Pain Management Nursing xxx (xxxx) xxx

Contents lists available at ScienceDirect

Pain Management Nursing

journal homepage: www.painmanagementnursing.org

Original Research

Brain Activation of Unpleasant Emotions Increases Catastrophizing in Patients with Chronic Pain

Kazuhiro Kimpara, Ph.D.[*,†,*,1], Shinichi Arizono, Ph.D.[*], Takako Tanaka, Ph.D.[‡], Taeko Kimpara, R.N.[†], Kazuhiro Terada, Ph.D.[†], Shohei Ohgi, Ph.D.[*]

[*] *School of Rehabilitation Sciences, Seirei Christopher University, Hamamatsu, Japan*
[†] *Terada Pain Clinic, Hamamatsu, Japan*
[‡] *Department of Physical Therapy, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan*

ARTICLE INFO

Article history:
Received 8 July 2022
Received in revised form 20 December 2022
Accepted 20 January 2023
Available online xxx

ABSTRACT

Background: Catastrophic thinking among patients with chronic pain impairs their quality of life and increases anxiety levels. Further, severe pain causes high emotional brain sensitivity and unpleasant feelings. However, the effects of emotional changes on catastrophic thinking in patients with chronic pain remain unclear.

Aims: We hypothesised that emotional brain activity during mild pain stimuli would affect catastrophic thinking in these patients. We aimed to examine the relationship between unpleasant emotional brain activation and catastrophic thinking due to pain stimuli in patients with chronic pain.

Design: This was a prospective observational study.

Participants: We included patients with chronic pain and healthy individuals.

Methods: The impact of emotional brain activity on catastrophic thinking was evaluated, specifically, the skin conductance response and oxygenated haemoglobin levels using near-infrared spectroscopy. After receiving three different pain stimuli, the participants were evaluated using the Numeric Rating Scale, Pain Catastrophising Scale, and McGill Pain Questionnaire.

Results: There were 28 patients in the chronic pain group and 33 patients in the healthy group. There was no between-group difference in oxygenated haemoglobin levels during pain stimulation. The chronic pain group showed a higher Pain Catastrophising Scale score and skin conductance response than the healthy group ($p < .05$). In the chronic pain group, oxygenated haemoglobin levels after pain stimuli were significantly associated with the Pain Catastrophising Scale score and skin conductance response ($p < .05$).

Conclusions: Brain activity of unpleasant emotions may influence catastrophic thinking in patients with chronic pain.

Chronic pain (CP) is a major public health problem that causes significant economic and social burdens (Langley et al., 2011; Dueñas et al., 2016). People with CP present exaggerated negative cognitive and emotional responses, including catastrophizing, anxiety, and depression (Larsson et al., 2017; Bäckryd et al., 2018). Specifically, catastrophizing, which is characterized by helplessness, magnification, and ruminative thoughts regarding pain, is a potent predictor of negative pain-related outcomes (Campbell et al., 2015). Catastrophizing in patients with CP is strongly affected by emotions as well as pain intensity measured using an 11-point numerical rating scale (Cheng et al., 2018; Hülsebusch et al., 2016). Therefore, CP and catastrophizing could interact with each other and increase the total symptom burden, leading to greater challenges in the clinical management of patients with CP.

Compared with healthy individuals, people with CP present with unpleasant emotions, including strong fear and anxiety (Bushnell et al., 2013). Further, there is increased blood flow in the emotional area upon pain stimulation in people with CP (Apkarian et al., 2005). Anxiety and fear are produced by the insula and amygdala in the limbic system; moreover, they are recognized by the orbitofrontal cortex (Ogino et al., 2007). Unpleasurable emotions amplify the pain experienced by individuals with CP

Abbreviations: CP, Chronic pain; NIRS, Near-infrared spectroscopy; SCR, skin conductance response; PCS, Pain Catastrophising Scale; MPQ, McGill Pain Questionnaire; Oxy-Hb, oxygenated haemoglobin; NRS, Numerical Rating Scale.

[1] Address correspondence to Kazuhiro Kimpara, Ph.D., School of Rehabilitation Sciences, Seirei Christopher University, 3453 Mikataha Kitaku, Hamamatsu, Shizuoka 433-8558, Japan.

E-mail address: kazuhiro-k@seirei.ac.jp (K. Kimpara).

https://doi.org/10.1016/j.pmn.2023.01.005
1524-9042/

(Villemure & Bushnell, 2009; Bushnell et al., 2013). Therefore, it is important to address the problem of unpleasant emotions in the treatment of people with CP.

We previously reported that people with moderate pain showed higher brain activities responsive to emotional stimuli than healthy people (Kimpara, Ohgi, & Terada, 2013). Individuals with CP have been reported to experience moderate pain as severe pain due to unpleasant feelings (Adler-Neal et al., 2019).

Pain catastrophizing is characterized by magnified pain amplification and is associated with anxiety and fear disorders in elderly people with CP (Dong et al., 2020). Emotional brain activity influences pain catastrophizing and anxiety. However, the influence of emotional changes in people with CP on catastrophic thinking remains unclear. We hypothesized that increased emotional brain activity after pain stimuli would lead to catastrophizing in people with CP. Pain site stimulation may increase emotional activity to induce catastrophizing in people with CP undergoing pain management nursing. Accordingly, we aimed to examine the relationship between brain activities related to unpleasant emotions and catastrophic thinking due to pain stimuli in patients with CP.

