlation between clinical variables at baseline.

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)
(1) IRI-PT	1													
(2) IRI-FS	0.532*	1												
(3) IRI-EC	0.581*	0.407*	1											
(4) IRI-PD	-0.237*	-0.044	-0.070	1										
(5) SF-MPQ PRI sensory	-0.012	0.123	-0.172	0.165	1									
(6) SF-MPQ PRI affective	-0.075	0.027	-0.106	0.390*	0.633*	1								
(7) SF-MPQ PPI	0.056	0.061	-0.107	0.072	0.534*	0.357*	1							
(8) SF-MPQ VAS	0.021	0.162	-0.112	0.010	0.245*	0.121	0.308*	1						
(9) BDI	-0.128	-0.020	-0.256*	0.343*	0.461*	0.538*	0.452*	0.080	1					
(10) BAI	0.134	0.062	-0.032	0.190	0.587*	0.584*	0.524*	0.134	0.686*	1				
(11) WHOQOL physical health	0.071	-0.020	0.040	-0.221*	-0.387*	-0.460*	-0.416*	-0.287*	-0.628*	-0.599*	1			
(12) WHOQOL psychological	0.217*	0.066	0.156	-0.354*	-0.312*	-0.466*	-0.168	-0.195	-0.674*	-0.463*	0.730*	1		
(13) WHOQOL social relationships	0.129	-0.131	0.143	-0.257*	-0.255*	-0.356*	-0.285*	-0.222	-0.536*	-0.383*	0.467*	0.494*	1	
(14) WHOQOL environmental	0.149	-0.151	0.262*	-0.121	-0.308*	-0.331*	-0.326*	-0.355*	-0.530*	-0.343*	0.546*	0.538*	0.641*	1

IRI=interpersonal reactivity index, PT=perspective taking, FS=fantasy scale, EC=empathic concern, PD=personal distress, SF-MPQ=short-form McGill pain questionnaire, PRI=pain rating index, PPI=present pain intensity, VAS=visual analog scale, BDI=Beck depression inventory, BAI=Beck anxiety inventory, WHOQOL=World Health Organization quality of life abbreviated version. * $P < .05$.

display greater physiologic arousal in response to a filmed depiction of another’s emotional experience.^[44] Female patients also obtained higher SF-MPQ PRI affective scores did than male patients, which may be predictive of greater effectiveness of mindfulness-oriented CBT for female patients. The aim of CBT treatment is to help patients adapt and make desirable changes in the present rather than to deal with issues in the distant past; to this end, a large part of the treatment is focused on problem solving and the acquisition of new coping skills. The ultimate goal is to enable patients to become their own therapists; hence, the therapeutic relationship between the CBT therapist and the patient is collaborative and supportive. In contrast of our expectation that CBT might be helpful in reducing pain and psychologic distress,^[58] we could not find direct effect on CBT intervention in the present population. A previous meta-

analysis also showed that acceptance- and mindfulness-based interventions can have indirect effects on pain intensity since increased acceptance may buffer the degree to which pain sensations are experienced as stressful events to be immediately avoided.^[59,60] In addition, in patients with fibromyalgia, none or small effects of mindfulness-based CBT were found in (randomized) controlled studies.^[59,61,62] In our data, the rate of fibromyalgia in female patients was higher than in male patients, this may have affected the statistically insignificant effect of CBT in women.

Although the change was not statistically significant, the IRI-PD scores of both male and female patients decreased slightly following CBT in our study. A functional magnetic resonance imaging study found a positive correlation between IRI-PD scores and blood oxygen level-dependent activity in the right temporal pole, which is associated with social behavior and functioning.^[63,64] Moreover, previous studies have shown a positive correlation between the severity of depression and IRI-PD scores^[65] and have reported that patients with CRPS had higher IRI-PD scores than healthy controls.^[13] Scores on the IRI-PD and those measuring individual quality of life have been shown to have an inverse relationship,^[13] which explains why higher IRI-PD scores are associated with poor interpersonal relationships. Thus, the trend that IRI-PD scores decreased after CBT suggests that the treatment had a positive effect on the social functioning and individual quality of life of our patients. Although the evident result was not shown in this study, the present finding suggests that this therapy may be useful for improving social interactions in this population; it may be especially beneficial for females. There is evidence to suggest that empathy is essential to the establishment of effective therapeutic relationships within CBT.^[66,67] CBT techniques may benefit from empathic understanding and enhanced trust it suggests that, due to the nature of CBT formulations and intervention strategies, there are some unique empathy and outcome in CBT.^[66,68]

