Title: Ipsilateral primary sensorimotor cortical response to mechanical tactile stimuli

Running head**: iSMI response to mechanical stimuli**

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Abstract

We studied somatosensory evoked fields elicited by mechanical vs. electrical stimuli to index finger of healthy subjects. Mechanical stimulation was index pulp compression and decompression by using non-magnetic mechanical stimulator. Electrical stimulation was three times of sensory threshold and delivered to index pulp by using ball-shaped electrodes. Mechanical/electrical-stimuli evoked contralateral primary somatosensory cortical (cSI) responses in all respective subjects. Compressive-stimuli evoked ipsilateral primary sensorimotor cortical responses in all respective subjects, with dipole strengths less than cSI of compressive-stimuli. Mechanical/electrical-stimuli evoked secondary somatosensory (SII) cortical responses bilaterally; Electrical-stimuli SII dipole strengths were relatively stronger than compressive-stimuli SII responses. It is concluded that the use of mechanical stimulation may improve our understanding of functional sensory cortical responses compared to electrical stimulation.

Key words: Mechanical stimuli; Compression; Decompression; Electrical stimuli; Somatosensory evoked fields (SEFs).

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Introduction

The somatosensory evoked fields (SEFs) elicited by electrical stimulation of the index finger exhibit a first cortical component in the contralateral hemisphere that is considered equivalent to the N20m elicited by median nerve stimulation at the wrist [1]. In addition, its source exhibits a tangential current (with posterior-to-anterior direction) in the posterior bank of the central sulcus in area 3b of contralateral primary somatosensory (cSI) cortex [1,2]. In human glabrous skin, on the other hand, the majority of rapidly adapting mechanoreceptors with a skin indentation threshold below 0.5mm were found to evoke action potentials with compression and decompression by an object in contact with skin [3]. Various mechanical methods of sensory stimulation have therefore been developed, including the air-puff stimulus [4]. The source location of SEFs elicited by air-puff stimuli is almost always located in area 3b, has opposite direction (anterior-to-posterior), and peaks at 50~60ms [5]. In the later study, SEFs were only evoked when the skin was indented by the air-puff stimulation. However, SEFs could not be evoked when the air-puff stimulation came off the contacted skin (decrement in the skin indentation).

Recently, SEFs elicited by compressive and decompressive stimulation of the index finger glabrous skin [6] and of the great toe [7] have been determined. Although different cSI responses were obtained to compressive and decompressive stimuli, an examiner was needed to stimulate the glabrous skin. This subjective stimulation introduces variances that can be eliminated with the use of machine stimulation. Moreover, neither ipsilateral primary sensorimotor (iSMI) nor secondary somatosensory (SII) cortical responses could be detected with either compressive stimuli or decompressive stimuli. This was probably the result of the use of subjectively weak compressive stimuli and short inter-stimulus interval for decompressive stimuli ($\leq$ 1s).

The primary aim of this study was to establish objectively the existence of compressive/decompressive stimuli-related SEFs, by using non-magnetic machinery mechanical stimulator. The second aim was to carry out a comparison between mechanical and electrical stimuli, in terms of their relative ability to evoke iSMI and SII cortical responses.

Methods

Nine healthy right-handed males, aged 25-40 years, were tested. The instruments used in this study were approved by the Japanese Ministry of Health, Labour, and Welfare (No. 20800BZY0027000). Informed consent was obtained from subjects to participate in this study, which was approved by the ethics committees of Hiroshima University.

Glabrous skin contact was produced with a non-magnetic machinery stimulator that was designed specifically for this study to compress and decompress left index finger pulp. The machine was equipped with a smooth plastic piece, round surface, with a contact area of approximately 70mm^2. Two recording sessions with different trigger timings were carried out for each subject (Fig.1). A video-based 3D motion analysis system (APAS, Ariel Dynamics, Inc. USA) was used to measure the average speeds of compression, decompression, and the time intervals of machine cycle constituents.

The electrical stimulation was delivered using ball-shaped Ag electrodes (3mm in diameter, anode 4mm from cathode) to index finger pulp of 7 subjects out of our 9 subjects. The electrical stimuli were constant-current square-electrical pulse of 0.2ms duration, three times of sensory threshold, 1Hz frequency, and 2~3s random inter-stimulus interval. The method of electrical stimuli in this study was used in a previous study [8].

