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Visual Effect on Mechanical Pain Threshold According to Anatomical Regions

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Purpose: Pain perception is affected by a wide range of contributing factors, including biological, psychological, and social factors. Although the provision of visual information could have a modulatory effect on pain perception, it is unclear whether such a visual effect might vary depending on the anatomical site and stimulation type. This study aimed to analyze the modulatory effect of visual information on the perception of sharp and dull pain in the face and hand and to assess the influence of individual fear levels on modulatory visual information.

Methods: A total of 68 healthy male and female volunteers were recruited for this study. Pressure and pricking pain with and without visual information were induced on the masseter and thenar muscles, and alterations in pain threshold were evaluated. The survey was conducted using the Geop-Pain Questionnaire (GPQ).

Results: The pricking pain threshold of the hand was significantly elevated when viewing the stimulated hand. This result indicated that the provision of visual information could decrease sensitivity to sharp pain in the hand. However, when correlating the GPQ score with the alteration in thresholds induced by visual information, no significant correlation was observed between the GPQ score and the threshold difference induced by visual information. This finding showed that the visual effect was not significantly affected by the fear level.

Conclusions: This study showed that the effect of visual information on the pain threshold could vary according to the anatomical site and stimulation type. A better understanding of such a modulatory effect on pain perception might be useful for clinicians during painful therapeutic procedures.

Keywords: Anticipation; Fear; Nociception; Pain perception; Visual Perception

INTRODUCTION

According to the International Association for the Study of Pain, pain is defined as “an unpleasant sensory and emotional experience associated with or resembling that associated with actual or potential tissue damage.” Although nociceptive signals could be initially evoked by actual damage and stimuli to the body and subsequently conveyed to the central nervous system, pain perception has a subjective aspect because pain can be diversely interpreted depending on individual life experiences and conditions [1]. Therefore, pain perception can be attributed to various modulatory mechanisms.

Pain perception is determined by a wide range of contributing factors, including biological, psychological, and social factors [2]. As pain is primarily regarded as a conscious experience, psycho-cognitive factors, including focusing, arousal, and expectation, would also have a modulatory effect on pain perception [3]. The simultaneous application of multisensory inputs modulates perceived pain intensity through complex interactions between the sensory and cognitive networks during pain perception processing. It has been reported that nociceptive stimuli may be perceived under interaction with other sensory inputs, including tactile, olfactory, acoustic, and visual stimuli [4-6]. Various studies have reported that the attention level modulated by visual stimuli or information could also alter the perceived pain threshold and intensity [7-10].

The visual effects on pain perception have been studied using various methodological protocols, including viewing the stimulated site of their own body with painful events, viewing the non-stimulated site (e.g., contralateral hand) of their own body without painful events, and viewing the neutral object or scene event during painful stimulation [6,7,9,11]. Among various experimental protocols, viewing the stimulated body site with a painful event could be considered the most naturalistic condition of pain perception, as acute pain is generally perceived with visual information regarding pain-eliciting processes or objects as well as pain-sensing sites [7]. Previous studies reported that visual information on painful events might increase pain intensity, possibly through enhanced pain anxiety and fear [8,12]. Similarly, viewing a red-colored virtual hand perceived as a threat to the real hand decreased the pain threshold [13]. The hyperalgesic effect of visual information could be attributed to modulating the expectation of forthcoming pain [8]. Additionally, neuroimaging findings revealed that pain-intensity-related brain activation partially overlapped with expectation-related activation in regions, including the anterior insula and anterior cingulate cortex [14]. However, another study reported that the expectation of pain severity could make alterations to pain perception by rendering moderate pain stimuli more painfully perceived than when weak pain is expected [15]. Therefore, it was suggested that the modulatory effect of visual information could vary depending on the expected severity of pain, which might be subsequently influenced by the stimulating tool and stimulated body site as potential cues to anticipate the severity of painful damage.

The face is the unique region of the body most closely linked with an individual's emotions [16]. Conversely, an individual's psychological condition can also be affected by facial sensations. A previous study reported that facial pain is associated with enhanced pain-related fear compared with pain in the extremities [17]. In a general population with a depressive and/or anxiety disorder who were followed up for 2 years, Gerrits et al. [18] found that the most frequent pain location was the head (76.6%). Pain in the trigeminal system causes much higher psychological and neurophysiological distress than pain in other body regions [19]. Also, several studies have reported that both somatosensory amplification and trait anxiety are highly associated with facial pain [20,21]. Therefore, facial pain can be considered a more threatening condition than limb pain [17]. However, it remains to be determined whether there are any differences in the hyperalgesic effect of visual information between facial and extremity pain.