The CBT is effective for treating depression and anxiety and improving the quality of life in chronic pain patients.^[69,70] In depressed patients, cognitive symptoms are significant predictors not only of therapeutic response, but also of later everyday and psychologic function. Improving neurocognitive function is associated with a greater likelihood of functional remission.^[9]

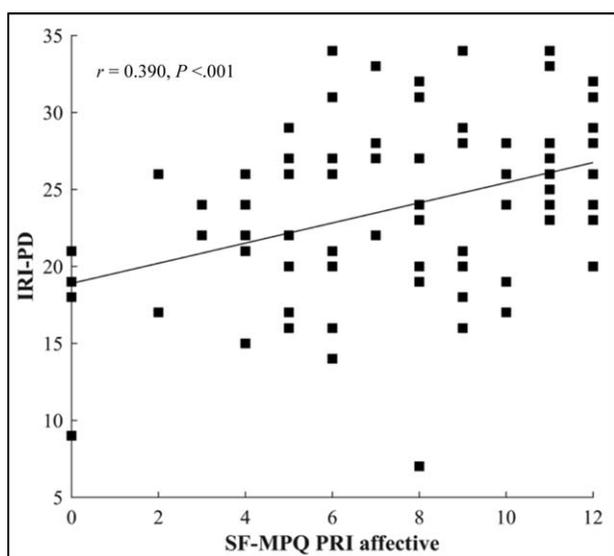


Figure 2. Correlation between affective score of pain severity and personal distress subscale score of interpersonal reactivity at baseline. IRI=interpersonal reactivity index, PD=personal distress, SF-MPQ=short-form McGill pain questionnaire, PRI=pain rating index.

However, despite decreasing trends, we found no significant changes in the BDI, BAI, and WHOQOL scores following CBT. This lack of significant effects may indicate that a 4-week CBT intervention was not sufficient to alleviate depression and anxiety and to improve the quality of life of patients in severe chronic pain. Furthermore, we could not find significant interaction between gender and the effect of CBT as stated above. To the best of our knowledge, no study has investigated relationships between the duration of CBT and psychologic symptoms; further investigations of these issues would be helpful in developing a treatment plan for chronic pain patients. Furthermore, as online mindfulness-based stress reduction and healing arts programs have been shown to be effective,^[71] the provision of online CBT training to chronic pain patients would be helpful, especially given that this modality is easily accessible and involves no time or space limitations.

Several limitations of this study should be considered when interpreting the findings. First, our sample size was small and heterogeneous populations, which may have resulted in selection bias; thus, our findings cannot be generalized to all patients with chronic pain. In addition, there was a significant gender difference in diagnosis of CRPS and fibromyalgia. However, these diagnoses correspond to only 30% among all of diagnosis, and distributions of other diagnoses were similar in 2 groups. Furthermore, corrections for multiple comparisons and correlations were not applied. We chose a rather liberal significance threshold because none of the variables were independent from each other. Thus, our conclusions should be treated with caution. Second, we did not compare chronic pain patients with normal controls; thus, we were not able to determine whether the changes in empathy were quantitatively meaningful in relation to a healthy population. Third, the duration of our study, which included 8 therapy sessions over the course of 4 weeks, was relatively short. Longitudinal investigations are necessary to evaluate the long-term effects of CBT on empathy in individuals with chronic pain. Finally, we did not consider the possible effects of medication. Future investigations in larger populations that include control subjects and consider several variables that may affect the results of CBT are warranted.

In conclusion, our investigation of the effects of CBT on empathy in patients with chronic pain showed that female patients revealed higher empathic abilities and reported more severe affective reactions to the intensity of their pain than did male patients both before and after CBT. Given the higher affective nature of pain and empathic abilities of female patients, this population may show different treatment outcomes from CBT compared to male patients. Although we could not confirm statistically significant effect on CBT in the present sample, pain control and reduction may not be the primary aims of mindfulness-based interventions.^[59] Mindfulness skills have been found to influence brain mechanisms that may alter pain experience.^[59,72] Based on the previous and current findings, we could expect that women might benefit from this treatment modality, as CBT is effective in the treatment of emotional distress. We recommend that clinicians consider the affective aspect of empathy when treating chronic pain patients, as this may be helpful in understanding the emotional distress and social difficulties that accompany chronic pain.

Author contributions

Conceptualization: Soo-Hee Choi, Jee Youn Moon, Yong Chul Kim, Do-Hyung Kang.

Data curation: Won Joon Lee.

