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Different patterns in mental rotation of facial expressions in complex regional pain syndrome patients

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Abstract

Although facial pain expressions are considered to be the most visible pain behaviors, it is known that the association between pain intensity and facial pain expression is weak for chronic pain. The authors hypothesized that the facial pain expressiveness was altered in chronic pain and investigated it with a mental rotation task using various facial expression, which seems to be associated with actual facial movements. As a task stimulus, 4 types of facial expression stimuli consisted of upper (tightening of eye and furrowed brows) and lower (raising upper lip) pain-specific facial expressions, and upper (eyeball deviation) and lower (tongue protrusion) facial movements not using facial muscles were used. Participants were asked to judge whether a stimulus presented at various rotation angles was left- or right-sided. The authors tested 40 patients with complex regional pain syndrome (CRPS) (12 women, age range 21–60) and 35 healthy controls (15 women, age range 26–64). In an analysis of reaction time (RT) using a linear mixed model, patients were slower to react to all types of stimuli ($P = .001$) and a significant interaction between group (patient or control) and type of facial expression was observed ($P = .01$). In the post hoc analysis only patients showed longer RTs to raising upper lip than other types of facial expressions. This reflects a deficit in mental rotation tasks especially for lower facial region pain expressions in CRPS, which may be related to the psychosocial aspects of pain. However, comprehensive intra- and interpersonal influences should be further investigated.

Abbreviations: ACC = anterior cingulate cortex, BDI = Beck Depression Inventory, CRPS = complex regional pain syndrome, EC = empathetic concern, ED = eyeball deviation, FACS = Facial Action Coding System, FS = Fantasy Scale, IRI = Interpersonal Reactivity Index, LFP = lower facial region pain expression, MPQ = McGill Pain Questionnaire, PD = personal distress, PT = perspective taking, RT = reaction time, TD = tongue deviation, UFP = upper facial region pain expression.

Keywords: complex regional pain syndrome, facial expression, mental rotation, pain behavior, psychosocial model of pain

1. Introduction

The degree of pain experienced can be assessed by pain behavior indices, most commonly in the form of self-reported verbal pain intensity and direct behavioral observation. Self-reported verbal pain intensity is often regarded as the gold standard for pain assessment.[1] However, there are many limitations to accepting self-reported verbal pain intensity as a credible assessment tool, because the ratings are retrospective and under the control of cognitive processes, which results in numerous emotional and self-presentation biases.[2] Thus, many clinicians instead assess patients' pain experiences based on their observations of nonverbal pain behaviors.[3] Among nonverbal pain behaviors, facial expressions are considered as a more important indicator of pain experiences than other bodily movements,[4] because the expressions are more reflex-like and are considered to be under involuntary control.[5,6]

Clinicians tend to underestimate the degree of pain reported by patients, especially in those suffering from chronic pain.[7] This includes cases where pain is evaluated by facial expressions.[8] This may be because the association between self-reported pain intensity and pain behavior in chronic pain is weak.[3] Although there is little research on the influence of pain underestimation on health outcomes in chronic pain, patients may also exaggerate pain-related behaviors to convince others that they are actually suffering from pain, according to the operant conditioning theory

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of chronic pain.[9] Thus, accurate assessment of pain is important in the treatment of chronic pain.

Complex regional pain syndrome (CRPS) is a chronic pain disorder, in which pain intensity is higher compared with of all other pain conditions.[10] Thus, in many cases, patients with CRPS are prescribed excessive opioid analgesics due to their severe pain, because these patients show poor responses to opioids[11] and thus require higher doses. As a result, patients with legitimate CRPS are often considered to be exaggerating their pain, or are mislabeled as addicts. It is uncertain whether underestimation of chronic pain is attributable to facial expressions of pain or to contextual factors associated with pain behaviors. We hypothesized that regulations associated with facial expressions of chronic pain would be altered, and evaluated this in patients with CRPS.

Motor imagery is a mental process in which an individual simulates an action without performing an actual movement.[12] Several studies have shown functional equivalence between actual motor movements and motor imagery.[13] Thus, motor imagery can be used as a tool for assessing the motor systems associated with actual actions.[14] In the field of pain, several studies have shown that performance on mental motor imagery tasks for painful versus nonpainful body parts was reduced.[15–18] In 1 study of facial pain that used mental rotation of faces, disrupted motor processing of facial expressions due to pain was found.[19] However, no reported study has assessed patients without facial pain, with respect to the function of facial expressions of pain, using various facial expression stimuli. Therefore, we devised a mental rotation task comprising various facial expressions and examined the difference between CRPS patients and normal controls.