The cortical SEFs were recorded using a whole-head 306-channel planar gradiometer system (Vector View Elekta Neuromag, Helsinki, Finland). Mutually orthogonal tangential magnetic field gradients were simultaneously obtained at 102 recording sites. The recording band-pass was 0.1~ 260Hz and the signal were digitized at 600Hz.

The exact location of the head with respect to MEG sensors were determined using the four head position indicator coils that were attached to specific sites on the subject`s head. For source identification, the head was assumed to be a sphere, the dimensions of which were determined on the basis of individual magnetic resonance (MR) images obtained using a GE Yokogawa SIGNA 1.5Tesla device (slice thickness of 2mm; 3D-SPGR). The two coordinate systems (MEG and MR) were aligned by applying markers in the MR image and by identifying these landmarks with a 3-D digitizer (Isotrack; Polhemus Navigation Sciences, Colchester, VT).

Source analysis was based on signals high-pass-filtered at 2Hz, low-pass-filtered at 100Hz, and analysis of a 1000ms period began 500ms before triggering. A total of 200 and 100 artifact-free evoked fields were averaged online separately for each mechanical and electrical stimulation sessions, respectively. Cerebral sources of the evoked responses were modeled as single-current dipoles. Then the equivalent current dipole was identified by a least-squares search using a subset of 20~30 channels over the rolandic region of SI, iSMI cortex, and anterior-lateral rolandic region of SII cortex. Only dipoles with goodness-of-fit of ≥80% were used for analysis.

One-way ANOVA was used for statistical comparisons of dipole latencies, orientations and strengths within each stimulation method, followed by post hoc analysis (Bonferroni test). Significance of differences was accepted at $P < 0.05$.

Results

The mean speeds of compression/decompression were 39.4±0.6cm/s and 10.1±1.2cm/s, respectively. One machine cycle comprised “decompression-- 0.6±0.02s -- compression-- 2.3±0.02s (sustained contact), and was repeated (Fig.1).

Table 1 summarizes the activated areas, dipole mean localization, strength, goodness-of-fit, and latency for each session. Compression was able to evoke cSI, iSMI, and iSII responses in all subjects (n=9), and cSII responses in three of them, whereas decompression was only able to evoke cSI responses in all subjects (n=9). On the other hand, electrical stimuli evoked cSI, cSII, and iSII cortical responses in all tested subjects (n=7). Posterior parietal cortical SEFs could not be detected either by mechanical or by electrical stimuli.

Results of ANOVA revealed significant differences in dipole strength values within the grouped data of mechanical stimuli (F=4.3, P=0.001) and electrical stimuli (F=2.7, P=0.035). Post hoc analysis indicated that dipole strength of compressive-cSI was larger than that of decompressive-cSI (P=0.004). In addition, dipole strength of compressive-iSMI was smaller than that of compressive-cSI (*P*=0.03). In electrical stimuli grouped data, dipole strength of electrical-cSII was larger than that of electrical-cSI (*P*=0.016).

Figure 2 shows that the source area of compressive/decompressive stimuli-cSI and electrical-cSI is in the posterior wall of the central sulcus, corresponding to the hand area. The dipole orientation of compressive/decompressive stimuli-cSI is anterior-to-posterior, whereas electrical-cSI dipole orientation has opposite polarity (posterior-to-anterior).The source area of compressive-iSMI also originated in the posterior wall of the central sulcus, but the dipole orientation was posterior-to-anterior. The source area of compressive/electrical stimuli cSII and iSII responses are in the parietal operculum (corresponding to the SII cortex), and the dipole orientations of bilateral SII evoked fields are inferior-to-superior.

Discussion

Our results objectively confirmed the findings of previous studies [6,7], that cortical cSI responses could be evoked not only by compressive stimuli but also by decompressive stimuli in all subjects. However, in our study, dipole strength of decompressive-cSI responses was smaller than that of compressive stimuli, since compression was approximately 4 times as fast as decompression (39.4±0.6cm/s and 10.1±1.2cm/s, respectively).