Methods

Ethics Statements

This study was approved by an independent ethics committee at Seirei Christopher University (approval number: 10069) and registered with the University Hospital Medical Information Network Center (UMIN000045273, http://www.umin.ac.jp/). All participants provided written informed consent before study participation.

Study Design and Participants

This was a prospective cohort study of patients with CP (CP group) and healthy participants (healthy group). The participants were recruited between July 2012 and July 2013. Patients with CP and healthy individuals were recruited from the Terada Pain Clinic (Hamamatsu, Japan) and Seirei Christopher University (Hamamatsu, Japan), respectively. The inclusion criteria for the CP group were as follows: (1) confirmed CP by the clinician defined as pain in more than one anatomical region (chronic musculoskeletal pain type) that persists or recurs for 3 months or longer and is related to significant emotional distress or functional disability (Treede et al., 2019); (2) having experienced pain for 3 months or longer; (3) aged 20 years or older; and (4) having a weekly average pain rating of 4 or greater on a 10-point Numerical Rating Scale. The inclusion criteria for the healthy group were as follows: (1) no history of pain or disease; (2) not currently taking analgesic medications; and (3) aged 20 years or older. We excluded healthy people who used medications that affect autonomic nervous system activity. Further, we excluded patients with CP who used medication that affected the autonomic nervous system activity (e.g., beta blocker, catecholaminergic agent, and Levodopa) or were unsuitable for physical pain stimulation due to severe disease (e.g., patients with Parkinson's disease, cerebral vascular disease, and ischemic heart disease).

Protocol

On the first visit, all participants received explanations regarding the study. On the second visit, the participants received three different electrical pain stimuli using a chronaxie meter (CX-3 OG; Giken, Tokyo Japan), which produced an electrical stimulus of 2.1 mA (stimulus duration, 0.3 ms at 1 Hz) on the palm side of the right forearm (Fig. 1). The pain stimuli were characterized by a tingling sensation with moderate intensity (the intensity at which a healthy adult usually feels a little pain). The participants were allowed to rest for 300 seconds and received three pain stimuli (1 s each) at 60-second intervals (Fig. 1). The chronaxie meter has confirmed validity and reliability for ethical use in pain research. Specifically, a previous Japanese study confirmed the safety of pain stimulation using a chronaxie meter with approximately the same stimulus and intensity (Andou, et al., 2000). Near-infrared spectroscopy (NIRS) was performed and the skin conductance response (SCR) was measured during the resting period and three pain stimuli to evaluate the transmission of pain stimuli to the limbic system. Pain stimuli transmission to the limbic system stimulates emotions and memory in the amygdala and hippocampus before transmission to the prefrontal cortex (Vachon-Presseau et al., 2016). The SCR was measured using a biologic polygraph recorder (MP100; Biopac Systems, Inc., Goleta, CA). After pain stimulation, the patients were asked to complete the Numerical Rating Scale, Pain Catastrophizing Scale (PCS), and McGill Pain Questionnaire. The experiment room was maintained at a comfortable temperature (26.1 ± 0.6 °C).

NIRS

Emotional brain activity in the prefrontal cortex was evaluated based on oxygenated hemoglobin (Oxy-Hb) using NIRS (optical topography device, ETG-7100; Hitachi, Ltd., Tokyo, Japan). NIRS is suitable for cerebral cortical measurements at a measurement depth of 2 to 3 cm. NIRS has a higher temporal resolution than functional magnetic resonance imaging (fMRI) (Hanaoka, 2007). NIRS measurement of the frontal lobe revealed that approximately 70% of the blood flow originated from the cerebral cortex (Funane et al., 2014). Another study that conducted simultaneous fMRI and NIRS measurements reported that NIRS signals (Oxy-Hb, Deoxy-Hb) showed good correlations (Sato et al., 2013). Accordingly, NIRS measurements have good reliability and validity.

The NIRS probe was placed on the head based on the international electroencephalography 10-20 method; further, Oxy-Hb and

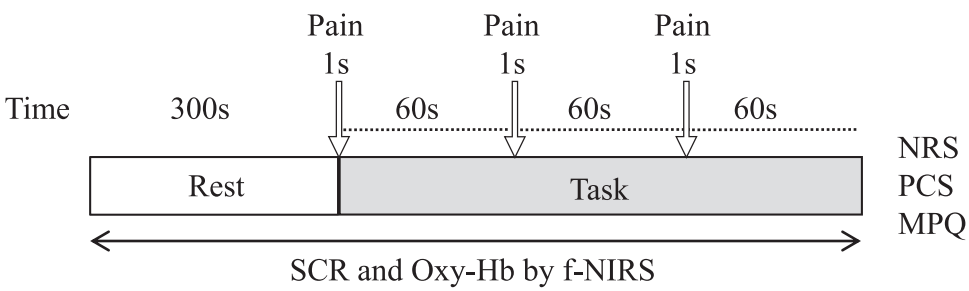

Figure 1. Three-time pain stimulus test protocol SCR = Skin conductance response; f-NIRS = functional near-infrared spectroscopy; NRS = Numeric Rating Scale; PCS = Pain Catastrophising Scale; MPQ = McGill Pain Questionnaire.