2. Methods

2.1. Subjects

Participants were recruited from the outpatient clinic of Seoul National University Hospital between April 2016 and October 2016. All patients were diagnosed with CRPS type 1 or 2 by a board-certified anesthesiologist, based on modified diagnostic research criteria.[20] Patients were excluded if they had difficulty understanding or performing the tasks due to severe pain. Age- and gender-matched controls were also recruited. In total, a convenience sample of 40 patients (12 women; age range: 21–60 years) and 35 healthy controls (15 women; age range: 26–64 years) was recruited.

The protocol was approved by the Institutional Review Board of Seoul National University Hospital. All participants gave written informed consent to participate. This study was conducted in accordance with the Declaration of Helsinki.

2.2. Mental rotation task

Selection of stimuli was based on the finding that 4 pain-indicative facial muscle movements are involved in pain expressions, across a range of different experimental pain modalities and clinical pain conditions.[21] However, instead of using the 4 pain-specific facial expressions, we constructed stimuli by dividing facial pain expressions into upper and lower regions of the face. Brow lowering and orbit tightening were the upper region expressions, and upper-lip raising was the lower region expression. We also included stimuli that did not use facial muscles to assess whether the ability to perform the task simply reflected the spatial difference between the upper and lower

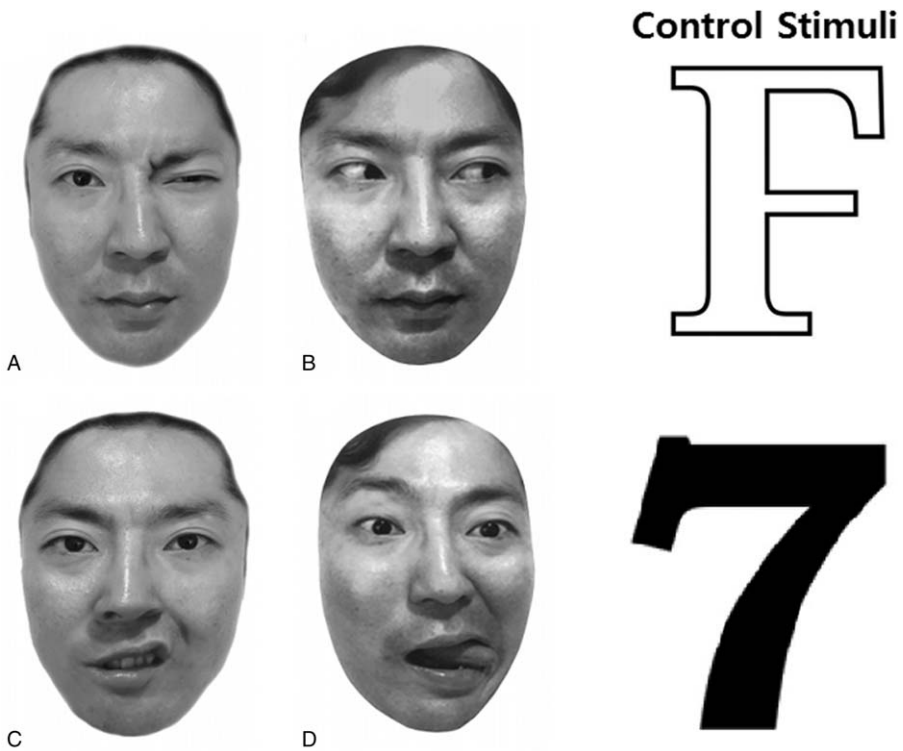

Figure 1. Stimuli used in mental rotation task. (A) Upper facial region pain expression. (B) Eyeball deviation. (C) Lower facial region pain expression. (D) Tongue deviation.

regions of the face, or differences between different types of facial expression. The nonfacial muscle stimuli were eyeball deviation (ED) (upper region) and tongue protrusion (lower region). The facial expression stimuli were presented only on the left or right side of the face, and the left- and right-sided images were mirror images of each other.

Two control stimuli, a letter and a number, were also used to assess whether any group difference resulted simply from a difference in the ability to perform mental rotation per se. Figure 1 shows the stimuli used in the task.

