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Itching-related somatosensory evoked potentials

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Abstract

Electrically evoked itching has the strong potential to be used to investigate the central processing associated with itching at high temporal resolution by employing magnetoencephalography, electroencephalography (EEG), and event-related functional magnetic resonance imaging. However, it has not been investigated whether time-locked brain activity can be measured using this stimulus, and whether the itching sensation induced by electrical stimulation of the skin is associated with C-fibers. Thus, we investigated these problems in this study. Itching sensations were elicited when electrical stimuli were applied to the skin of the right wrist and right forearm. EEG activity was recorded from 5 electrodes (Fz, FCz, Cz, CPz and Pz). When the right wrist was stimulated, the reaction time (RT) and latency of the positive component of somatosensory evoked potentials (P1) were 1215 ms and 963 ms, respectively. When the right forearm was stimulated, the RT and peak latency of the P1 were 1013 ms and 772 ms, respectively. The conduction velocity estimated from the RT and latency of the P1 was 1.04 m/s and 0.92 m/s, respectively. In addition, the itching sensation and P1 were inhibited when the current intensity was increased into the range eliciting pain and touch sensations, implying interaction between C- and A-fibers. These findings demonstrate that time-locked brain activity can be measured using electrically evoked itching and that the itching sensation induced by the electrically evoked itching is associated with C-fibers. Thus, this method is useful for research into the central processing of itching.

Keywords: Electrically evoked itching; Somatosensory evoked potential; C-fibers

1. Introduction

Itching sensations are associated with the excitation of C-fibers induced by histamine [7,22,24,25,29]. Therefore, in most studies of itching, histamine is used to elicit the itching sensation. Recently, functional neuroimaging techniques such as positron emission tomography and functional magnetic resonance imaging (fMRI) have been used to clarify the central mechanism of itching [4,8,15,16]. For example, Mochizuki et al. reported that the posterior cingulate cortex and posterior insula play important roles in itching perception [16]. Laknes et al. suggested that the itch–scratch-cycle, a serious problem among patients with atopic dermatitis, was partly associated with enhanced activity in the striato-thalamo-orbitofrontal circuit [12]. These studies used histamine-induced itching. When histamine is applied to the skin, an itching sensation gradually develops and remains for a long time (5–20 min), then slowly decreases. Therefore, such a chemical stimulus is not useful for measuring time-locked brain activity with magnetoencephalography (MEG), electroencephalography (EEG), and event-related fMRI. However, it has also been reported that a special electrical stimulation

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of the skin can elicit an itching sensation [5,23,28]. Since electrical stimulation has a great advantage over chemical stimulation in terms of time-locked averaging, it can be a powerful tool with which to investigate the brain processing associated with itching at high temporal resolution (ms). Therefore, we considered that electrically evoked itching is useful for basic and clinical research on itching. However, it is still unclear whether time-locked brain activity (i.e., somatosensory evoked potential (SEP)) can be measured using the electrically evoked method. Thus, we investigated this problem. In addition, we also estimated the conduction velocity (CV) of peripheral signals responsible for SEP. This is the first study to measure the CV of itch signals conducted through peripheral nerves following electrical stimulation of the skin.

2. Methods

2.1. Subjects

Nine healthy male volunteers (28 ± 4 years (mean ± standard deviation (SD))) participated in this study. Subjects with a history of allergy, atopic eczema, or other dermatological diseases were excluded. The study was approved by the Ethics Committee at our Institute. Written informed consent was obtained from each subject, and the study was performed in compliance with the relevant laws and institutional guidelines.