Please cite this article as: K. Kimpara, S. Arizono, T. Tanaka et al., Brain Activation of Unpleasant Emotions Increases Catastrophizing in Patients with Chronic Pain, Pain Management Nursing, https://doi.org/10.1016/j.pmn.2023.01.005

deoxyhemoglobin levels were measured at all 47 channels (sampling frequency, 10 Hz). We used the number 5 channel, the Brodmann Area 10, which recognizes unpleasant emotions. We used NIRS to measure activity in the orbitofrontal cortex, which is responsible for emotional perception in Brodmann Area 10. We calculated the difference in Oxy-Hb representative data averaged for 10 seconds before and after pain stimulation.

SCR

SCR measures mental sweating of the palms and feet bottom. The central mechanism of mental sweating mainly involves the limbic system and hypothalamus (Asai, 2013). Electroencephalogram studies have reported palmar sweating after stimulation of the amygdala-hippocampus-limbic system (Homma et al., 1998). The SCR does not reflect the actual sweating amount; instead, it evaluates perspiration activity as the electrical potential. Accordingly, SCR measurements have good reliability and validity. We calculated the difference in SCR representative data averaged for 10 seconds before and after pain stimulation.

Patient-Reported Outcomes

The patients completed the Numerical Rating Scale, PCS, and McGill Pain Questionnaire after the pain stimulation.

Numerical Rating Scale

Pain intensity was assessed using a 10-point Numerical Rating Scale [0 ('no pain'), 10 ('worst imaginable pain')]. The Numerical Rating Scale is well correlated with the visual analog scale (Faries et al., 1991), which indicates the reliability of Numerical Rating Scale measurements.

PCS

The PCS measures catastrophic thinking, which is an emotional and psychological state in people with CP. We assessed pain catastrophizing using the Japanese version of the PCS (PCS-J) (Matsuoka and Sakano, 2007). It comprises 13 items that are scored to provide an overall composite catastrophic measure; further, it has three subscales representing rumination, magnification, and helplessness. Each item is rated on a 5-point Likert scale ranging from 0 (not at all) to 4 (all the time). The validity and reliability of the PCS-J have been demonstrated (Matsuoka and Sakano, 2007).

McGill Pain Questionnaire

The McGill Pain Questionnaire is a self-report questionnaire that assesses the quality and intensity of subjective pain. It provides the total score of four categories using 78 descriptive words for pain (sensory, emotional, evaluative, and miscellaneous factors of pain). Further, it has been shown to be useful and reliable for patients with high psychogenic factors (Ogasawara & Watanabe, 1991).

Statistical Analysis

All data are presented as mean ± standard deviation (SD). Between-group differences in outcome measures were assessed using unpaired *t* tests. Further, the correlations of Oxy-Hb levels during pain stimulation with other measurements were assessed using Pearson's correlation analysis. Statistical analyses were performed using SPSS 24.0 for Windows (IBM Corp., Armonk, NY). Statistical significance was set at $p < .05$.

Table 1
Characteristics of the Participants

	CP group	Healthy group
n	28	33
Age (y)	43.2 ± 13.9[a]	22.1 ± 2.5
Male (%)	18 (62.0 %)	32 (97.0%)
Height (cm)	164.1 ± 8.0	170.2 ± 5.0
BMI (kg/m^2)	23.1 ± 1.9	22.0 ± 2.7
Period of illness (months)	6.1 ± 2.2	n.a
Site of pain	Neck: 8 Shoulders: 9 Waist: 13 Hips: 1 Knees: 2 Ankles: 1 Other: 1	n.a
Medication (n)	NSAIDs: 10 Antidepressant: 13 Anxiolytic: 4 Opioid analgesics: 12	n.a

Data are presented as mean ± standard deviation; number (male %).
CP = chronic pain; BMI = body mass index; NSAIDs = nonsteroidal anti-inflammatory drugs.
[a] $p < .01$.

Table 2
Correlation analysis between Oxy-Hb and measures.

	CP group		Healthy group	
	r	*p*	r	*p*
SCR	- 0.48	.01	- 0.19	.34
NRS	0.33	.10	0.34	.07
MPQ	0.41	.03	0.39	.04
PCS	0.52	.01	0.22	.26

SCR = skin conductance response; NRS = Numerical Rating Scale; MPQ = McGill Pain Questionnaire; PCS = Pain Catastrophizing Scale.

Results

Initially, there were 29 and 33 participants in the CP and healthy groups, respectively. We excluded data from one patient with CP due to missing values. Finally, we included 28 patients with CP and 33 healthy individuals (Fig. 2). Table 1 presents the demographics of the included participants. All participants in the CP group had diagnoses of chronic musculoskeletal pain and had multiple musculoskeletal pain sites.

Oxy-Hb levels were negatively correlated with the PCS score and SCR in the CP group ($p < .01$) but not in the healthy group (Figs. 3 and 4). Oxy-Hb levels were significantly associated with McGill Pain Questionnaire scores in both groups (Table 2).