In the face mental rotation task, left- and right-sided stimuli for 4 types of facial expression were presented at 0°, 90°, 180°, and 270° of rotation, giving a total of 32 stimuli. Participants were asked to report whether the presented pictures were left- or right-sided in the face mental rotation task. In the control stimuli task, an upright stimulus was presented on the left side of the screen and the same, or a mirror-image, stimulus was presented at 90°, 180°, and 270° of rotation on the right side; in total, there were 12 stimuli. Participants were asked to report whether the stimuli presented on the right side were the same as, or mirror images of, the upright stimuli on the left side in the control stimuli task.

Participants completed 10 practice tasks for familiarization with the task prior to the experimental trials. There were 3 trials, each of which comprised 32 facial and 12 control stimuli; the stimuli were presented in a random order. A short break was provided between each trial.

Participants were seated in front of a laptop and placed their right index finger on the "m" key, and their left index finger on the "z" key. They were asked to judge whether the presented facial expression was left- or right-sided, pressing "m" for the right side and "z" for the left side. For the control stimuli, participants were asked to judge whether stimuli presented on the left, and rotated control stimuli on the right, were the same or mirror images of each other, pressing "m" to indicate that they were the same image, and "z" to indicate that they were mirror images. Participants were instructed to press the buttons as fast as they could.

The primary outcome measures were reaction time (RT) and response accuracy. RT was indexed by the mean of 3 repeated measurements. Only RTs in which the correct response was made were considered. RTs that were 2.5 standard deviations above the mean were discarded before the analysis.

The task was designed using E-Prime software (Psychology Software Tools, Sharpsburg, PA) and executed on a laptop computer. On average, it took about 8 min to complete the task.

2.3. Self-reported measures

As other variables can also influence task performance, pain severity was measured with the short-form McGill Pain Questionnaire (MPQ), and depression with the Beck Depression Inventory (BDI). The MPQ consists of 15 items, rated on Likert-type scales (0 = none, 1 = mild, 2 = moderate, 3 = severe) and measuring sensory (11 items) and affective (4 items) dimension of pain. In addition, 1 item measures present pain intensity (0 = none, 1 = mild, 2 = discomfort, 3 = distressing, 4 = horrible, 5 = excruciating).

The Interpersonal Reactivity Index (IRI) was used to assess the influence of changes in facial expression on empathetic ability.[22] The IRI is a 28-item self-reported questionnaire, composed of 4 subscales, which assesses cognitive and emotional aspects of empathy. The 4 subscales of the IRI are the Fantasy Scale (FS), perspective taking (PT), empathetic concern (EC), and personal distress (PD); the former 2 represent the cognitive dimension and the latter 2 represent the emotional dimension. The FS measures the tendency to imagine oneself as a character in, or in situations from, films, or books, while the PT scale measures the ability to take another's perspective. The EC scale measures the tendency to sympathize and identify with others and the PD scale measures the tendency to feel pain and discomfort on observing the suffering of others.

Table 1

Demographics and clinical characteristics in participants.

	Patients (N = 40)	Controls (N = 35)	P
Demographics			
Sex (M/F)	28/12	20/15	.36
Age, y	43.65 ± 9.84	41.43 ± 9.73	.33
Education, y	13.40 ± 2.26	16.62 ± 1.26	<.001*
Marital, %	55	77.1	.054
Occupation, %	12.5	85.7	<.00*
Clinical characteristics			
BDI	35.31 ± 12.85	7.49 ± 6.52	<.001*
IRI			
IRI-FS	13.36 ± 5.37	15.23 ± 4.62	.12
IRI-PT	14.79 ± 6.04	18.14 ± 3.14	.004*
IRI-EC	17.33 ± 5.48	18.57 ± 3.35	.24
IRI-PD	14.79 ± 6.17	12.23 ± 4.74	.050*
Diagnosis (CRPS I/II)	33/7		
Affected extremity (upper/lower)	14/26		
Duration of illness, mo	63.48 ± 43.82		
SF-MPQ			
Sensory	22.49 ± 7.21		
Affective	7.26 ± 3.01		
PPI	3.59 ± 0.99		

BDI = Beck Depression Inventory, CRPS = complex regional pain syndrome, EC = empathic concern, FS = Fantasy Scale, IRI = Interpersonal Reactivity Index, PD = personal distress, PPI = present pain intensity, PT = perspective thinking, SF-MPQ = short form of McGill Pain Questionnaire.
* $P < .05$.