Only compressive stimuli were able to evoke iSMI at a latency of 159.4±17ms, and we could not obtain iSMI response prior to this latency. This is because dipole strength of earlier iSMI response elicited electrically in a previous study [9] was 4~16 times smaller than those in cSI cortex. Therefore, it is assumed that we might detect such earlier iSMI response if we averaged a larger number of trials (e.g. more than 200 trials).

Consistent with previous studies [9,10,11,12], which detected iSMI responses to electrical stimulation of the median nerve at the wrist, the source localization of compressive-iSMI response was also in area 3b, and dipole orientation of compressive-iSMI response, posterior-to-anterior, is opposite to that in compressive-cSI response (Fig.2). Dipole strength of compressive-iSMI response was weaker than that of compressive-cSI response (Table 1), and this is also consistent with the findings of electrical evoked iSMI studies [10,11].

However, iSMI responses to compressive stimuli could be detected in all of our subjects, while our electrical stimuli to index finger pulp could not evoke any iSMI responses. Furthermore, electrical stimuli to median nerve could evoke iSMI responses in only 2~50 % of examined subjects or/and patients in previous studies [9,10,11,12,13].

One possible explanation is that when electrical stimulation is applied to a given nerve (e. g. median nerve), simultaneous excitation of different sensory afferents occurs [5]. These all-or-none-activated afferents of different related receptors (i.e. nociceptive, thermal, proprioceptive, tactile, and others) have different time responses and also exhibit differences in cortical integration [14]. Although many researchers [2,5,15] recommend that electrical stimuli be applied to a tested fingers rather than to mixed nerves, in order to avoid proprioceptive components from interfering with the tactile inputs at the cortical level, our electrical stimuli to index finger pulp failed to evoke iSMI responses. We therefore hypothesize that neural interaction between the inputs of different sensory afferents, elicited electrically at the cortical level, suppresses the iSMI evoked fields.

On the other hand, mechanical stimuli can selectively activate cutaneous mechanoreceptors [16,17]. As a result, it is hypothesized that mechanical stimuli delivered a more selective tactile sensory input without the non-tactile inputs (proprioceptive, thermal, and others); in this way, iSMI responses can be consistently detected with mechanical stimuli rather than electrical stimuli.

One question that may still exist is that the touch corresponding sensory afferents are a part of the whole nerve sensory afferents (touch, proprioceptive etc.); hereby one may expect that touch-related cortical activation (compression-SEFs) would be a part of nerve-related cortical activation (electrical-SEFs). However, why did our results indicate that the opposite is the case, that compressive stimuli elicited more cortical areas (e.g. iSMI) than electrical stimuli? A study [17] shows that subjects` perception of mechanical skin indentation of a specific rapid mechanoreceptor receptive field was larger than subjects` perception of peripheral electro-microstimulation to the corresponding single afferent fiber of that receptive field. Therefore, the conclusion there [17] is that more cortical nerve cells and cortical regions need to be activated at the somatosensory level to produce a perception experience evoked mechanically rather than a perception experience evoked electrically. Moreover, pain-related SEFs studies [18,19] show the existence of separate and different activated cortical areas between selective nociceptive afferent stimulation (e.g. CO_2 laser beam) and painful electrical stimuli to the corresponding nerve bundle.

Another possible explanation is that electrical-iSII responses were relatively stronger than those in compressive-iSII responses. Therefore, iSMI evoked field could be masked by the relatively strong electrical-iSII activation, whereas the less activated compressive-iSII did not conceal or mask the iSMI. Therefore, we could detect iSMI response with compressive stimuli rather than electrical stimuli.

The overall pathway of sensory input to iSMI cortex has been the subject of considerable debate, based on observed iSMI evoked field latencies. One possible pathway is the transcallosal pathway, since it is assumed that the transcallosal pathway may contribute to the slow iSMI response with a peak latency of 80~300ms [10,11], and the iSMI response of a wide wave form that appeared at 40~50ms and peaked at 180ms [13].

Also of note, compressive stimuli were able to evoke iSII (n=9) and cSII (n=3) responses. The cSII response, with compressive stimuli, could also be observed around 70~100ms in the rest of our subjects (n=6 out of 9), but there no successful dipole fitting could be made. This was probably due to the strong compressive-cSI responses, in terms of recorded amplitudes that SQUID can detect.

