Activitas Nervosa Superior Rediviva Volume 62 No.1 2020

ORIGINAL ARTICLE

Cognitive task suppresses extra-epidermal electrical stimulation evoked potentials

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Submitted: 2019-12-17 *Accepted: 2020-04-15* *Published online: 2020-05-10*

Key words: **Extra-epidermal electrical stimulation evoked potentials; pain cognition; Rehabilitation; chronic pain; pain distraction**

Act Nerv Super Rediviva 2020; **62**(1): 5–9 ANSR62120A01

Abstract

OBJECTIVES: To examine the pain-reducing effects of distracting cognitive tasks, measured by Extra-epidermal electrical stimulation evoked potentials (EES-EPs), as an occupational therapy technique in patients experiencing pain.
PARTICIPANTS AND SETTING: Nine healthy male volunteers (mean age, 23.9±3.0 years) participated in this study conducted at Nishikyushu University.
METHODS: Participants were asked to perform two cognitive tasks (calculation and memorization) to measure pain cognition. EES-EPs were recorded using a ring-electrode on the right index finger while the tasks were performed. Visual Analog Scale (VAS) and peak-to-peak (N2-P2) amplitude of EES-EPs were measured to determine functional outcomes.
RESULTS: Subjective pain decreased during cognitive tasks relative to resting in all subjects tested. Additionally, the amplitude of the P2 component at the Cz position decreased significantly in the calculation and memorization tasks in comparison to the amplitude at rest. Our findings show that the amplitude of the P2 component of EES-EPs was affected by the distraction tasks.
CONCLUSION: The late positive component of LEPs that appears at a latency of 250-300 msec, known as P2, reflects the emotional and cognitive aspects of nociceptive processing. Overall, our data show that cognitive tests provide a sufficient distraction to induce a reduction in subjective pain and affect nociceptive processing.

Abbreviations & units:
Extra-epidermal electrical stimulation evoked potentials (EES-EPs); Visual Analog Scale (VAS); anterior cingulate cortex (ACC); functional magnetic resonance imaging (fMRI); cognitive-behavioral therapy (CBT); Laser-evoked potentials (LEPs); analysis of variance (ANOVA).

Introduction

Pain is a subjective, unpleasant sensation that can have negative effects on an individual's emotional state (Merskey & Bogduk 1994). Numerous diseases can cause pain, independent of age or sex. The neural mechanisms underlying pain are complex. In short, signals initiating in somatosensory pathways are processed in the somatosensory cortex and can ultimately activate brain regions that control emotion/ cognition, such as the anterior cingulate cortex. The International Association for the Study of Pain (IASP) defines chronic pain as "pain that extends beyond the expected period of healing or progressive pain due to non-cancer diseases" (Merskey & Bogduk 1994). Chronic pain represents a significant health burden, affecting over 1.5 billion people worldwide (Borsook 2012). In Japan, as much as 13–39.3% of the population suffers from chron ic pain (Hattori *et al.* 2004; Nakamura *et al.* 2011; Inoue *et al.* 2015). Inoue *et al.* (2015) reported that the most common locations of chronic pain are the lower back (30.6%), knees (19.8%), shoulders (17.0%), and neck (8.3%).

Currently, brain imaging techniques are used to examine and better understand brain regions involved in pain transmission and the resulting cognitive effects. Previous studies have shown that the coordinated network of brain regions activated during acute pain are the primary and secondary somatosensory (S2) cortex, insular cortex, anterior cingulate cortex (ACC), prefrontal cortices, and thalamus (Apkarian *et al.* 2005). Interestingly, functional magnetic resonance imaging (fMRI) studies have illustrated that many of these brain regions are also active during virtual pain and form a "pain matrix" (Craig 2009; Gogolla *et al.* 2014; Menon & Uddin 2010). Another study reported that the imagination of pain even without physical injury engages the cortical representations of the pain-related neural network (Ogino *et al.* 2007). The ability to virtually activate this pain matrix, independent of a physical painful stimulus, indicates that individuals can anticipate pain and that these brain regions play a key role. Therefore, individuals can learn about "pain" through painful past experiences, which allow them to predict the extent of pain independent of an actual painful stimulus. Treatments for chronic pain commonly consist of exercise therapy, pharmacotherapy, cognitive-behavioral therapy (CBT), and many other therapy types. CBT has shown to be an effective tool for chronic pain management (Morley *et al.* 1999; Astin *et al.* 2002; Ociskova *et al.* 2019). Basic research suggests that CBT, Laser-evoked potentials (LEPs) with CO2 laser stimulation, and electrical stimulation can affect nociceptive processing of pain by inducing a "pain distraction" (Chen et at 2004; Kakigi *et al.* 2000; Yamasaki *et al.* 1999, 2000). Specifically, these studies state that the negative component of LEPs appearing at a latency of 150 msec, known as N2, can measure sensory-discriminative-related activation of the primary somatosensory cortex (Bentley *et al.* 2001; Christmann *et al.* 2007). In addition, they show that the late positive component of LEPs that appears at a latency of 250–300 msec, known as P2, reflects the emotional and cognitive aspects of nociceptive processing. Moreover, previous studies have reported a selective change in these measurements upon repeated stimuli, as well as a change in determining response habituation (Torta *et al.* 2012). Thus, the psychological factors that are regulated by pain-related brain activations have been well studied. However, few studies have shown how pain distraction during a task affects the P2 of nociceptive-related potentials elicited by transcutaneous electrical stimulation. This study investigates the pain-reducing effect from very simple cognitive tasks that are free from invasive medical intervention or pharmacotherapy. Here, we sought to examine how subjective pain and nociceptive processing of pain is affected by distraction from pain using EES-EPs.