The CP group showed a significantly higher SCR than the healthy group ($p < .05$) (Table 3). There were no between-group differences in the Numerical Rating Scale and McGill Pain Questionnaire scores (Table 4). The CP group showed significantly higher PCS scores than the healthy group ($p < .05$). There was no significant correlation between the PCS and age in both groups. Further, there were no between-group sex differences.

Table 3
Results of Oxy-Hb and SCR

	CP group	Healthy group	*p*
Oxy-Hb (mMmm)	0.05 ± 0.10	0.06 ± 0.14	.67
SCR (μS)	0.20 ± 0.19	0.08 ± 0.36	.01

Oxy-Hb = oxyhemoglobin; SCR = skin conductance response.

Please cite this article as: K. Kimpara, S. Arizono, T. Tanaka et al., Brain Activation of Unpleasant Emotions Increases Catastrophizing in Patients with Chronic Pain, Pain Management Nursing, https://doi.org/10.1016/j.pmn.2023.01.005

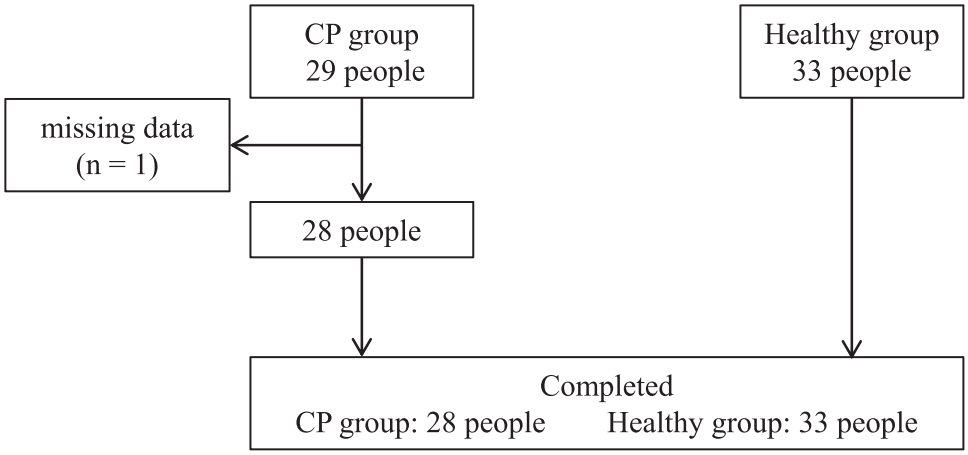

Figure 2. Participant flow diagram. CP = Chronic Pain.