2.2. Stimuli

To evoke itching, a modified version of the method that Ikoma et al. recently developed was used [9]. In brief, the electrode for the electrical stimulus was composed of 4 crossed stainless steel wires (diameter: 0.1 mm, The Nilako Co. Ltd., Tokyo, Japan) and a plastic plate ($1.5 \times 1.5\ cm^2$) (Fig. 1A). The electrode was attached to the right wrist and right forearm in the wrist and forearm stimulus conditions, respectively. A saline-soaked gauze pad ($1.5 \times 1.5\ cm^2$) serving as the reference electrode (cathode) was placed on the right wrist 2.0 cm proximal to the electrode center (Fig. 1B). On the basis of a previous study [9], current-constant square wave pulses (pulse duration, 2 ms; frequency, 50 Hz) were applied to the skin through the electrodes. Twenty pulses were given in one stimulus. Before the experiment, the intensity of the current at which a clear itching sensation was felt was defined for each subject, 0.24 ± 0.06 mA. The electrical stimulus was applied to the right wrist (area: $4 \times 4\ cm^2$) or the right forearm (area: $4 \times 4\ cm^2$). Forty stimuli were given to the subjects in each condition. In addition, before and after the recording of SEP, the electrical stimulus was applied 10 times to obtain the reaction time (RT) and a mean value was used for analysis. In a preliminary study, we observed that repeated stimuli markedly reduced the itching sensation when the inter stimulus interval (ISI) was less than 30 s. Therefore, we considered it better to have a long ISI. Thus, the ISI was over 30 s in this study. Each session included ten stimuli. It took about 7 min in one session. Four sessions were conducted for recording SEP and two sessions for recording RT. The subjects rested for about 10 min between each session. During this time, we changed the site of stimulation within the restricted area ($4 \times 4\ cm^2$) in each condition. In total, it took at least 1.5 h to measure the SEP and RT in one condition (e.g., the wrist stimulus condition). Therefore, it was very tough for subjects to be measured SEP and RT following the stimulation of two different body parts (i.e., the right wrist and right forearm) on the same day. Therefore, the two conditions were performed on different days for each subject.

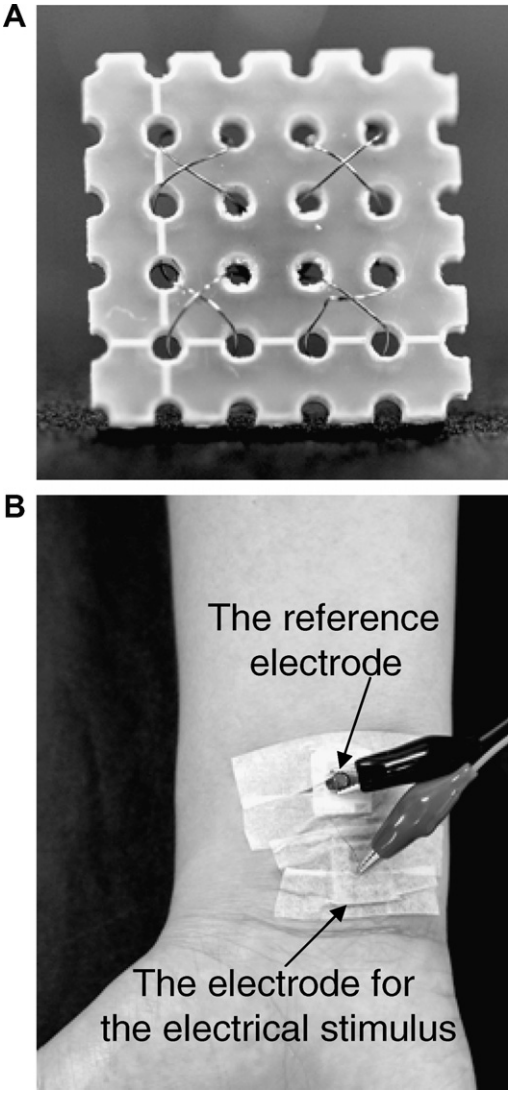

Fig. 1. The electrode used to elicit itching (A) and the right wrist when the electrical stimulus was applied (B).

After each stimulus during the SEP recording, the subjects evaluated itching sensations using a scaling bar whose color gradually changes from white to red (0–20 cm). The left side (0 cm, color: white), middle (10 cm, color: pink), and right side (20 cm, color: red) of the scaling bar indicated no itching sensation, an itching sensation with a strong urge to scratch, and an itching sensation with a very strong urge to scratch, respectively (the itching score).