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Impaired Recognition of Social Emotion in Patients With Complex Regional Pain Syndrome

Na Young Shin,* Do-Hyung Kang,† Joon Hwan Jang,† Soo Young Park,‡ Jae Yeon Hwang,§ Sung Nyun Kim,† Min Soo Byun,† Hye Youn Park,† and Yong Chul Kim‡

**Interdisciplinary Cognitive Science Program, Seoul National University, Seoul, Republic of Korea.*
†Department of Psychiatry, Seoul National University College of Medicine, Seoul, Republic of Korea.
‡Department of Anesthesiology and Pain Medicine, Seoul National University Hospital, Seoul, Republic of Korea.
§Department of Psychiatry, SMG-SNU Boramae Medical Center, Seoul, Republic of Korea.

Abstract: Multiple brain areas involved in nociceptive, autonomic, and social-emotional processing are disproportionally changed in patients with complex regional pain syndrome (CRPS). Little empirical evidence is available involving social cognitive functioning in patients with chronic pain conditions. We investigated the ability of patients with CRPS to recognize the mental/emotional states of other people. Forty-three patients with CRPS and 30 healthy controls performed the Reading Mind in the Eyes Test, which consists of photos in which human eyes express various emotional and mental states. Neuropsychological tests, including the Wisconsin Card Sorting Test, the stop-signal test, and the reaction time test, were administered to evaluate other cognitive functions. Patients with CRPS were significantly less accurate at recognizing emotional states in other persons, but not on other cognitive tests, compared with control subjects. We found a significant association between the deficit in social-emotion recognition and the affective dimension of pain, whereas this deficit was not related to the sensory dimension of pain. Our findings suggest a disrupted ability to recognize others' mental/emotional states in patients with CRPS.

***Perspective:** This article demonstrated a deficit in inferring mental/emotional states of others in patients with CRPS that was related to pain affect. Our study suggests that additional interventions directed toward reducing distressful affective pain may be helpful to restore social cognitive processing in patients with CRPS.*

***Key words:** Complex regional pain syndrome, chronic pain, emotion, cognitive function, social cognition, social perception.*

Complex regional pain syndrome (CRPS) is a chronic neuropathic pain condition characterized by spontaneous pain, hyperalgesia, allodynia, and motor dysfunction that hampers quality of life and social functioning of patients.[27] There is evidence that functional reorganization in pain-related brain regions occurs in patients with CRPS.[23] Imaging studies have shown that multiple brain areas involved in nociceptive, autonomic, and emotional processing are disproportionally changed in patients with this syndrome.[10,21,22] It is interesting that the altered cortical areas in patients with CRPS encompass the ventromedial prefrontal cortex, insula, amygdala, and anterior cingulate cortex, which are engaged in emotional processing,[10,26] understanding of others' affective mental states,[30] and empathy for pain of other persons.[31] The abnormalities in these neural regions suggest a possible deterioration of social cognitive and emotional functioning in patients with CRPS.[9,18] However, few studies have considered social cognitive and emotional functioning in CRPS. A single study observed specific cognitive disability when performing an emotionally laden task that involves loss and gain in patients with CRPS.[1] No study investigates social cognitive function in chronic pain, including CRPS.

In the present study, we explored the ability of patients with CRPS to perceive another person's mental and

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Address reprint requests to Do-Hyung Kang, PhD, MD, Department of Psychiatry, Seoul National University College of Medicine, 28 Yeongon-dong, Chongno-gu, Seoul, Korea 110-744. E-mail: basuare@paran.com
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emotional states. On the basis of the neurobiological evidence and a limitation in social functioning in patients with CRPS,[27] we hypothesized that the ability to recognize mental states from subtle emotional and social cues may be impaired in patients with CRPS. Additionally, we assessed other cognitive function that has been found to be deficient in chronic pain patients[25] to investigate whether the deficit is specific to social-emotional skill or generalized to other cognitive domains.