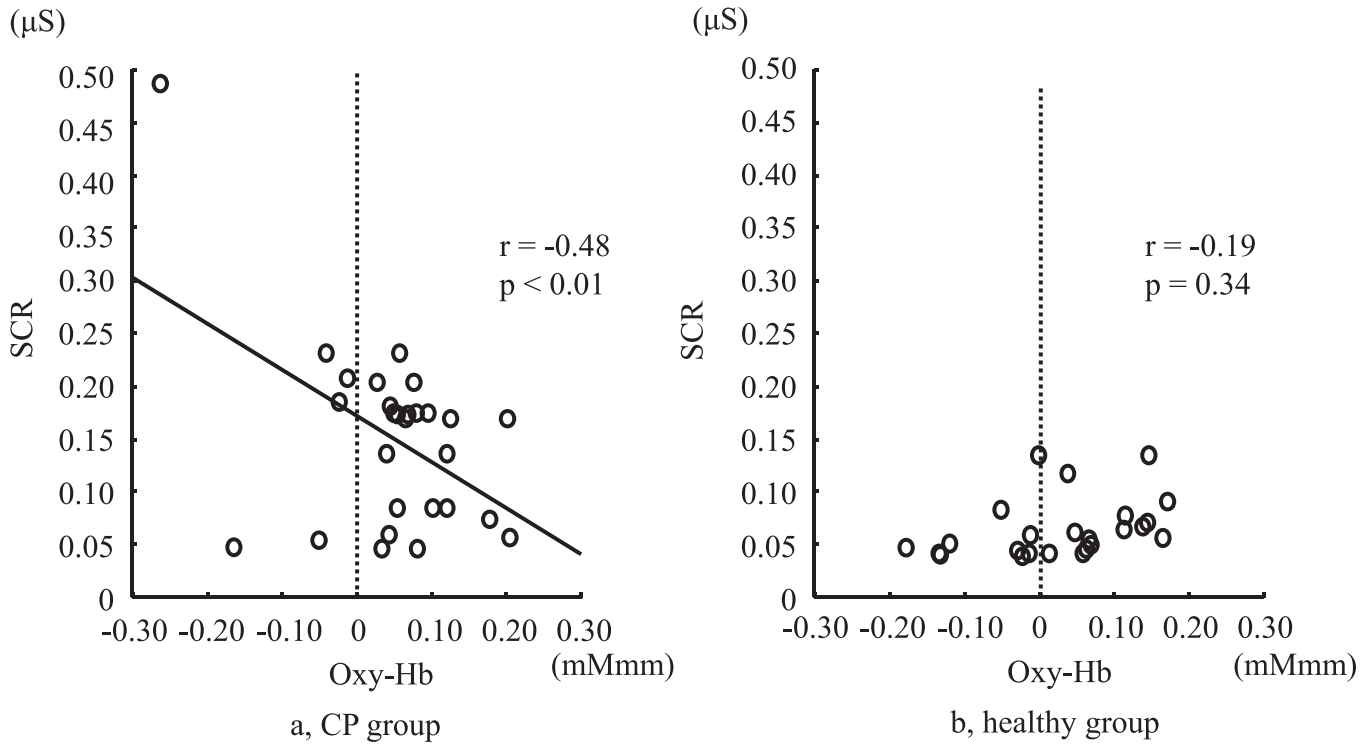

Figure 3. Correlation between SCR and Oxy-Hb at pain stimuli in the chronic pain group and healthy group. Oxy-Hb = Oxygenated Hemoglobin; SCR = Skin Conductance Response.

Table 4
Results of Patient-Reported Outcomes

	CP group	Healthy group	*p*
NRS	4.4 ± 1.8	4.9 ± 1.4	.33
MPQ	18.8 ± 14.3	16.3 ± 8.6	.40
PCS	25.2 ± 10.3	18.5 ± 10.3	.01

NRS = Numerical Rating Scale; MPQ = McGill Pain Questionnaire; PCS = Pain Catastrophizing Scale.

Discussion

To our knowledge, this is the first study to evaluate the association between the PCS score and emotional brain activity due to pain stimulation in patients with CP. Our findings showed that the brain activity of unpleasant emotions during pain stimulation correlated with catastrophizing in patients with CP, which confirmed our hypothesis. However, there was no between-group difference in the NIRS findings. In the CP group, the NIRS findings were correlated with the SCR and PCS score; further, the neurophysiologic responses were correlated with limbic system activity (SCR) and orbitofrontal cortex activity (NIRS). Long-term pain may have sensitized the central nervous system in patients. Furthermore, in the CP group, the PCS score was correlated with the NIRS findings but not with the SCR. This further indicates that patients with CP may have developed a brain network related to catastrophic thinking due to long-term pain.

In the CP group, brain activation of unpleasant emotions at moderate pain intensity correlated with severe catastrophic thinking, as measured by the PCS. Dong et al. (2020) reported that

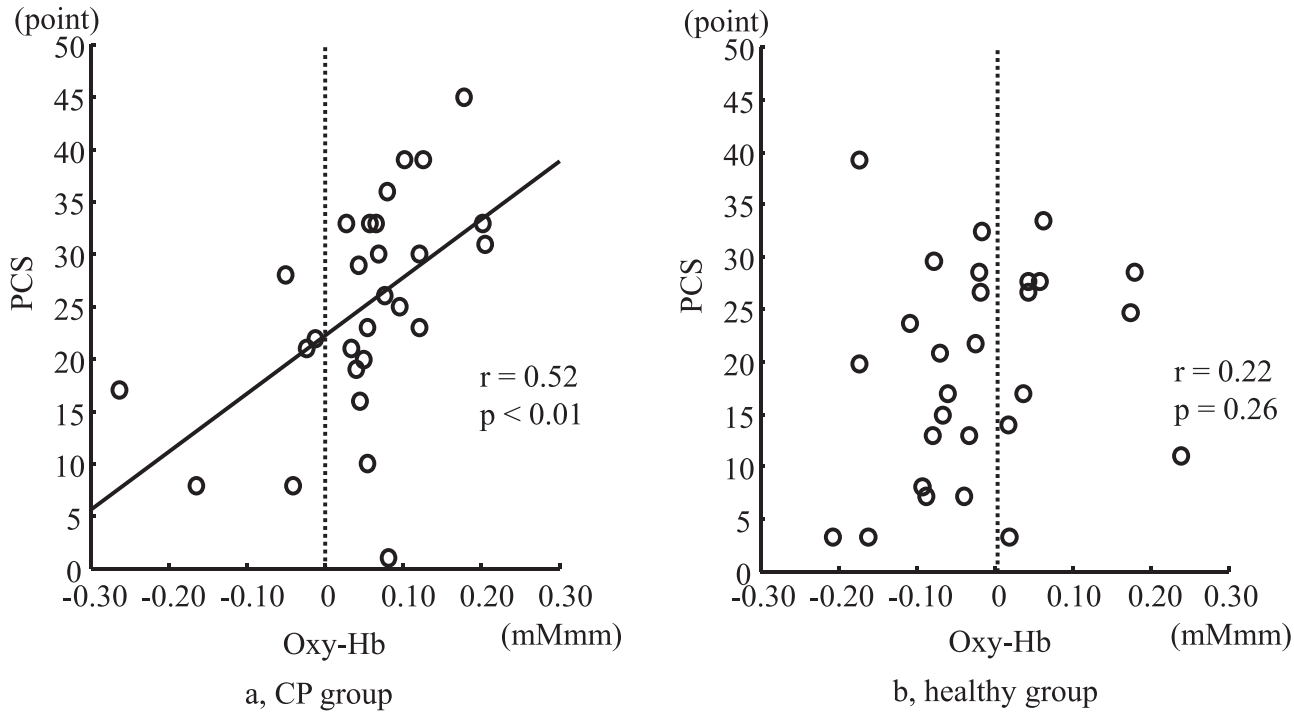

Figure 4. Correlation between PCS and Oxy-Hb in the CP group and healthy group. PCS = Pain Catastrophising Scale; Oxy-Hb = Oxygenated Hemoglobin; CP = Chronic Pain.