Therefore, this study aimed to determine the comparative effect of visual information on the perception of sharp and dull pain experimentally induced on the face and hand and to assess the influence of individual fear levels on pain perception using visual information.

MATERIALS AND METHODS

1. Participants

A total of 68 healthy individuals (34 males, mean age=27.7±4.29 years, range 23-38 years; 34 females, mean age=24.3±2.26 years, range 20-30 years) with normal or corrected-to-normal vision were enrolled from among students and staff of Kyungpook National University and Dental Hospital. Individuals with a history of chronic pain, sleep disorders, neurologic pain disorders, local damage or illness, and medications influencing pain perception were excluded from this study. Written informed consent was obtained from all participants after a full explanation of the objectives and procedures of the study. This study was approved by the Institutional Review Board of the Kyungpook National University Dental Hospital (KNUDH-2021-02-01-00).

2. Determination of Pain Threshold

The pressure pain threshold (PPT) and pricking pain threshold (PkPT) were measured to determine the sensitivity for dull and sharp pain, respectively [22,23]. These measurements were performed on the middle part of the right facial masseter muscle and the palm side of the right thenar muscle. The experimental site on the masseter muscle was determined as the midpoint on an arbitrary line paralleling 1 cm posterior to the anterior border [24,25]. The experimental site on the thenar muscle was determined as an intersectional point between the two longitudinal axes of the thumb and index finger [24]. All examinations were performed by the same examiner (KHK) to minimize variability resulting from the examination technique. The experimenter was trained to deliver the stimulation as constantly as possible. All measurements were performed in a quiet room under fixed environmental conditions (room temperature, approximately 24°C; humidity, approximately 30%-40%; illumination intensity, approximately 600 lx), with the participants sitting in a relaxing chair with a headrest and armrest.

1) PPT

The PPT of each muscle was measured using a pressure algometer (Somedic Algometer type 1; Somedic AB, Stockholm, Sweden) with a 12 mm diameter rod. The rod tip was covered with 2 mm flat rubber to avoid tissue damage and perpendicular contact with the test site. PPT was defined as the amount of pressure the participants perceived as painful at the first moment [25]. The participants were instructed to push a small switch with their left hand to stop the stimulation as soon as the pain was perceived. At this moment, the pressure (kPa) was displayed on the monitor. The stimuli were gradually increased at a constant rate of 30 $\mathrm{kPa \cdot s^{-1}}$ [24,25]. While the pressure was applied to the right masseter muscle, the test performer placed their hand on the participants' left zygomatic region as counter-pressure to prevent their head from being rotated or moved. The participants were instructed to keep their teeth slightly apart during stimulation to prevent various amounts of masseter muscle contraction [24]. Once pressure stimulation was applied, the same area was not stimulated for 1 minutes to avoid sensitization [25]. These measurements were performed three times at each point [24]. The mean values of the three measurements were used for statistical analysis.

2) PkPT

The PkPT was measured using a digital force gauge (M7-2; Mark-10 Corporation, Copiague, NY, USA) [26]. The participants were instructed to step on the footswitch with their left foot as soon as the pricking stimulation was perceived as pain. The amount of pricking force (gF) was displayed on the monitor. The pricking tip was made moderately sharp as a ball pen tip of diameter 0.38 mm made using dental resin to prevent possible skin damage. The probe tip contacted the test site perpendicularly at a constant rate of 10 $\mathrm{gF \cdot s^{-1}}$ [27]. The pricking force steadily increased until the participants first experienced pain. The same site was not stimulated for 3 minutes to avoid sensitization [24]. These measurements were performed three times. The mean values of three measurements were used for statistical analysis.

3) Visual information

Visual information during the application of pain stimuli was conditioned using a square mirror (70×70 cm) placed 20 cm in front of the participants (Fig. 1). For the condition without any visual information, the participants were instructed to keep their eyes closed until the measurements were completed. Wearing a blindfold was not considered because adding unfamiliar tactile senses might affect pain perception in the facial region. Instead, the participants were given repeated instructions to keep their eyes closed. Subsequently, the PPT and PkPT were measured alternately in the right masseter and thenar areas with their eyes closed. For the condition with visual information, the participants were instructed to open their eyes and observe the noxious stimulus applied to their faces and hands through the mirror. Their right hands were hidden by a mirror, so the direct vision of the right hand was blocked [11]. Subsequently, the PPT and PkPT were measured alternately in the right masseter and thenar areas, as previously described (Fig. 2). The entire experimental procedure lasted for approximately 25 minutes.