Materials and Methods

Participants

Nine healthy volunteers participated in this study (9 men, mean age, 23.9±3.0 years). We excluded volunteers with neuropathy, trauma, and pain in the upper limbs. This study was approved by the Research Ethics Committee (020) at Kouradai Rehabilitation Hospital. Written informed consent was obtained from all subjects. The subjects received no compensation for participation in this study.

Extra-epidermal electrical stimulation-evoked potentials using a ring electrode

A ring electrode on the right index finger was used as an electrical stimulus. The pain rating for each subject was determined using a visual analogue scale (VAS). The electrical stimulus strength was determined to be the amount of stimulus that elicited a score of 8/10 on the VAS. The inter-stimulus duration was 0.5 msec at random for between 1.0 and 3.0 sec.

Cognitive tasks

During the experiment, each subject sat comfortably in a chair. In accordance with Yamasaki *et al.* (1999, 2000), we used two kinds of cognitive tasks (calculation and memorization) with a control task (rest). Each task was displayed on the monitor in front of the subjects. The calculation and memorization tasks required concentration by the subject. Therefore, we advised the subjects to relax and perform the tasks intensively. The calculation task involved 25 random two-digits numbers (5 × 5 lines) displayed on a 15-inch monitor placed at a distance 1 m away. The calculation task was to add the 5 numbers on each line (Figure 1). The subjects were instructed to add the top row numbers verbally. If the answer was correct, they were asked to add the next line. If incorrect, they were asked to add the same line again. The Memorization task involved memorizing as many numbers as possible (Figure 2). Immediately after each task was finished, the subjects were asked to report a number for pain sensation (VAS) during both the distraction tasks and rest.

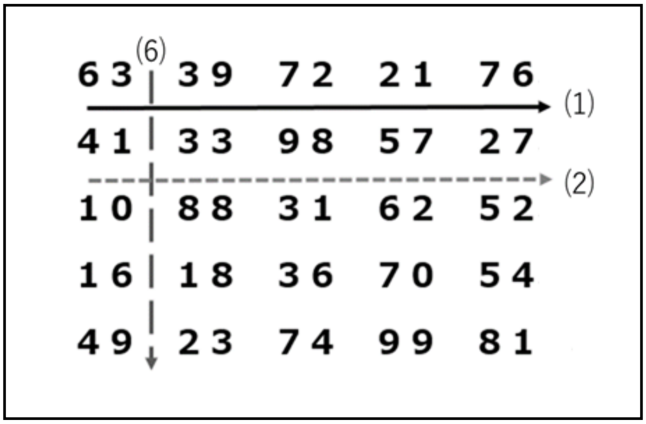

Fig.1. Method was to add the 5 numbers on line(1). When the answer was correct, to add the next line(2). The total was 10 lines.

