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The Neural Mechanism of Audio-Tactile Integration in Human Somatosensory Cortices

인간 체성감각 피질에서의 청각-촉각 연합 신경 메커니즘

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이 논문을 이학석사 학위논문으로 제출함
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Abstract

The Neural Mechanism of Audio−Tactile Integration in Human Somatosensory Cortices

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Humans perceive the roughness of texture using tactile information, but sound information presented simultaneously with tactile information can affect the roughness judgment. However, the neural mechanism of integrating the two modalities of sensory information to determine roughness is largely unknown. In this study, we investigated whether the population neural activity in the human primary somatosensory cortex (S1) and secondary somatosensory cortex (S2) represents audio−tactile integrated information by using electrocorticography (ECoG).

In the experiment, we induced tactile illusion, through which we changed how subjects felt the roughness of texture, by presenting them with modulated friction sound simultaneously with texture.

We found that when tactile illusion occurs, the high gamma (HG, 60–150Hz) power in S2 varies according to the modulation methods of friction sound as well as texture. On the other hand, the HG power in S1 fluctuated according to the type of texture, without the influence of friction sound. These results may indicate that the HG power in S2 represents the degree of roughness felt by the subject, while the HG power in S1 represents the physical parameter of texture stimuli. Furthermore, we confirmed that the linear SVM classifier could predict the subject's judgment with the HG power data in S2. The results provide evidence that the HG activity in S2 represents audio–tactile integrated information.

Therefore, we propose that auditory information is integrated in S2 for the sequential processing of tactile information in human somatosensory cortices.

Keyword : Multisensory integration, Secondary somatosensory cortex, High–gamma activity, Roughness, Electrocorticography, Human brain

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Contents

1. Introduction

1.1. Study Background

Tactile perception is essential to fully understand the environment. Roughness perception, which is the most representative among various types of tactile perception, usually requires an intricate interplay between tactile and auditory information[1,2]. It has been believed that the two sensory modalities are deeply interconnected, as both texture and sound information are characterized by frequency[3]. Previous behavioral experiments demonstrate that auditory information affects tactile roughness judgments[4–6], but the underlying neural mechanism has not yet been revealed.

Most studies on multisensory process have focused on audio–visual integration, and little is known about audio−tactile integration[7,8]. In the past, there was a strong belief that multisensory integration occurs in high−level association cortices after unisensory processing in each low−level sensory cortex[9,10]. However, recent studies using high−resolution techniques have suggested that multisensory integration occurs in low−level sensory cortices, providing electrophysiological and neuroimaging evidence of integration−related responses in the sensory cortices[11–13]. From the perspective of roughness perception, it is well known that texture information is processed sequentially in the primary somatosensory cortex (S1) and the secondary somatosensory cortex (S2)[14–16]. Therefore, it is worth investigating whether audio−tactile integration process also occurs in the somatosensory areas during roughness perception.

Recent human fMRI studies have shown that auditory stimulation can activate S1 and S2, namely the somatosensory areas[17]. More specifically, it has been found that the activation patterns in the somatosensory areas are related to auditory frequency information[18], which may imply that the integration of auditory and tactile information can occur in the somatosensory areas. In fact, it has been recently reported that both touch selective neurons and sound selective neurons coexist in S2 of mice, and the degree of neuronal activity of each sensory modality is affected by the other[19]. Therefore, to verify that audio−tactile integration indeed occurs in the human somatosensory cortices, it is necessary to confirm that neural responses in S1 and S2 are affected by auditory input and consequently correspond to what people actually perceive.