3. Questionnaire for Analysis of the Fear of Pain

The Geop-Pain Questionnaire (GPQ) was used to evaluate

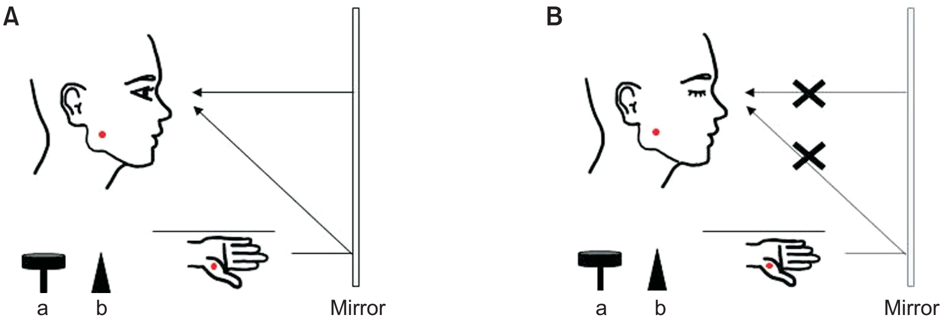

Fig. 1. The experimental set-up with the two types of mechanical stimulations. (A) The condition with visual information. (B) The condition without visual information. Stimulating rods with (a) flat end or (b) sharp end.

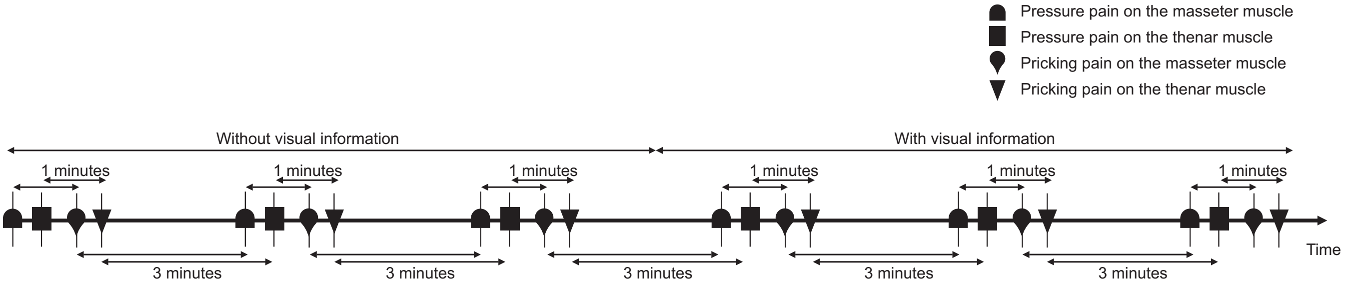

Fig. 2. Timetable for experimental procedures.

if pain-related psychological conditions such as fear, anxiety, or catastrophizing (in Korean, "Geop") had an underlying influence on the effect of visual information in threshold value (Supplementary Tables 1, 2). The GPQ was first developed as a pain-sensitivity-specific questionnaire composed of 15 items [28]. It was verified that three sections of the questionnaire had a strong correlation with the Pain Sensitivity Questionnaire (for questions 1-5 of GPQ), the Pain Anxiety Symptoms Scale (questions 6-10), and Pain Catastrophizing Scale (questions 11-15) [28]. The questionnaire was administered after the end of the entire experiment to exclude the possibility that the involved contents may cause fearful emotions in the participants before the measurement [29].

4. Statistical Analysis

Quantitative data were presented as mean±standard deviation. Before performing any analyses, the data sets were tested for the normality of the parameters using the Shapiro–Wilk test. Paired t-test and Wilcoxon signed-rank test were used to compare the difference in the mean threshold of the PPT and PkPT according to the visual information during the application of noxious stimuli. Differences in the altered PPT and PkPT according to sex were statistically compared using a two-sample t-test. The correlation between GPQ scores and the alterations in the PPT and PkPT according to visual information was also analyzed using Spearman's correlation. Statistical analyses were performed using PASW Statistics for Windows, Version 18.0 (SPSS Inc., Chicago, IL, USA). The significance level was set at $p<0.05$ for all statistical procedures.