Methods

Subjects

Forty-three patients with CRPS were recruited from the outpatient clinic at the Seoul National University Hospital. The patients (26 men and 17 women) fulfilled the research criteria of the International Association of Study of Pain for CRPS I (n = 35) or CRPS II (n = 8). The mean age of the patients was 38.8 ± 11.9 years (range, 20–59 years), and the mean years of education was 12.4 ± 2.7 years. The mean duration of the disease was 46.5 ± 42.3 months. The upper limbs were affected in 14 patients, the lower limbs in 15, and both in 14 patients. Thirty-two patients (74%) had comorbid Axis I psychiatric disorders: major depressive disorder (n = 19), other mood disorders (n = 12), and anxiety disorders (n = 1). One patient did not use any drugs, but the others were taking various analgesic drugs including opioids (n = 20), nonsteroidal anti-inflammatory drugs (n = 10), anticonvulsants (n = 37), antidepressants (n = 36), antipsychotics (n = 13), and anxiolytics (n = 33). Exclusion criteria for patients included intellectual disabilities, neurologic disorders, history of head injuries, and substance abuse.

Thirty healthy control subjects (22 men, 8 women) with a mean age of 29.9 ± 7.8 years (range, 19–48 years) and a mean educational level of 15.0 ± 1.9 years were recruited from the community though internet advertisements. These participants had no history of hospitalization due to any kind of disease and were screened for psychiatric disorders using the Structured Clinical Interview of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth edition,* nonpatient version. Exclusion criteria for controls were intellectual disabilities, psychiatric illnesses, history of head injury, and neurologic disorders. This study was approved by the institutional review board of the Seoul National University Hospital, and written informed consent was obtained from all subjects before testing.

Measurements

Clinical Assessment

The Korean version of the short-form McGill Pain Questionnaire[20,28] was employed to quantify patient pain. This questionnaire measures sensory (11 items) and affective (4 items) dimensions of pain, which are self-rated on a Likert-type scale (0 = none, 1 = mild, 2 = moderate, 3 = severe). This scale also includes the single-item present pain intensity scale (0 = none, 1 = mild, 2 = discomfort, 3 = distressing, 4 = horrible, 5 = excruciating) and the visual analog scale (0 = no pain; 10 = maximum imaginable pain) to evaluate pain intensity. The 21-item clinician-rated Hamilton Rating Scale for Depression (range, 0–66)[13] and the 14-item clinician-rated Hamilton Rating Scale for Anxiety (range, 0–44)[12] were used to evaluate the levels of depressive and anxiety symptoms in patients, respectively. In addition, the self-reported Beck Depression Inventory[6] and Beck Anxiety Inventory,[5] which are composed of 21 items (range, 0–63), were administered to all subjects to measure depressive and anxiety symptoms.

Neurocognitive Tests

Trained researchers administered the following neuropsychological tests during a single session in a quiet room: 1) The Reading Mind in the Eyes test (RMET)[4] was administered to evaluate the ability to infer another person's emotional and mental state from eye expressions. Thirty-seven photographs (including 1 practice item) depicting the eye region of human faces were presented. Participants were asked to select the word that best described the mental state from among 4 choice words. A preliminary study showed overall accuracy of 74.8% in 110 Korean undergraduate university students, which was comparable to that previously reported in a study by Baron-Cohen et al.[4] The RMET items were classified as positive (8 items), neutral (16 items), or negative (12 items) to examine a role of emotional valence on the performance.[14] 2) The reaction time (RTI) test from the Cambridge Neuropsychological Test Automated Battery (Cambridge Cognition, Cambridge, United Kingdom) was used to measure psychomotor speed and attention. The subjects were asked to release a pad button (reaction time) or touch a stimulus after button release (movement time) in response to the onset of a stimulus in a single location (simple) or in 1 of 5 locations (5-choice) as quickly as possible. 3) The stop-signal test from the Cambridge Neuropsychological Test Automated Battery was employed to evaluate the ability to inhibit an ongoing motor response. The subjects were instructed to press the right or left button, depending on the direction of the arrow, and to suppress their response when an auditory signal (beep) occurred. The stop-signal reaction time, an estimate of the time taken to withhold a response, was measured. 4) The Wisconsin Card Sorting Test (WCST)[16] was used to measure cognitive flexibility. Subjects were given 4 stimulus cards with symbols differing in color, form, and number and were asked to match 128 response cards to one of the stimulus cards according to color, form, or number. The criterion shifted after 10 consecutive correct selections. This procedure was repeated until 6 criteria were completed. The number of perseverative errors and the number of categories completed, which are sensitive to frontal lobe damage,[32] were used for the analysis.

Statistical Methods

Analysis of covariance (ANCOVA) was performed, with RMET accuracy rate and the stop-signal test scores as dependent variables, the CRPS patient and control