Although electrical stimuli with inter-stimulus interval of ≥1s could evoke SII responses [20] and we set it for decompression at 2.3s, we detected no SII cortical responses with decompression. One possible explanation is that the SII responses were related to stimulus strength, in terms of faster stimulus being a stronger stimulus and vice versa, since compression were approximately 4 times as strong (fast) as decompression. However, subjectively strong (fast) decompressive stimuli could not evoke SII responses [6,7]. In addition, despite the difference in nature of the stimuli, weak electrical stimuli (at twice the sensory threshold) could evoke SII responses [21].

An alternative explanation is that SII responses were sensitive to changes in tactile inputs [22], which are related to subject attention [23]. In short, a 2.3s period of subject adaptation after strong compression reduced attention to weak decompression. On the other hand, weak decompression followed by strong compression with relatively short inter-stimulus interval (0.6s) may have increased attention. However, this hypothesis requires further testing, since our study protocol and design could neither confirm it nor rule it out.

Conclusion

We confirmed the existence of cortical responses to decompressive as well as compressive stimuli using non-magnetic stimulation. Mechanical stimuli evoked consistent iSMI and iSII responses, and may be useful for improving understanding of functional sensory cortical responses, since they yield more selective nerve stimulation compared with electrical stimuli.

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Figure legend

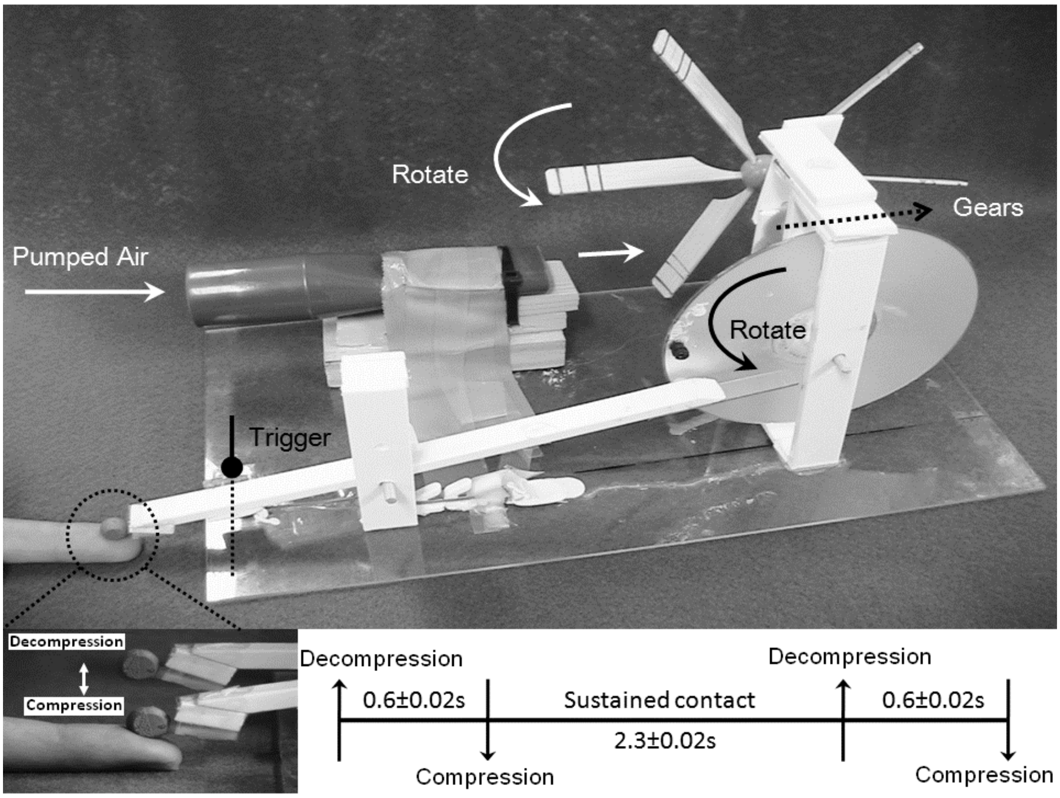

Fig.1

The tactile stimulator is activated by an air pump that is placed outside the MEG room, which pumps air into a pipe through a plastic tube. The air rotates a fan that in turn rotates a disk through a drive shaft and reduction gears. A pusher (a plastic piece mounted on the disk) pushes a plastic lever arm downward, moving its opposite end away from the index finger. In one session, this movement elicits the optic fiber trigger, and delivers decompression stimuli. When the arm is released from contact with the pusher, an elastic rubber band (attached to the base of the device and the lever arm) brings it back to compress the index finger; in this second session movement delivers compressive stimuli.