RESULTS

This study found no significant difference in pain threshold according to visual information, except for the PkPT of the hand region (Table 1). With respect to the stimulation type, the PPT on either test site showed no significant alteration according to visual information, while the PkPT on the hand showed a significant increase with visual information. The difference in the PPT according to the presence or absence of visual information was −0.97±14.44 ($p=0.583$) and −0.45±30.39 ($p=0.895$) on the masseter and thenar muscles, respectively. The difference in the PkPT was +5.27±30.25 ($p=0.171$) and 14.07±25.48 ($p=0.000$) on the masseter and thenar muscles, respectively (Table 1). These findings indicated that the perceived sensitivity for sharp pain significantly decreased with the application of visual

Table 1. Effect of the visual information on pain thresholds according to the experimental body sites

Test	Site	Without visual information	With visual information	Visual effect (⊿ without and with visual information)	p-value
PPT (kPa)	Face	104.83±35.19	105.79±36.05	−0.97±14.44	0.583[a]
	Hand	207.78±63.16	208.23±68.01	−0.45±30.39	0.895[b]
PkPT (gF)	Face	129.61±42.99	124.35±46.55	5.27±30.25	0.171[b]
	Hand	125.41±32.85	139.48±37.74	−14.07±25.48	<0.001[b]

PPT, pressure pain threshold; PkPT, pricking pain threshold.
Values are presented as mean±standard deviation.
[a]Paired t-test. [b]Wilcoxon signed-rank test.

Table 2. Comparison of GPQ scores between males and females and the correlation of GPQ with the visual effect

GPQ	Male	Female	p-value (between males and females)	Total	Correlation with visual effect (p-value)			
					⊿ PPT		⊿ PkPT	
					Face	Hand	Face	Hand
Total	24.09±7.18	22.94±6.78	0.500	23.51±6.95	0.702	0.846	0.227	0.599
Sense (Q1-5)	8.65±2.78	8.06±2.71	0.380	8.35±2.74	0.963	0.914	0.347	0.438
Experience (Q6-10)	7.76±2.95	7.44±2.39	0.621	7.60±2.67	0.952	0.645	0.270	0.709
Catastrophizing (Q11-15)	7.68±2.46	7.44±2.51	0.698	7.55±2.47	0.796	0.432	0.288	0.862

GPQ, Geop-Pain Questionnaire; PPT, pressure pain threshold; PkPT, pricking pain threshold.
Values are presented as mean±standard deviation.
Spearman's correlation was used to assess correlations between GPQ scores and threshold alterations.

Table 3. Comparison of visual effects between males and females

Test	Site	Male	Female	p-value (between males and females)
⊿ PPT (kPa)	Face	0.65±15.49	−2.58±13.34	0.361
	Hand	4.97±35.83	5.56±23.96	0.937
⊿ PkPT (gF)	Face	−0.85±37.28	−0.04±22.02	0.913
	Hand	−14.65±29.03	−13.50±21.78	0.854

PPT, pressure pain threshold; PkPT, pricking pain threshold.
Values are presented as mean±standard deviation.
A two-sample t-test was used to assess the differences between males and females. ⊿ denotes the difference (without and with visual information) in the pain thresholds.

information.

Further assessment of whether the visual effect was related to the fear of pain level revealed no significant correlation between the GPQ score and the threshold difference (the threshold with visual information minus the threshold without) (p>0.05) (Table 2). This finding showed that the phenotypic variation of mild-to-moderate GPQ could not be significantly linked with any threshold difference according to visual information (PPT on the face, p=0.702; PPT on the hand, p=0.846; PkPT on the face, p=0.227; PkPT on the hand, p=0.599). Additionally, the mean GPQ score was 24.09±7.18 and 22.94±6.78 in the male and female groups, respectively, but no significant differences were observed between both groups (p=0.500) (Table 2).

Further statistical analysis revealed no significant interaction between sex and threshold difference (p>0.05) (Table 3). With respect to the stimulation type, the PkPT with visual information was increased in both the male and female groups, but no significant differences were observed between both groups. The difference in the PkPT on the face was −0.85±37.28 and −0.04±22.02 in the male and female groups, respectively (p=0.913). The difference in the PkPT on the hand was −14.65±29.03 and −13.5±21.78 in the male and female groups, respectively (p=0.854).