1.2. Purpose of Research

At the population level, it is known that high−gamma (HG) power is related to local high−frequency synaptic and spiking activity[20–22]. We previously confirmed that HG power in human S1 and S2 depends on the roughness of textures through experiments in which only tactile information was provided[16]. Based on these results, we hypothesized that the HG power in S1 and S2 represents the degree of roughness perceived through audio−tactile integration rather than the physical parameters of textures. To test this hypothesis, we designed two alternative forced choice tasks to confirm that tactile illusion had occurred, which signifies that roughness was perceived differently due to auditory information. Subjects were instructed to compare the roughness of textures presented in pairs under various auditory conditions. We verified our hypothesis in three steps. First, we aimed to investigate whether the HG power in S1 and S2 differ according to the roughness of textures when only tactile stimuli are presented. Second, we tested whether the HG power differ according to the roughness of textures even while unmodulated friction sounds are presented simultaneously. Finally, we investigated whether the HG power differ according to the modulation of friction sound, which is when tactile illusion occurs. At the end of these steps, we found out that the HG power in S1 and S2 differ according to the roughness of textures regardless of the existence of auditory information. We discovered, however, that only the HG power in S2 differs according to the auditory stimuli. Additionally, we could predict subjects' behavioral responses with high accuracy through the HG power data in S2. This suggests that human S2 plays a key role in audio−tactile integration after receiving tactile information processed primarily in S1.

2. Materials and Methods

2.1. Subjects

8 patients (6 females) participated in this study, and were implanted with subdural electrode arrays for the purpose of localizing the epileptogenic zone. Electrode arrays were placed across multiple brain regions in each subject to suit the purpose of monitoring, and the electrodes covered S1 (Subject 1-6) or S2 (Subject 7, 8) areas. All subjects underwent preoperative MRI and postoperative CT. All procedures were approved by the Institutional Review Board of Seoul National University Hospital (H-1810-023-978). Prior to the experiment, direct consent was obtained from all subjects.

2.2. Experimental design

We aimed to induce tactile illusion in which roughness is perceived differently due to the influence of modulated friction sound as well as to confirm whether the HG power in the somatosensory areas represents the degree of roughness that subjects perceive through audio-tactile integration.

We used two-alternative forced choice paradigm, of which the main task was the discrimination of roughness between two sequentially presented tactile stimuli. The duration of each stimulation period was 1.8 seconds, and the interstimulus interval was 1.5 seconds. Subjects were instructed to answer which one was rougher by pressing the button after the second stimulation.

For tactile stimulation in each trial, two texture stimuli were presented in pairs to the index finger pad contralateral to the implantation hemisphere by a custom-made "Texture Drum" equipment. We used sandpaper, a standardized texture, for texture stimulation. Texture conditions were created by using two types of sandpaper: "Rough texture" (600-grit sandpaper, average particle diameter: 25.8 μm) and "Smooth texture" (1200-grit sandpaper, average particle diameter: 15.3 μm). We selected the sandpapers after the pilot test, which confirmed that the subject could distinguish the two textures with about 80% accuracy and experienced no pain after a long period of contact. It should be noted that the roughness of the two textures is quite similar. In the trials, two conditions of tactile stimuli were presented in random sequence: In T1 condition, Rough texture was presented first and Smooth texture was presented second. In T2 condition, Smooth texture was presented first and Rough texture was presented second (Figure. 1A).

For auditory stimulation, while texture stimuli were being presented, friction sounds generated by touch between the finger pad and the textures were also presented. In order to confirm the effect of auditory information on roughness perception, the friction sounds were modulated in various ways. We utilized four modulations: "Mute," "Unmodulated," "Amplified," and "Attenuated" [4,5]. No sound was delivered to the subjects during the Mute period, while unmodulated friction sound was delivered to the subjects during the Unmodulated period. In the real-time-recorded sound spectrum, the magnitude of sound above 2kHz was amplified or attenuated by 15dB. Then the modulated sound was delivered to subjects during the Amplified period and Attenuated period, respectively. In the trials, four conditions of sound stimuli were presented in random sequence: In A1 condition, only tactile information was presented during the first and second stimulation periods without any sound. In A2 condition, Unmodulated friction sound was presented during the first and second stimulation periods. In A3 condition, Amplified friction sound was presented in pair with the Rough texture and Attenuated friction sound was presented in pair with the Smooth texture. In A4 condition, contrary to A3 condition, Attenuated friction sound was presented in pair with the Rough texture and Amplified friction sound was presented in pair with the Smooth texture (Figure. 1A).

After the subjects pressed the response button, the next trial begun. The experiment was conducted over two blocks with a short break in between each block. In each block, stimulus pairs were presented 40 times (5 repetitions × 8 pairs (combination of 2 tactile conditions and 4 auditory conditions)), comprising a total of 80 trials (stimulus pairs). Each block took about 7 minutes.