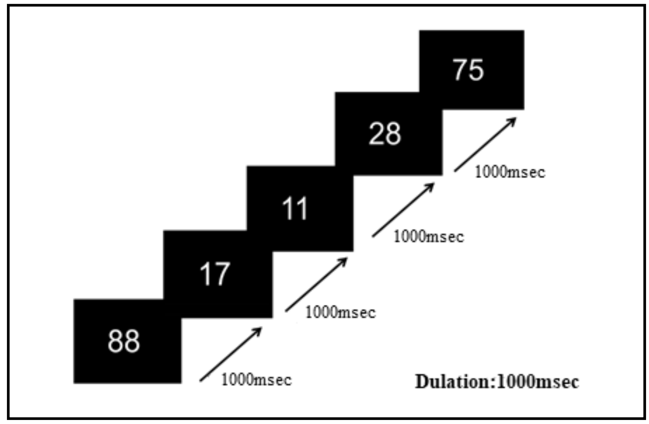

Fig. 2. The memorization task was to memorize as many as possible of the numbers.

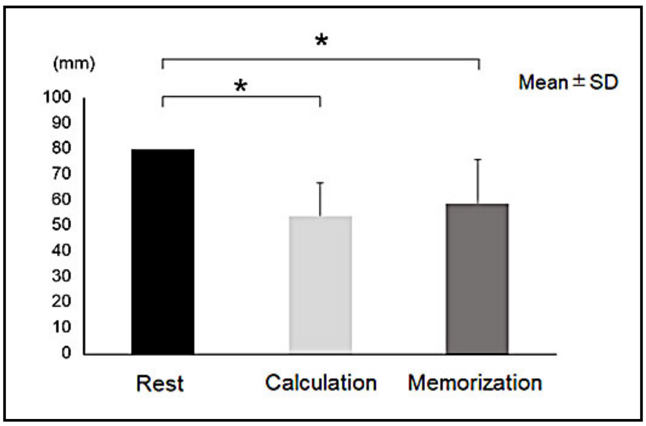

Fig 3. Subjective pain (VAS) of three conditions. The calculation and memorization task was significantly lower than at rest. ANOVA followed by Fisher's PLSD test was used for three tasks.

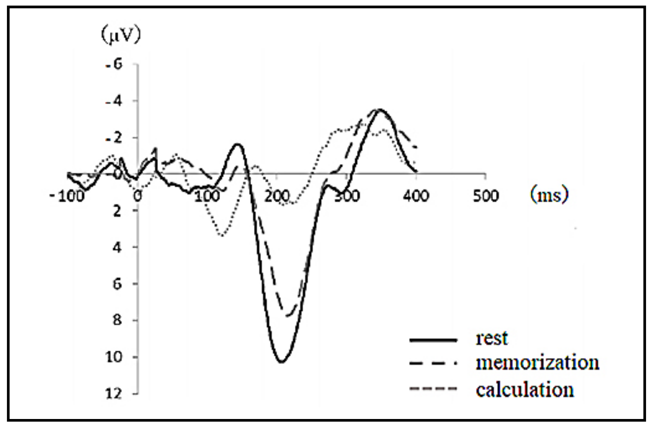

Fig 4. Grand average waveform on the Cz in the s in each condition (n=9).

Measurement method

The EES-EPs were measured with a signal processor (Neuropackμ MEB-9100 system, NIHON KOHDEN, Tokyo, Japan) and analyzed with a data processing device (EPILYSER2, Kissei Comtec, Matsumoto, Japan) and the visual presentation equipment (Multi Trigger System, Tokyo, Japan). The electroencephalographic responses were recorded utilizing Ag/AgC1 electrodes from the Cz and Pz positions on the scalp according to the International 10–20 system. A reference electrode was attached to the earlobe, and a neutral electrode was attached to the Fpz position on the scalp. The impedance was carefully balanced and maintained below 5 kΩ. During the recordings in each condition, 100 artifact-free sweeps were averaged. The amplitude of each component in the LEPs was calculated as the difference between the peak N2-P2 components.

Data analysis

The amplitudes of the P2 components of EES-EPs were measured and averaged for all subjects in the cognitive and control tasks. Statistical analysis was performed using an analysis of variance (ANOVA) followed by Fisher's Protected Least Significant Difference with a significance level of p<0.05%.

Results

Subjective pain rating

The perceived VAS in the two distraction tasks was lower compared to rest in all three subjects. The VAS was reduced from 8.0 at rest to 5.4±1.3 in the calculation task and 5.9±1.7 in the memorization task (Figure 3). VAS scores in the calculation and memorization tasks were significantly lower than at rest (Figure 3). There were comments from the subjects that pain was hardly felt because they were focused on the tasks, and, that the level of subjective pain and the degree of difficulty between tasks were not majorly different.