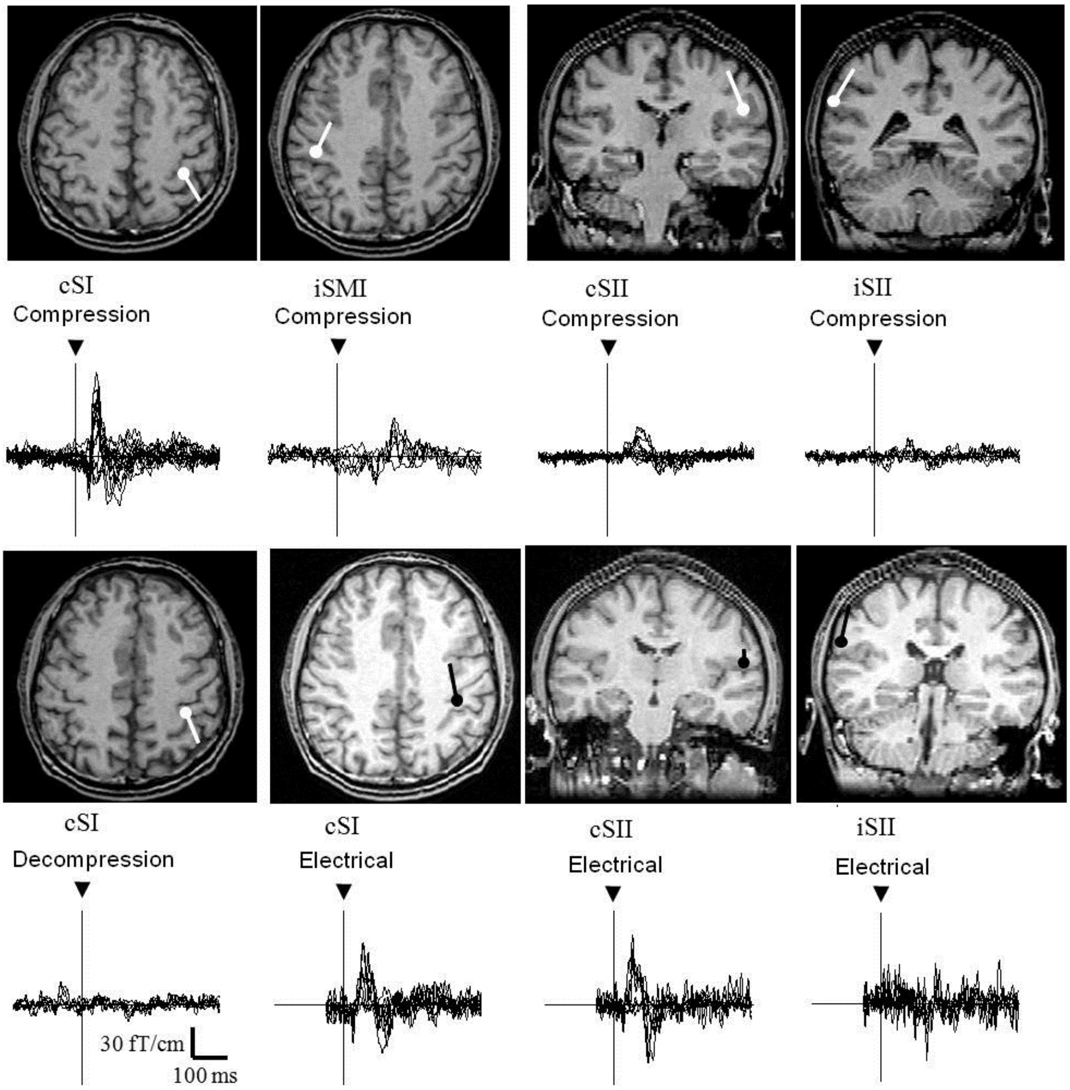

Fig.2

The source locations and SEF superimposed waveforms in a representative subject elicited by compressive, decompressive, and electrical stimuli delivered to the glabrous skin of the left index finger pulp.