the PCS score was significantly related to anxiety and depression in 6,611 older adults. They reported that anxiety and depression were emotional distresses that should be addressed in the pain management of older adults with CP. Anxiety and depression are considered unpleasant emotions, which were reported by Cheng et al. (2018) to affect catastrophizing and impair self-efficacy in 664 older adults with CP. They measured unpleasant emotions using patient-reported outcomes; contrastingly, we measured brain activation of unpleasant emotions with pain stimuli using NIRS, which yielded new findings in the research field. We found that Oxy-Hb levels in the emotional region were negatively correlated with the SCR in patients with CP. The SCR represents the variance in emotional ratings evaluated from the limbic system (Zakrzewski et al., 2018; Herrero et al., 2020; Gatti et al., 2018). The negative response related to Oxy-Hb levels was lower in brain activities with stimuli than in those without stimuli; moreover, it influenced the increased limbic cortical activity (high SCR). We found that moderate pain stimulation in patients with CP led to emotional activation in the cerebral cortex and limbic system. Decreased Oxy-Hb levels lead to low blood flow in the pleasant and unpleasant emotional regions. People with CP may experience a shift toward unpleasant emotions rather than pleasant emotions. Furthermore, the SCR is negatively correlated with the Oxy-Hb response in the emotional region. These findings show that patients with CP recognize low unpleasant emotions as highly sensitive to pain. Patients with CP have an elevated SCR and decreased blood flow in the emotional area due to central sensitization resulting from chronic pain exposure (Wager et al., 2004). Seifert et al. (2013) reported that the SCR with heat pain stimulation was negatively correlated with activity in the contralateral medial prefrontal cortex as measured through fMRI in healthy individuals. Since their painful stimulus was higher than ours (Numerical Rating Scale score, 6.1 versus 4.9), a correlation was observed even in healthy participants. A previous study showed that patients with CP experienced weak pain stimuli strongly; accordingly, patients experienced pain stimulation at a Numerical Rating Scale score of 4.4 as strong pain in the prefrontal cortex (Apkarian et al., 2005).

The CP group showed a higher SCR than the healthy group. Woelk et al. (2020) reported that the SCR to cold pain stimuli was higher than that at rest in 120 participants with CP. Individuals with low back pain have poor sleep quality and an increased SCR, with these parameters being correlated (Woelk et al., 2020). Sleep quality in individuals with CP may have influenced our results. The SCR represents limbic cortex activity, including emotion in the amygdala and insula, which has a high sensitivity to pain (McCarberg and Peppin, 2019). Central sensitization is characterized by the hyperexcitability of central nervous system neurons to noxious stimuli and involves multiple somatosensory processing changes (Woolf, 2011), which amplifies the responsiveness of the primary afferent nociceptors (Hucho and Levine, 2007). People with CP experience severe pain due to high central sensitization; moreover, the SCR of the amygdala and insula is increased during unpleasant emotion processing (Coghill et al., 2003).

The response of Oxy-Hb levels in the emotional region to moderate pain was significantly related to the McGill Pain Questionnaire score in both groups. Li et al. (2021) reported that depression and the McGill Pain Questionnaire score in patients with low back pain are closely related to activity in the dorsolateral prefrontal cortex based on fMRI findings. Most patients with CP develop depression; accordingly, there is a need to elucidate the influence of depression on prefrontal cortex activity. We previously reported that pain catastrophizing and anxiety were significantly improved after watching relaxation videos and dual-task training in people with CP (Kimpara et al., 2019). Accordingly, pain management nursing care targeting pleasant emotions may improve catastrophic thinking in people with CP.

Limitations

This study has several limitations. First, this was a single-center study on patients of a single race with preserved functionality,

Please cite this article as: K. Kimpara, S. Arizono, T. Tanaka et al., Brain Activation of Unpleasant Emotions Increases Catastrophizing in Patients with Chronic Pain, Pain Management Nursing, https://doi.org/10.1016/j.pmn.2023.01.005

which limits the generalizability of our findings. Second, we did not match the age between the CP and healthy groups. The healthy group had relatively young participants since they lacked a history of pain or disease. Third, we did not evaluate brain activation using fMRI. Fourth, the sample size was not sufficient to evaluate between-sex differences. Differences in age and sex in both groups may influence pain catastrophizing. Finally, we did not evaluate the effect of pain rehabilitation and pharmacologic therapy in patients with CP.

Conclusions

In conclusion, we clarify that unpleasant emotional brain activity due to pain stimuli is associated with catastrophic thinking in patients with CP. The brain activity of unpleasant emotions is a crucial factor in the brain plasticity changes responsible for catastrophic thinking. Our findings indicate that treatment strategies for decreasing unpleasant emotions are important for people with CP.