Formal analysis: Jae-A Lim.

Funding acquisition: Do-Hyung Kang.

Project administration: Do-Hyung Kang.

Supervision: Joon Hwan Jang, Do-Hyung Kang.

Validation: Joon Hwan Jang.

Writing – original draft: Jae-A Lim.

Writing – review & editing: Soo-Hee Choi.

References

- [1] Simons LE, Elman I, Borsook D. Psychological processing in chronic pain: a neural systems approach. *Neurosci Biobehav Rev* 2014;39:61–78.
- [2] Borsook D, Becerra L, Carlezon WA, et al. Reward-aversion circuitry in analgesia and pain: Implications for psychiatric disorders. *Eur J Pain* 2007;11:7–20.
- [3] Elman I, Zubieta J-K, Borsook D. The missing P in psychiatric training: why it is important to teach pain to psychiatrists? *Arch Gen Psychiatry* 2011;68:12–20.
- [4] Perl ER. Ideas about pain, a historical view. *Nat Rev Neurosci* 2007;8:71–80.
- [5] Becker S, Gandhi W, Schweinhardt P. Cerebral interactions of pain and reward and their relevance for chronic pain. *Neurosci Lett* 2012;520:182–7.
- [6] Shin NY, Kang D-H, Jang JH, et al. Impaired recognition of social emotion in patients with complex regional pain syndrome. *J Pain* 2013;14:1304–9.
- [7] Reedijk WB, van Rijn MA, Roelofs K, et al. Psychological features of patients with complex regional pain syndrome type I related dystonia. *Mov Disord* 2008;23:1551–9.
- [8] Marinus J, Moseley GL, Birklein F, et al. Clinical features and pathophysiology of complex regional pain syndrome. *Lancet Neurol* 2011;10:637–48.
- [9] Gonda X, Pompili M, Serafini G, et al. The role of cognitive dysfunction in the symptoms and remission from depression. *Ann Gen Psychiatry* 2015;14:27.
- [10] Lee DH, Noh E, Kim YC, et al. Risk factors for suicidal ideation among patients with complex regional pain syndrome. *Psychiatry Investig* 2014;11:32–8.
- [11] Üçeyler N, Sommer C. Status of immune mediators in painful neuropathies. *Curr Pain Headache Rep* 2008;12:159–64.
- [12] Marchand F, Perretti M, McMahon SB. Role of the immune system in chronic pain. *Nat Rev Neurosci* 2005;6:521–32.
- [13] Sohn H-S, Lee D-H, Lee K-J, et al. Impaired empathic abilities among patients with complex regional pain syndrome (type I). *Psychiatry Investig* 2016;13:34–42.
- [14] Geha PY, Baliki MN, Harden RN, et al. The brain in chronic CRPS pain: abnormal gray-white matter interactions in emotional and autonomic regions. *Neuron* 2008;60:570–81.
- [15] Barad MJ, Ueno T, Younger J, et al. Complex regional pain syndrome is associated with structural abnormalities in pain-related regions of the human brain. *J Pain* 2014;15:197–203.
- [16] Kim JH, Choi SH, Jang JH, et al. Impaired insula functional connectivity associated with persistent pain perception in patients with complex regional pain syndrome. *PLoS One* 2017;12:e018479.
- [17] Lumley MA, Cohen JL, Borszcz GS, et al. Pain and emotion: a biopsychosocial review of recent research. *J Clin Psychol* 2011;67:942–68.
- [18] Ochsner KN, Zaki J, Hanelin J, et al. Your pain or mine? Common and distinct neural systems supporting the perception of pain in self and other. *Soc Cogn Affect Neurosci* 2008;3:144–60.
- [19] Saarela MV, Hlushchuk Y, Williams ACDC, et al. The compassionate brain: humans detect intensity of pain from another's face. *Cereb Cortex* 2007;17:230–7.
- [20] Singer T, Seymour B, O'Doherty J, et al. Empathy for pain involves the affective but not sensory components of pain. *Science* 2004;303:1157–62.
- [21] Decety J, Lamm C. Human empathy through the lens of social neuroscience. *Sci World J* 2006;6:1146–63.
- [22] Thompson E. Empathy and consciousness. *J Conscious Stud* 2001;8:1–32.
- [23] Cano A, Barterian J, et al. Empathic and nonempathic interaction in chronic pain couples. *Clin J Pain* 2008;24:678–84.