P2 component of EES-Eps

Figure 4 shows the grand average wave form on the Cz in the P2 for each task. The amplitude of the P2 component at Cz was significantly decreased in both the calculation (6.9 ± 1.3 μv) and the memorization tasks (11.8 ± 3.1 μv) relative to rest (17.1 ± 2.4 μv) (Figure 5). However, the amplitude of the P2 component between

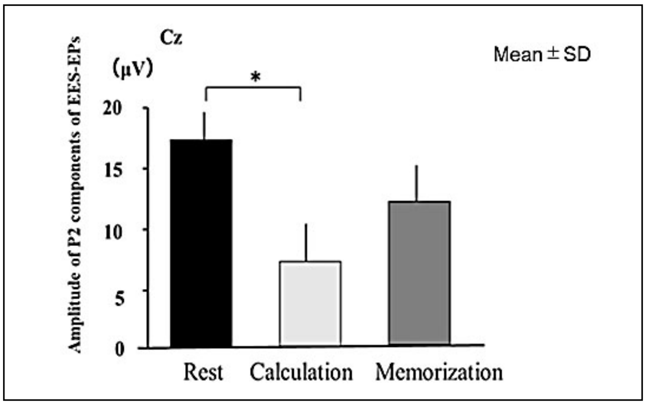

Fig. 5. Comparison of the amplitude of the P2 component of EES-EPs in each tasks.

the calculation memorization tasks showed no significant difference ($p<0.05$; Figure 5).

Discussion

In this study, the cognitive effects of pain distraction from a painful stimulus, recorded using EES-Eps, were investigated to answer the following questions. Does pain distraction cause a change in subjective pain intensity? Does pain distraction cause changes in the amplitude of the P2 component, which is related to the emotional and cognitive aspects of nociception?

Change in subjective pain rating

In this study, the stimulus intensity was set at VAS 8/10. Reported VAS scores in all subjects decreased significantly during both the calculation and memorization tasks compared to rest. The VAS is the most widely used tool for estimating both severity of pain and the extent of pain relief. There are many studies using the VAS (Kelly 2001; Bodian *et al.* 2001; Nadar *et al.* 2016). Previous studies have reported results from a trial comparing acupuncture to placebo needling for the treatment of acute low back pain (Kennedy *et al.* 2008). The VAS is a useful tool to quickly provide approximations of pain in patients. However, focusing on the specific aspects of pain may decrease a person's motivation for activity. Therefore, a useful tool during rehabilitation is to use distracting activities to redirect a patient's attention to help reduce feelings of pain.

In the present study, we found that while focusing on a task, such as calculation and memory tasks, volunteers experienced a decrease in subjective pain sensation.

P2 component of the EES-Eps

In a previous study, the P2 component of LEPs was found to be correlated with the cognitive and emotional aspects of nociceptive processing. In agreement with this, our study found that the amplitude of P2 components at the Cz electrode were significantly decreased in the calculation and memorization tasks relative to rest. Therefore, our data show that pain distraction can have positive effects on nociceptive processing. Furthermore, the P2 component is correlated with activity in the brain regions associated with cognition of pain, such as the somatosensory cortex, anterior cingulate cortex, and insular cortex. fMRI research has revealed that a sustained focus on pain and medical issues that may underlie pain could influence pain perception by increasing attention to pain-related stimuli (Apkarian *et al.* 2005; Torta *et al.* 2012; Moayedi *et al.* 2015). Patients with chronic pain tend to demonstrate a cognitive bias toward pain-related information, which may negatively affect patient functioning (Dehghani *et al.* 2004; Haggman *et al.* 2010). Therefore, attention bias modification training was administered to patients with chronic pain. As hypothesized, we found that simple distracting tasks, such as calculation and memory tasks, could reduce pain and affected nociceptive processing as measured by EES-EPs. Thus, during rehabilitation for chronic pain, pain perception can be reduced by providing temporary distraction. Future research should focus on further understanding the effects of various tasks and differing degrees of difficulty on pain perception. This study used an invasive intervention for healthy volunteers. It is ethically questionable to give an invasive intervention to patients with chronic pain. The stimulation site in this study was the finger, but actual pain patients experience pain in various places.

Conclusions

The main result of this study was that the amplitude of the P2 component during EES-EPs was affected by distraction tasks. We showed a reduction in subjective pain and nociceptive processing in the brain while diverting the subject's attention. These data demonstrate that distraction from pain by simple cognitive tasks may be an effective rehabilitation for chronic pain patients.

Acknowledgments

We sincerely thank for the students of Nishikyushu University, the graduate students, and the physical and occupational therapists of Kouradai Rehabilitation Hospital.

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