References

Adler-Neal, A. L., Emerson, N. M., Farris, S. R., Jung, Y., Coghill, R. C., & Zeidan, F. (2019). Brain moderators supporting the relationship between depressive mood and pain. *Pain, 160*(9), 2028–2035.

Andou, M., & Kanou, H. (2000). The development of the method for examining pain detection threshold by the chronaximeter (Japanese). *Physical Therapy Research., 27*, 133–138.

Apkarian, A. V., Sosa, Y., Sonty, S., Levy, R. M., Harden, R. N., Parrish, T. B., & Gitelman, D. R. (2005). Chronic back pain is associated with decreased prefrontal and thalamic gray matter density. *Journal of Neuroscience, 17*, 10410–10415.

Asai, K. (2013). *Autonomic nerve function test* (pp. 224–229). Japan Society of Neurovegetative Research.

Bäckryd, E., Persson, E. B., Larsson, A. I., Fischer, M. R., & Gerdle, B. (2018). Chronic pain patients can be classified into four groups: Clustering-based discriminant analysis of psychometric data from 4665 patients referred to a multidisciplinary pain centre (a SQRP study). *PloS One, 13*(12), Article e0192623.

Bushnell, M. C., Ceko, M., & Low, L. A. (2013). Cognitive and emotional control of pain and its disruption in chronic pain. *Nature Reviews. Neuroscience, 14*(7), 502–511.

Campbell, C. M., Buenaver, L. F., Finan, P., Bounds, S. C., Redding, M., McCauley, L., Robinson, M., Edwards, R. R., & Smith, M. T. (2015). Sleep, pain catastrophizing, and central sensitization in knee osteoarthritis patients with and without insomnia. *Arthritis Care & Research, 67*(10), 1387–1396. https://doi.org/10.1002/acr.22609.

Cheng, S. T., Leung, C., Chan, K. L., Chen, P. P., Chow, Y. F., Chung, J., Law, A., Lee, J., Leung, E., & Tam, C. (2018). The relationship of self-efficacy to catastrophizing and depressive symptoms in community-dwelling older adults with chronic pain: A moderated mediation model. *PloS One, 13*(9), Article e0203964.

Coghill, R. C., McHaffie, J. G., & Yen, Y. F. (2003). Neural correlates of interindividual differences in the subjective experience of pain. *Proceedings of the National Academy of Sciences of the United States of America, 100*(14), 8538–8542.

Dong, H. J., Gerdle, B., Bernfort, L., Levin, L. Å., & Dragioti, E. (2020). Pain Catastrophizing in older adults with chronic pain: The mediator effect of mood using a path analysis approach. *Journal of Clinical Medicine, 9*(7), 2073.

Dueñas, M., Ojeda, B., Salazar, A., Mico, J. A., & Failde, I. (2016). A review of chronic pain impact on patients, their social environment and the health care system. *Journal of Pain Research, 9*, 457–467.

Faries, J. E., Mills, D. S., Goldsmith, K. W., Phillips, K. D., & Orr, J. (1991). Systematic pain records and their impact on pain control. *A pilot study. Cancer Nursing, 14*(6), 306–313.

Funane, T., Atsumori, H., Katura, T., Obata, A. N., Sato, H., Tanikawa, Y., Okada, E., & Kiguchi, M. (2014). Quantitative evaluation of deep and shallow tissue layers' contribution to fNIRS signal using multi-distance optodes and independent component analysis. *NeuroImage, 85*, 150–165.

Gatti, E., Calzolari, E., Maggioni, E., & Obrist, M. (2018). Emotional ratings and skin conductance response to visual, auditory and haptic stimuli. *Scientific Data, 5*, Article 180120.

Hanaoka, N., Aoyama, Y., Kameyama, M., Fukuda, M., & Mikuni, M. (2007). Deactivation and activation of left frontal lobe during and after low-frequency repetitive transcranial magnetic stimulation over right prefrontal cortex: A near-infrared spectroscopy study. *Neuroscience letters, 414*(2), 99–104.

Herrero, H., Tarrada, A., Haffen, E., Mignot, T., Sense, C., Schwan, R., El-Hage, W., Maillard, L., & Hingray, C. (2020). Skin conductance response and emotional response in women with psychogenic non-epileptic seizures. *Seizure, 81*, 123–131.

Homma, S., Nakajima, Y., Toma, S., Ito, T., & Shibata, T. (1998). Intracerebral source localization of mental process-related potentials elicited prior to mental sweating response in humans. *Neuroscience Letters, 247*(1), 25–28.

Hucho, T., & Levine, J. D. (2007). Signaling pathways in sensitization: Toward a nociceptor cell biology. *Neuron, 55*(3), 365–376.

Hülsebusch, J., Hasenbring, M. I., & Rusu, A. C. (2016). Understanding pain and depression in back pain: the role of catastrophizing, help-/hopelessness, and thought suppression as potential mediators. *International Journal of Behavioral Medicine, 23*(3), 251–259.

Kimpara, K, Ohgi, S., & Terada, K. (2013). Relationship between subjective evaluation of pain and neurophysiological examination in people with chronic pain, (Japanese). *Journal of the Japanese Society for the Study of Chronic Pain, 32*, 183–188.