- [24] Chibnall JT, Tait RC, Jovel A. Accountability and empathy effects on medical students' clinical judgments in a disability determination context for low back pain. *J Pain* 2014;15:915–24.
- [25] Cohen M, Quintner J, Buchanan D, et al. Stigmatization of patients with chronic pain: the extinction of empathy. *Pain Med* 2011;12:1637–43.
- [26] Hurter S, Paloyelis Y, Amanda AC, et al. Partners' empathy increases pain ratings: effects of perceived empathy and attachment style on pain report and display. *J Pain* 2014;15:934–44.
- [27] Leonard MT, Issner JH, Cano A, et al. Correlates of spousal empathic accuracy for pain-related thoughts and feelings. *Clin J Pain* 2013;29:324–33.
- [28] Tracy LM, Giummarra MJ. Sex differences in empathy for pain: what is the role of autonomic regulation? *Psychophysiology* 2017;54:1549–58.
- [29] Hoffman ML. Sex differences in empathy and related behaviors. *Psychol Bull* 1977;84:712–22.
- [30] Hofmann SG, Asnaani A, Vonk IJJ, et al. The efficacy of cognitive behavioral therapy: a review of meta-analyses. *Cognit Ther Res* 2012;36:427–40.
- [31] Morley S, Eccleston C, Williams A. Systematic review and meta-analysis of randomized controlled trials of cognitive behaviour therapy and behaviour therapy for chronic pain in adults, excluding headache. *Pain* 1999;80:1–3.
- [32] Butler AC, Chapman JE, Forman EM, et al. The empirical status of cognitive-behavioral therapy: a review of meta-analyses. *Clin Psychol Rev* 2006;26:17–31.
- [33] Wetherell JL, Afari N, Rutledge T, et al. A randomized, controlled trial of acceptance and commitment therapy and cognitive-behavioral therapy for chronic pain. *Pain* 2011;152:2098–107.
- [34] Lee D-H, Park HY, Lee US, et al. The effects of brain wave vibration on oxidative stress response and psychological symptoms. *Compr Psychiatry* 2015;60:99–104.
- [35] Hoffman BM, Papas RK, Chatkoff DK, et al. Meta-analysis of psychological interventions for chronic low back pain. *Health Psychol* 2007;26:1–9.
- [36] Andrasik F, Grazzi L, Usai S, et al. Pharmacological treatment compared to behavioural treatment for juvenile tension-type headache: results at two-year follow-up. *Neurol Sci* 2007;28(Suppl 2):S235–8.
- [37] Aggarwal VR, Lovell K, Peters S, et al. Psychosocial interventions for the management of chronic orofacial pain. *Cochrane Database Syst Rev* 2011;11: Art. No.: CD008456.
- [38] Astin JA, Beckner W, Soeken K, et al. Psychological interventions for rheumatoid arthritis: a meta-analysis of randomized controlled trials. *Arthritis Rheum* 2002;47:291–302.
- [39] Glombiewski JA, Sawyer AT, Gutermann J, et al. Psychological treatments for fibromyalgia: a meta-analysis. *Pain* 2010;151:280–95.
- [40] Andrasik F. What does the evidence show? Efficacy of behavioural treatments for recurrent headaches in adults. *Neurol Sci* 2007;28(Suppl 2):S70–7.
- [41] Pieh C, Altmeppen J, Neumeier S, et al. Gender differences in outcomes of a multimodal pain management program. *Pain* 2012;153:191–202.
- [42] Eisenberg N, Lennon R. Sex differences in empathy and related capacities. *Psychol Bull* 1983;94:100–31.
- [43] Kabat-Zinn J, Lipworth L, Burney R. The clinical use of mindfulness meditation for the self-regulation of chronic pain. *J Behav Med* 1985;8:163–90.
- [44] Davis MH. Measuring individual differences in empathy: evidence for a multidimensional approach. *J Pers Soc Psychol* 1983;44:113–26.
- [45] Kang I, Kee S, Kim SE, et al. Reliability and validity of the Korean-version of interpersonal reactivity index. *J Korean Neuropsychiatr Assoc* 2009;48:352–8.
- [46] Konrath S. Critical synthesis package: interpersonal reactivity index (IRI). *MedEdPORTAL* 2013;9:9596.
- [47] Dworkin RH, Turk DC, Revicki DA, et al. Development and initial validation of an expanded and revised version of the short-form McGill pain questionnaire (SF-MPQ-2). *Pain* 2009;144:35–42.
- [48] Melzack R. The short-form McGill pain questionnaire. *Pain* 1987;30:191–7.