2.4. Statistical analysis

Demographic data were compared using χ^2 or independent t tests. A linear mixed model was used for the mental rotation task, with RT and accuracy as the dependent variables, and group (patients vs controls), gender, age, type of facial expression, side, and rotation angle as the independent variables; BDI was included as a covariate. The same analysis was performed for the control task using type of control stimuli instead of type of facial expression. Post hoc comparisons were carried out using the Bonferroni correction. Linear regression analyses were used to assess the relationships among clinical variables and the group difference in RT. Statistical analyses were performed using SAS software (ver. 9.0; SAS Institute, Cary, NC) and significant interactions were evaluated by a simple main-effect test ($P < .05$).

3. Results

3.1. Demographic profile

The demographic and clinical characteristics of the participants are shown in Table 1. The mean age of the CRPS patients was 43.65 years and 70% of these patients were male. The lower extremities (65%) were more affected than the upper extremities (35%) in patients with CRPS. The gender and affected limb

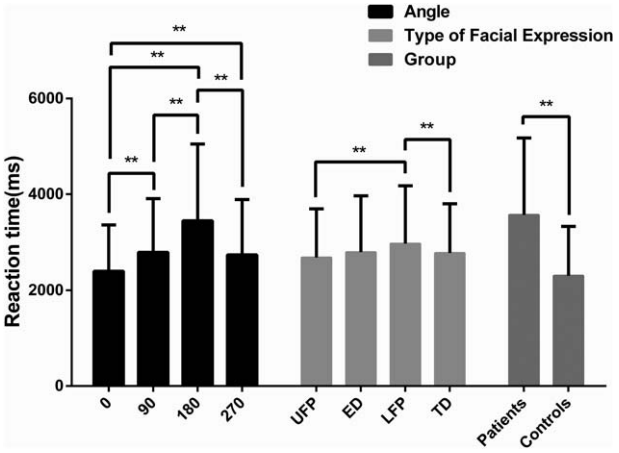

Figure 2. Reaction times according to rotation angle, type of facial expression, and group (patients vs controls). ED = eyeball deviation, LFP = lower facial region pain expression, TD = tongue deviation, UFP = upper facial region pain expression. ** Bonferroni adjusted $P < .05$.

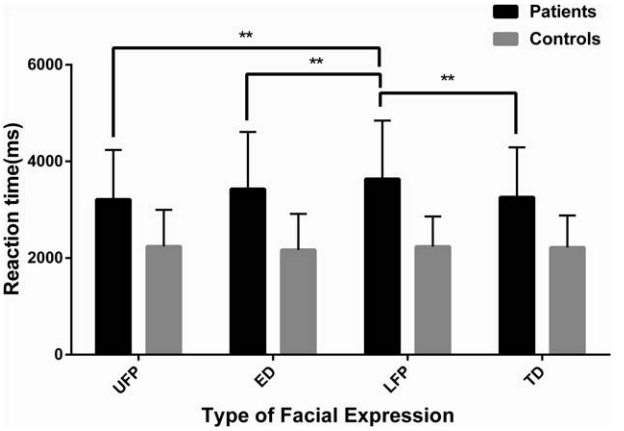

Figure 3. Reaction times according to type of facial expression in patients versus controls. ED = eyeball deviation, LFP = lower facial region pain expression, TD = tongue deviation, UFP = upper facial region pain expression. ** Bonferroni adjusted $P < .05$.

region ratios of our CRPS patients differed from those reported previously.[23]

In the patient group, occupational status ($P < .001$) and education level ($P < .001$) were both significantly lower than those of the control group, and depression severity, as assessed by the BDI ($P < .001$), was significantly higher than in the control group. Patients showed significantly impaired empathetic ability on the IRI-PT ($P = .004$) and IRI-PD ($P = .005$) subscales compared with controls; the IRI results were consistent with previously reported findings, except for IRI-EC ($P = .24$).[24]

3.2. Reaction time

Repeated data analysis, using a linear mixed model for RTs to facial expression stimuli, showed statistically significant main effects of age ($P = .001$), rotation angle ($P < .001$), type of facial expression ($P < .001$), and group ($P = .006$), but not gender ($P = .17$) or side ($P = .29$). Concerning rotation angle, RTs were significantly faster for 0° (2536.77 ms) than for the other 3 orientations (90°: 2923.10 ms, 180°: 3603.26 ms, 270°: 2848.41 ms), and slower for 180° than for the other 3 orientations (Fig. 2).