However, the PPT decreased, except for the facial region, in the female group. The difference in the PPT on the face was +0.65±15.49 and −2.58±13.34 in the male and female groups, respectively (p=0.361). The difference in the PPT on the hand was +4.97±35.83 and +5.56±23.96 in the male and female groups, respectively (p=0.937). The PPT of the face showed a contradictory decrease in males and an increase in females. However, no significant difference was observed between the male and female groups (p=0.361) (Table 3). Therefore, these findings indicated no significant interaction between sex and visual effect on pain perception.

DISCUSSION

Although noxious stimuli are physical stimuli with objectively invariable values, pain perception is a psychophysiological response with subjectively variable cognition [30]. The cognitive processes involved in pain perception are complex, potentially due to various psychological and physiological factors such as anxiety and visual information [4,7,10].

It has been reported that the perceived intensity of pain can vary depending on the presence and extent of visual inputs. Visual information provided in previous studies was as follows: (1) real visual information by viewing the pain-inducing tool applied on one's own body [6,7,9], (2) fake visual information by viewing the pain-inducing tool suppositiously applied on the contralateral side of one's own body [6,29], and (3) blocked visual information by closing their own eyes or covering the eyes with a blindfold [14]. Various studies have found that the provision of visual information on painful events can usually increase pain intensity and/or decrease pain threshold. It has been reported that these effects of visual information might be related to the possibility of anticipating a more enhanced upcoming threat [3,31]. However, a recent study reported that pain intensity decreased despite visual information. These findings indicated that the visual effect on pain could vary according to the vulnerability of the stimulated site, irritability of noxious stimuli, expected tissue damage, and psychological condition.

Dental treatment is commonly regarded as a highly anxious procedure by the general population [32,33]. A previous study reported that extreme dental anxiety affects approximately 12% of the general population [34]. A nationwide survey and other studies have revealed that approximately one-third of the adult population in the UK is influenced by dental anxiety, which contributes to the avoidance of dental care [35-37]. Sharp syringes, the sound of rotary instruments, and other sharp tools used in dental procedures can make individuals more susceptible to fear and anxiety [33]. Moreover, it was revealed that pain experiences resulting from dental pain and insufficient anesthesia experience had a marked influence on dental fear levels [38]. It could be helpful to better understand the mechanisms of orofacial pain perception by determining the detailed effects of contributing factors for the establishment of a more effective pain control strategy. Therefore, this study investigated the difference in the visual effect on pain between anatomical regions (face and hand) and mechanical pain stimulation types (sharp and dull pain). Additionally, the psychological state was determined using a questionnaire scale to determine the effect of visual information on pain perception. In this study, the same number of male and female participants of similar ages were recruited to eliminate the effects of sex and age.

This study showed that the sharp pain threshold of the hand increased significantly by viewing the stimulated hand compared with stimulation without visual information (Table 1). This finding was contrary to that of previous studies, which showed that visual information could enhance the fear and attention to a noxious stimulus, possibly altering pain sensitivity [8,24]. However, recent studies reported that pain intensity decreased when participants looked directly at their stimulated right hand [9,13]. These studies provide a probable underlying mechanism for the increased pain threshold with visual information. They suggested that the sense of body ownership and agency could be consolidated when viewing one's own body site stimulated with noxious but low stimuli, subsequently decreasing pain intensity by mitigating fear and attention [9,39]. A sense of enhanced ownership might induce psychological stability and belief in bodily control, possibly lowering pain levels by making it possible for individuals to perceive noxious stimuli realistically without exaggeration [40]. The other mechanism is that visual information could readily activate endogenous descending analgesic neural pathways in advance [41]. In terms of the homeostatic model, for example, the predictable pain of consecutive stimulation could prepare the neuromuscular system to activate and thereby could invoke a rapid reaction to escape or cope with pain [42]. Furthermore, these responses appeared to depend on the expected severity of the noxious stimuli. Previous research revealed that moderately painful stimuli were experienced as more painful when the participants expected to receive intense pain and less painful when they expected to receive mild pain [43]. Because the pain threshold in this experiment was determined when initially recognizing mild painful stimuli, the severity of pain was graded as mild. Therefore, the influence of visual information on painful stimuli may vary depending on the experimental context. Observing noxious stimulation does not always increase pain. However, pain perception can be reduced through positive pain prediction.