Kimpara, K, Sakuma, S., Yang, H., Adachi, K., Tanaka, M., Tawara, Y., Arizono, S., & Terada, K. (2019). Effects of dual task in chronic pain patients (Japanese). *The Journal of the Japanese Society for the Study of Chronic Pain, 38*, 158–165.

Langley, P. C., Ruiz-Iban, M. A., Molina, J. T., De Andres, J., & Castellón, J. R. (2011). The prevalence, correlates and treatment of pain in Spain. *Journal of Medical Economics, 14*(3), 367–380.

Larsson, B., Gerdle, B., Bernfort, L., Levin, L.-Å., & Dragioti, E. (2017). Distinctive subgroups derived by cluster analysis based on pain and psychological symptoms in Swedish older adults with chronic pain—A population study (PainS65+). *BMC Geriatrics, 17*(1), 200.

Li, H., Song, Q., Zhang, R., Zhou, Y., & Kong, Y. (2021). Enhanced temporal coupling between thalamus and dorsolateral prefrontal cortex mediates chronic low back pain and depression. *Neural Plasticity, 2021*, Article 7498714. https://doi.org/10.1155/2021/7498714.

Matsuoka, H &, & Sakano, Y. (2007). Assessment of cognitive aspect of pain: Development, reliability, and validation of Japanese version of pain catastrophizing scale (Japanese). *Japanese Journal of Psychosomatic Medicine, 47*, 95–102.

McCarberg, B., & Peppin, J. (2019). Pain pathways and nervous system plasticity: learning and memory in pain. *Pain Medicine, 20*(12), 2421–2437.

Ogasawara, T., & Watanabe, N. (1991). Examination of the reliability and validity of the McGILL pain questionnaire. *Journal of Japan Academy of Nursing Science, 11*, 96–97.

Ogino, Y., Nemoto, H., Inui, K., Saito, S., Kakigi, R., & Goto, F. (2007). Inner experience of pain: imagination of pain while viewing images showing painful events forms subjective pain representation in human brain. *Cerebral Cortex, 17*(5), 1139–1146.

Sato, H., Yahata, N., Funane, T., Takizawa, R., Katura, T., Atsumori, H., Nishimura, Y., Kinoshita, A., Kiguchi, M., Koizumi, H., Fukuda, M., & Kasai, K. (2013). A NIRS-fMRI investigation of prefrontal cortex activity during a working memory task. *NeuroImage, 83*, 158–173.

Seifert, F., Schuberth, N., De Col, R., Peltz, E., Nickel, F. T., & Maihöfner, C. (2013). Brain activity during sympathetic response in anticipation and experience of pain. *Human Brain Mapping, 34*(8), 1768–1782.

Treede, R. D., Rief, W., Barke, A., Aziz, Q., Bennett, M. I., Benoliel, R., Cohen, M., Evers, S., Finnerup, N. B., First, M. B., Giamberardino, M. A., Kaasa, S., Korwisi, B., Kosek, E., Lavand'homme, P., Nicholas, M., Perrot, S., Scholz, J., Schug, S., Smith, B. H., Svensson, P., Vlaeyen, J. W. S., & Wang, S. J. (2019). Chronic pain as a symptom or a disease: The IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). *Pain, 160*(1), 19–27.

Vachon-Presseau, E., Centeno, M. V., Ren, W., Berger, S. E., Tétreault, P., Ghantous, M., Baria, A., Farmer, M., Baliki, M. N., Schnitzer, T. J., & Apkarian, A. V. (2016). The emotional brain as a predictor and amplifier of chronic pain. Journal of Dental Research, *95*(6), 605–612.

Villemure, C., & Bushnell, M. C. (2009). Mood influences supraspinal pain processing separately from attention. *Journal of Neuroscience, 29*(3), 705–715. https://doi.org/10.1523/JNEUROSCI.3822-08.2009.

Wager, T. D., Rilling, J. K., Smith, E. E., Sokolik, A., Casey, K. L., Davidson, R. J., Kosslyn, S. M., Rose, R. M., & Cohen, J. D. (2004). Placebo-induced changes in FMRI in the anticipation and experience of pain. *Science, 303*(5661), 1162–1167.

Woelk, J., Goerlitz, D., & Wachholtz, A. (2020). I'm tired and it hurts! Sleep quality and acute pain response in a chronic pain population. *Sleep Medicine, 67*, 28–32.

Woolf, C. J. (2011). Central sensitization: Implications for the diagnosis and treatment of pain. *Pain, 152*(3), S2–S15.

Zakrzewski, J. J., Datta, S., Scherling, C., Nizar, K., Vigil, O., Rosen, H., & Mathews, C. A. (2018). Deficits in physiological and self-conscious emotional response to errors in hoarding disorder. *Psychiatry Research, 268*, 157–164.

Please cite this article as: K. Kimpara, S. Arizono, T. Tanaka et al., Brain Activation of Unpleasant Emotions Increases Catastrophizing in Patients with Chronic Pain, Pain Management Nursing, https://doi.org/10.1016/j.pmn.2023.01.005