Table 2

Linear mixed model statistics for reaction times and post hoc analysis for significant factors with contrasts.

Effect			Post hoc			
Factor	F	P	Contrast	t		P*
Sex	1.92	.17				
Age	10.46	.001				
BDI	0.03	.87				
Group	7.69	.006				
Type of facial expression	9.86	<.001				
			UPF vs ED	−1.78		.45
			UPF vs TD	−0.08		1.00
			UPF vs LPF	−4.71		<.001
			ED vs TD	1.71		.53
			ED vs LPF	−2.94		.02
			TD vs LPF	−4.65		<.001
Angle	71.73	<.001				
			0 vs 90	−4.21		<.001
			0 vs 180	−13.98		<.001
			0 vs 270	−3.42		.004
			90 vs 180	−9.88		<.001
			90 vs 270	0.79		1.00
			180 vs 270	10.64		<.001
Group × Type of facial expression	3.99	.008		Control	Patient	Control	Patient
			UPF vs ED	−0.18	−2.38	1.00	.20
			UPF vs TD	−0.28	0.17	1.00	1.00
			UPF vs LPF	−1.4	−5.35	1.00	<.001
			ED vs TD	−0.1	2.58	1.00	.12
			ED vs LPF	−1.22	−3	1.00	.036
			TD vs LPF	−1.13	−5.58	1.00	<.001
Group × Angle	0.79	.50					
Group × Angle × Type of facial expression	1.53	.073					

BDI = Beck Depression Inventory, ED = eyeball deviation, LFP = lower facial region pain expression, TD = tongue deviation, UFP = upper facial region pain expression.
* Bonferroni adjusted *P*.

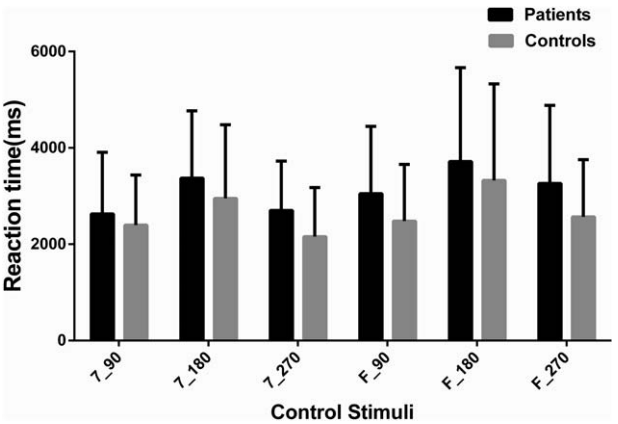

Figure 4. Reaction times for control stimuli in patients versus controls.

Concerning type of facial expression, RTs for lower facial region pain expressions (LFPs) (3212.19 ms) were significantly slower than those for the other 3 types of facial expression (upper facial region pain expression [UFP]: 2836.99 ms, ED: 2966.33 ms, tongue deviation [TD]: 2892.46 ms). The RTs of patients (3112.62 ms) were significantly slower than those of controls (2740.70 ms) (Fig. 2). There was a significant interaction only for group × type of facial expression ($P = .008$). In the post hoc analysis with Bonferroni correction, although RTs by type of facial expression were not significantly different within the control group (UFP: 2285.40 ms, LFP: 2372.15 ms, ED: 2253.08 ms, TD: 2316.20 ms), RTs for LFPs (3926.51 ms) were significantly slower than those for UFPs (3354.10 ms, Bonferroni adjusted $P < .001$), ED (3593.42 ms, Bonferroni adjusted $P = .039$), and TD (3399.58 ms, Bonferroni adjusted $P < .001$) within the patient group (Fig. 3; Table 2) (Supplemental Table 1, http://links.lww.com/MD/B895).

In the analysis of control stimuli, there was no significant group difference in RTs ($P = .077$); angle ($P < .001$), and type of stimuli ($P < .001$) were the factors for which there were significant group differences (Fig. 4) (Supplemental Table 2, http://links.lww.com/MD/B895).