Regarding the visual effect according to visual information, viewing the approaching stimulation in the facial area did not make a significant difference in the pain threshold in both stimulation types (Table 1). Craniofacial pain sensation is qualitatively different from bodily nociception [17]. Furthermore, a previous study reported that the visual information from the face could carry negative emotions presented by facial expressions [44]. Previous findings revealed that viewing approaching stimuli could enhance the interconnection with pain perception through emotional influence [44]. Other studies also showed that participants reported higher pain-induced fear scores when stimuli with the same pain intensity were applied to the face than to the extremities [17]. This study showed that neither aggravation nor analgesic effects of visual information were apparent in the facial area, whereas an analgesic effect was manifested in the hand area. These results might partially be explained by the fact that the neuro-emotional sensitivity of the facial area could counteract the analgesic effect of visual information.

The perception of pain stimuli on the face could be attributed to the complex interaction between the physiological and cognitive-emotional aspects. Because the emotional effects underlying pain perception might be considered to influence the visual effects, especially in the facial region, an apparent threshold difference in individuals with higher fear of pain levels would be expected. However, the GPQ score analysis showed no significant correlation with the threshold difference induced by visual information. This result might partially be explained by the fact that there was a mild-to-moderate difference in GPQ scores between individuals (Table 2). Another possible explanation may be that pain-modulating factors could vary widely across individuals, so the fear of pain scale alone may not reflect the contribution of pain perception. It has been reported that not only the fear of pain but also self-efficacy, anxiety, and predictability of pain stimulation could be involved in pain perception [39]. Therefore, future research is needed to address the complex interactions between psychological factors and visual effects on pain perception.

In this study, the visual effect according to the noxious type was additionally evaluated. Although the analgesic effect of visual information was revealed on the PkPT on the hand, no significant visual effects were observed on the PPT on any body part, which predominantly reflects muscle nociception [22]. This result might be related to previous findings that dull muscle pain would be more affected by psychological factors than sharp cutaneous pain [45,46]. Although dull and aching muscle pain is typically perceived with more unpleasant negative emotions [46], cutaneous pain is considered a psychological aspect that is less involved in its perception [45]. Additionally, previous findings from brain imaging studies supported perception differences in the two types of pain [47,48]. Although cutaneous pain was found to activate the secondary somatosensory cortex in a region-specific manner, muscular pain activated the anterior midcingulate cortex, insular cortex, and posterior insular cortex in a network-specific manner instead of a region-specific manner, which could imply a stronger interaction between emotion and somatosensation [48]. Therefore, negative expectations of muscular pain might result in negative amplification of pain perception [47]. Thus, the comparative visual effects according to noxious types might be partial because neuro-emotional involvement in the perception of muscular pain could counteract the analgesic effect of visual information.

In this study, we also compared sex differences in the visual effects on pain thresholds. A previous study has revealed that women reported higher pain intensity ratings and lower threshold and tolerance levels [49]. Considering the biological and psychological factors, women are more susceptible to both acute and chronic pain [50]. In this study, it was expected that the visual effects on pain perception might differ between the male and female groups. However, this was not supported by our results. When viewing the stimulated hand, both the male and female groups showed increased pain thresholds (Table 3). These data suggest that the visual effect is sex-independent. However, further detailed studies are needed to clarify the sex differences in neuroimaging features underlying visual effect-related brain activity.

This study has a few limitations. First, it is difficult to say that the experimenter completely controlled the participants' vision because of not using a blindfold. However, participants were repeatedly instructed to follow the visual conditions outlined in the experimental protocol. Second, a selection bias might be present since we only recruited all participants from our university. Thus, the results cannot be generalized to the rest of the population. Within the study limitations, it can be concluded that the application of visual information could alter the pain perception threshold, which differed according to the anatomical region and stimulation type.

In conclusion, this study showed that visual information could have an analgesic effect on the perceived pain threshold depending on the anatomical region and stimulation type. The pain threshold of the mechanical pricking stimulation was significantly increased by viewing one's own hand. A better understanding of the modulatory mechanisms of pain perception is helpful for clinicians to apply painful therapeutic procedures.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

Conceptualization: JKJ, KHK. Data acquisiton: KHK. Project administration: JKJ. Visualization & Writing original draft: KHK. Writing review & editing: JRK, JSB, JKJ.

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