- [49] Choi SA, Son C, Lee J-H, et al. Confirmatory factor analysis of the Korean version of the short-form McGill pain questionnaire with chronic pain patients: a comparison of alternative models. *Health Qual Life Outcomes* 2015;13:15.
- [50] Beck AT, Ward CH, Mendelson M, et al. An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:561–71.
- [51] Lee YH, Song JY. A study of the reliability and the validity of BDI, SDS, and MMPI-D scales. *Kor J Clin Psychol* 1991;10:98–113.
- [52] Beck AT, Steer RA. Beck anxiety inventory manual. Harcourt Brace and Company, San Antonio, TX:1993.
- [53] Yook SP, Kim JS. A clinical study on the Korean version of Beck anxiety inventory: comparative study of patient and non-patient. *Kor J Clin Psychol* 1997;16:185–97.
- [54] Beck AT, Epstein N, Brown G, et al. An inventory for measuring clinical anxiety: psychometric properties. *J Consult Clin Psychol* 1988;56:893–7.
- [55] Min SK, Kim KI, Lee CI, et al. Development of the Korean versions of WHO Quality of Life scale and WHOQOL-BREF. *Qual Life Res* 2002;11:593–600.
- [56] The WHOQOL Group. Development of the World Health Organization WHOQOL-BREF quality of life assessment. *Psychol Med* 1998;28:551–8.
- [57] Flor H. Psychological pain interventions and neurophysiology: implications for a mechanism-based approach. *Am Psychol* 2014;69:188–96.
- [58] Tang NKY. Cognitive behavioural therapy in pain and psychological disorders: towards a hybrid future. *Prog Neuropsychopharmacol Biol Psychiatry* 2017;1–9.
- [59] Veehof MM, Trompetter HR, Bohlmeijer ET, et al. Acceptance- and mindfulness-based interventions for the treatment of chronic pain: a meta-analytic review. *Cogn Behav Ther* 2016;45:5–31.
- [60] Shapiro SL, Carlson LE, Astin JA, et al. Mechanisms of mindfulness. *J Clin Psychol* 2006;62:373–86.
- [61] Lakhan SE, Schofield KL. Mindfulness-based therapies in the treatment of somatization disorders: a systematic review and meta-analysis. *PLoS One* 2013;8:e71834.
- [62] Lauche R, Cramer H, Dobos G, et al. A systematic review and meta-analysis of mindfulness-based stress reduction for the fibromyalgia syndrome. *J Psychosom Res* 2013;75:500–10.
- [63] Moriguchi Y, Ohnishi T, Lane RD, et al. Impaired self-awareness and theory of mind: an fMRI study of mentalizing in alexithymia. *Neuroimage* 2006;32:1472–82.
- [64] Bachevalier J. Medial temporal lobe structures and autism: a review of clinical and experimental findings. *Neuropsychologia* 1994;32:627–48.
- [65] Berthoz S, Wessa M, Kedia G, et al. Cross-cultural validation of the empathy quotient in a French-speaking sample. *Can J Psychiatry* 2008;53:469–77.
- [66] Thwaites R, Bennett-Levy. Conceptualizing empathy in cognitive behaviour therapy: making the implicit explicit. *Behav Cogn Psychother* 2007;35:591–612.
- [67] Hardy G, Cahill J, Barkham M, Gilbert P, Leahy RL. Active ingredients of the therapeutic relationship that promote client change: a research perspective. *The Therapeutic Relationship in the Cognitive-Behavioural Psychotherapies* Routledge, London:2007;24–42.
- [68] Bohart A, Elliott R, Greenberg LS, Norcross JC, et al. Empathy. *Psychotherapy Relationships that Work* Oxford University Press, New York:2002;89–108.
- [69] Butler AC, Chapman JE, Forman EM, et al. The empirical status of cognitive-behavioral therapy: a review of meta-analysis. *Clin Psychol Rev* 2006;26:17–31.
- [70] Castro MM, Daltro C, Krachete DC, et al. The cognitive behavioral therapy causes an improvement in quality of life in patients with chronic musculoskeletal pain. *Arq Neuropsiquiatr* 2012;70:864–8.
- [71] Jung YH, Ha TM, Oh CY, et al. The effects of an online mind-body training program on stress, coping strategies, emotional intelligence, resilience and psychological state. *PLoS One* 2016;11:e0159841.
- [72] Zeidan F, Martucci KT, Kraft RA, et al. Brain mechanisms supporting the modulation of pain by mindfulness meditation. *J Neurosci* 2011;31:5540–8.