3.3. Accuracy data

In the analysis of face expression stimuli, there were only 2 significant main effects, of side ($P = .009$) and rotation angle ($P < .001$), within the accuracy data, and there was no significant difference by group ($P = .09$). In a post hoc analysis of side, accuracy for right-sided stimuli (0.873) was significantly lower than that for left-sided stimuli (0.893). In a post hoc analysis of angle, accuracy at 180° (0.821) was significantly lower than that at 0° (0.910, $P < .001$), 90° (0.895, $P < .001$), and 270° (0.907, $P < .001$). No significant interactions were observed within the accuracy data.

3.4. Correlation analysis

Because RTs for LFPs were significantly longer than those for the 3 other types of facial expression, mean differences in RT for LFP versus other types of facial expression were calculated. In univariate regression analyses that included other variables, such as pain severity, pain duration, BDI and IRI subscale scores, only IRI-EC ($r = -0.422$, $P = .04$) and IRI-PD ($r = -0.443$, $P = .03$) correlated significantly with the difference in RT between the LFP and ED, and between LFP and TD, respectively (Table 3).

4. Discussion

We investigated performance on a mental rotation task, according to type of facial expression, in CRPS patients using various facial expression stimuli. Overall, the patient group showed a decrease in motor imagery performance compared with controls for facial expression stimuli, as evaluated by RT, especially for LFP stimuli (i.e., upper lip raising). It seems that this was not due to a defect in mental rotation ability per se in the patients, because they showed no difference in RT for the control stimuli compared with the control group.

However, evaluations of facial expressions in a motor imagery task may differ from evaluations of actual facial expressions. Among the various methods used to estimate facial expression evaluations, the Facial Action Coding System (FACS), an anatomically based index of visible facial muscle movements, is considered the gold standard.[25] In studies of facial pain expressions in chronic pain using FACS,[26,27] patients' facial pain expressions in response to an acute pain stimulus were not different from those of healthy controls. This is in contrast to another study in which, in chronic pain, the correlation between pain intensity and facial pain expressions was weak.[3] Patients with chronic pain do not elicit facial pain expressions habitually, but only during exacerbations of pain. Thus, when we assess facial expressions of chronic pain under natural conditions, neural representations associated with facial expressiveness would be more important than the virtual facial expressions on which FACS analysis is based. Given this, motor imagery tasks may be advantageous in that they investigate the underlying mechanisms of the various motor systems that control actual movements.

Pain is a multidimensional experience encompassing sensory and affective aspects. Several neuroimaging studies have reported that when cues related to a person's experience of pain are presented, the anterior cingulate cortex (ACC) and insula, but not

Table 3

Correlation coefficients of IRI subscales and reaction time differences.

	IRI-PT		IRI-FS		IRI-EC		IRI-PD	
Reaction time difference	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*
LFP–UFP	0.0412	.86	0.177	.44	−0.0980	.63	0.117	.62
LFP–ED	0.129	.54	0.204	.33	−0.223	.28	−0.443	.027*
LFP–TD	−0.151	.47	−0.0787	.71	−0.422	.035*	−0.0548	.80

EC = empathic concern, ED = eyeball deviation, FS = Fantasy Scale, IRI = Interpersonal Reactivity Index, LFP = lower facial region pain expression, *P* = statistical significance, PD = personal distress, PT = perspective thinking, *r* = correlation coefficient in univariate regression for the difference between reaction time for LFP and reaction times for the other type of stimuli and IRI subtype, TD = tongue deviation, UFP = upper facial region pain expression.

* $P < .05$.

the sensory cortex, are activated in the observer's brain.[28–30] Thus, the perception of pain in others has been suggested to be mediated by the affective processing of pain. When facial expressions of painful conditions were presented, similar findings were obtained,[31–33] and the ACC was found to be involved in assessing the facial pain intensity of others.[33] Taking these imaging studies together, perception of pain in others, based on their facial expressions, seems to be mediated by affective, and not sensory, mechanisms.[34] According to the experimental research of Kunz et al,[35] facial pain expressions can be decoded into affective and sensory aspects, and movements of the eye brows and upper lip were suggested to be associated with the affective dimension of pain. Thus, the longer RTs that we observed to the raising of the upper lip, which is one of the affective dimensions of facially expressed pain, may reflect altered facial expressiveness for affective aspects of pain that can be detected by others.[34] In such cases, observers may think that facial pain expressions are incongruent with reported pain intensity, which can lead to underestimation of the pain experienced by patients with CRPS.