2.3. Apparatus

For tactile stimulation, we used a custom-made “Texture Drum” equipment inspired by the system at Bensmaia’ s Laboratory of Chicago university[23]. It is comprised of a rotating drum, where four pairs of texture strips are attached at the front and the back. In this study, only two pairs of textures were used. With the subjects' hands immobilized, the drum was rotated to present texture stimuli to the subjects' index finger pad contralateral to the implantation hemisphere. In each trial, the drum rotated once, and a pair of texture stimuli were presented in the front-touch section and back-touch section, once in each section, respectively. After the subjects pressed the response button, the drum moved to the side for the next trial (Figure. 1B). Two motors were used to control drum movement, one to rotate the drum and the other to move the drum from side to side. The motors were shielded to prevent potential noise generation (Figure. S1A). The width of the drum was 12 cm, while the diameter of the no-touch and touch section was 14cm and 15 cm, in the respective order. The subjects' fingertip and the textures touched at 10 cm/s. The equipment was controlled through micro control unit(atmega128) and MATLAB commands were delivered to the unit via serial communication. We attached a curtain to the equipment to prevent the subjects from acquiring visual information about the textures during the experiment (Figure. S1B).

For auditory stimulation, a microphone (EM-XSW 2, Sennheiser) was installed around the touch site to let the patients hear the friction sound in real time. To deliver the sound, we used earphones (Earphone Insert 10 ohm 1/4 Stereo, Neuroscan) to which earplugs were attached for the purpose of blocking external noise. The earphones delivered sound via air tube, not via electric wire, thereby preventing possible artifacts generation. We used an audio mixer (Studiolive AR12 usb, Presonus) for modulation, and in each trial, the demultiplexer sent the input sound to the adequate mixer line in the order of the stimuli. During the experiment, the sound delivered to the patient was stored through DAQ system and used for further analysis (Figure. S1C).

2.4. ECoG data acquisition and preprocessing

ECoG data were recorded with Neuroscan (Compumedics) or Neuvo (Compumedics) at a sampling rate of 2000Hz. Then, all analysis was performed using Matlab. The data was band-pass filtered at 0.1~150Hz and notch filtered with a FIR filter to remove systematic noise at 60, 120Hz to prevent noise from the power source. Channels with impedance greater than 20 kΩ or those with epileptiform activities were excluded from analysis. The data was re-referenced to the common average reference (CAR) and epoched with a window of −2.5s to 10s of the first stimulus onset. Considering that the subjects' hand size varies and that the position of the hand may vary slightly from trial to trial, we tried to select the onset point as accurately as possible using the recorded sound.

For a time-frequency analysis, the complex Morlet wavelet transform was applied to the epochs. Transformed single-trial data were squared for calculating power and then normalized by the mean and standard deviation of the baseline (−1.5s to −1s of the first stimulation onset) power of each frequency. Note that the normalized data does not indicate the Z-score[16]. Thereafter, the normalized power values between 60 Hz and 150 Hz were averaged for HG power analysis. A trial in which the HG power during the baseline and stimulation periods deviated from the 3-standard deviation of all trials was considered as an outlier and excluded from the analysis. A trial in which the subject' s response time deviated from the 3-standard deviation of all trials was also excluded from the analysis.

2.5. S1, S2 electrodes selection

Talairach coordinates of every electrode were obtained from MRI-CT co-registration with CURRY software (version 7.0 or 8.0, Compumedics). We chose S1 and S2 electrodes based on anatomical landmark (S1: the hand knob of the post central gyrus, S2: the upper limb of the Sylvian fissure in the parietal region) and neural responses demonstrated in previous ECoG studies (S1: The high peak pattern immediately after onset, immediately before offset, and the continuous activities between them, S2: Delayed and long-lasted activation)[16,24].

The perception of roughness is a tactile-dominant process that occurs regardless of the presence of an auditory input, and the process occurs in both the first and second stimulation periods. Therefore, only electrodes that show significant HG responses during both the first and second stimulation periods in A1 condition were included in further analysis. We performed the two-tailed Wilcoxon signed rank test ($p<0.001$) to select electrodes that show significant HG activities in both stimulation periods compared to the baseline.