The control of facial expressions has been suggested to be organized across the upper–lower axis based on the results of facial blend paradigms, where facial expressions in the lower facial region are involved in modulating social emotions.[36] Thus, changes in facial expressions of pain in the lower region of the face may be due to social motivation. This appears to be supported by a recent neuroimaging study showing that not only the motor cortex but also additional neural substrates associated with social cognition and reward processing were activated during facial pain expressions in chronic pain.[27]

According to the communication model, which is one of several psychosocial models of pain, pain behavior should be understood in a framework that includes not only pain expressers but also the perceivers of that pain.[37,38] In chronic pain conditions, pain behavior is known to be controlled by operant conditioning mechanisms,[9] and facial expression-related pain behavior has also been shown to be influenced by operant conditioning under experimental conditions.[39] Thus, it is important to consider the responses of the observer to changes in facial pain behavior in chronic pain. It is known that, within couples, reactions to spouses with chronic pain are dependent on the level of pain and the degree of marital satisfaction, but less is known about the effects of chronic pain on the observer.[40] Responses to others who are in pain can take 2 different forms: moving away from the subject to avoid distress, or approaching the subject to offer help or support. In many cases, CRPS patients show no apparent injury, so it is difficult to empathize with their pain. In addition, because the treatment response of these patients is poor, the duration of treatment is often long and the treatment cost burden is considerable.[41] Therefore, the severity of the suffering of observers (e.g., caregivers of CRPS patients) is high; this may act as motivation for negative responses, such as neglect or avoidance, instead of solicitous responses. This type of response in observers may negatively reinforce a patient's pain-related behavior and, as a result, the patient may suppress facial expressions of pain. Longer RTs to upper lip rising may reflect this suppression of facial pain expressions.

In a subanalysis, we analyzed correlations between RT differences and several other variables. RT differences were calculated by subtracting RTs for the 3 other types of facial expression from those for LFPs (Table 3). Only IRI-EC and IRI-PD, which correspond to the emotional component of IRI, correlated significantly with RT differences. However, it is difficult to interpret the meaning of a negative correlation between IRI-PD and RT differences, although the IRI-PD of patients was higher than of controls.

According to facial reflex theory, a decrease in the function of muscles that produce facial expressions is known to result in a decrease in empathy for others.[42] Thus, our results suggest that the change in facial expression resulted in a decrease in empathic ability, as assessed by IRI.

The correlation between longer RTs for LFPs and impaired empathic ability suggests that this impairment could lead to misinterpretation, as reflected in the observer's behavioral response, which may impede social interactions. From the patient's perspective, altered facial expressiveness is an adaptive change resulting from the motivation to promote social interaction. However, this is maladaptive in that the patients showed impaired empathic ability and may not receive appropriate pain management due to their pain being underestimated by observers.

In conclusion, because changes in facial pain behavior occur through complex interactions between the patient and observer, both interpersonal aspects (such as the effect on the observer of chronic pain, as well as the observer's response to the patient) and intrapersonal aspects (such as the personality of the pain sufferer and degree of empathetic ability in accordance with the experience of chronic pain) must be considered. Considering all of these factors, the extent and direction of changes in facial pain behavior may vary.

Our study had some limitations, including the small number of subjects. Although the control stimuli condition showed that there was no group difference in the ability to perform the mental rotation task, the reduction in task performance associated with facial expression may reflect a cognitive deficit in CRPS patients.[43] Although we used control face stimuli with ED and tongue protrusion to control for regional differences in the face, the response to stimuli based on other, nonpain indicative facial expressions should be evaluated before a strong claim can be made that processing of LFPs is impaired. Using a mental rotation task, we aimed to show the neural representations that were responsible for specific facial expressions of pain, but many other factors may also be involved. Control over these factors may be seen more clearly in subsequent neuroimaging studies.

5. Conclusions

In this study, we found that recognition of pain facial expressions in a mental rotation task differed between CRPS patients and healthy controls. In particular, LFPs had longer RTs versus the other types of facial expression. Overall consequences of these changes in chronic pain may be related to psychosocial aspects of pain, but the impact of the intra- and interpersonal characteristics of pain suffers should be investigated further.

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