2.6. Averaged HG power comparison

We wanted to confirm that the HG power represents the degree of roughness for all subjects consistently. However, since the number of electrodes was different by subject, the statistical result could be biased towards certain subjects with greater number of electrode implants. Therefore, to prevent bias, HG power from previously selected electrodes of each subject was averaged. Furthermore, the HG power was averaged across the stimulus period that ranged from 300ms after stimulation onset to 300ms before stimulation offset, in which the stimuli were presented at constant intensity (the dashed box in Fig. 2B). The HG power immediately after the stimulation onset and immediately before the stimulation offset, where the intensity of the stimuli changes, was not included in subsequent analysis.

We hypothesized that the HG power in S1 and S2 represents the degree of roughness perceived through audio−tactile integration rather than the physical parameters of textures. We verified our hypothesis in three steps: First, we compared the HG values during the Rough and the Smooth texture periods in trials where tactile information was presented without auditory information (A1 condition). Second, we compared the HG power during the Rough and the Smooth texture periods in trials where tactile information was presented with Unmodulated friction sound (A2 condition). Finally, in order to confirm whether the HG power in S1 and S2 differ according to the modulation of friction sound, we compared the HG power during the Amplified friction sound periods and the Attenuated friction sound periods. Before statistical analysis, the Kolmogorov–Smirnov test was performed to test the normality of the HG power data, but the null hypothesis was not rejected, so the Wilcoxon test was used for further analysis.

In the first step, the Wilcoxon signed–rank test (two–tailed) was performed for each subject to evaluate the difference in the HG power between the two texture periods. In addition, we wanted to ensure that the difference pattern was consistent among subjects. We averaged the HG power across the trials in A1 condition for each subject. One pair of data, consisting of the HG power value from the Rough texture period and that of the Smooth texture period, was obtained for each subject. The average HG power data of the subjects with electrodes on S1 were included in the same sample. After constructing the samples, we conducted the Wilcoxon signed–rank test again. Since there were two subjects with electrodes on S2, statistical processing was not performed for S2 data. In the second step, the same process was performed as in the first step with HG power data in A2 condition.

In the third step, we evaluated the difference in the HG power between the Amplified friction sound and Attenuated friction sound periods. We conducted the Wilcoxon signed–rank test (two–tailed) with the HG power data in A3, A4 conditions. The test was conducted for the data of each subject.

2.7. Predicting the subjects' behavioral responses using HG power data

First, we confirmed whether the HG power data was classified according to the subject's behavioral response, during which the subjects successfully discriminated the roughness of the texture in A1 or A2 conditions. For the classification, the linear support vector machine (SVM) was used. The HG power value during the first and second stimulation periods in each trial were provided as input. It should be noted that only the HG power data of the correct trials were used for classification. Therefore, the classification made according to the subjects' behavioral responses is consistent with the classification made according to the tactile stimulation conditions.

Subjects made decisions corresponding to what they perceived through a combination of tactile and auditory information. Therefore, we thought that if the HG power values in S1 and S2 represent the perceived roughness, it should be possible to predict the subjects' behavioral responses through the HG power. The previous SVM model, which classified the HG power data in A2 condition, eventually mimics the roughness discrimination process using tactile information and auditory information. We checked whether the previous SVM model could predict the subject's response even when the HG power data in A3 and A4 conditions were provided as input.

3. Results

3.1. Behavioral results showing the induction of tactile illusion

First, in order to confirm that the presence of auditory information has an effect on roughness discrimination, we compared the subjects' discrimination accuracies in A1 and A2 conditions (Figure. 2A). Subjects distinguished the roughness of the two textures with an average accuracy of 89.03% and 90.88% in A1 and A2 conditions, respectively. There was no significant difference in accuracy between A1 and A2 conditions (two-tailed Wilcoxon signed-rank test; $p = 0.297$).

Secondly, in order to confirm the effect of modulated auditory information on roughness discrimination, we compared the subjects' discrimination accuracies in A3, A2, and A4 conditions (Figure. 2B). The average discrimination accuracy was 92.45%, 90.88% and 77.45% in A3, A2, and A4 conditions, respectively. Although the discrimination accuracies of subjects were significantly different between A3 and A4 conditions (two-tailed Wilcoxon signed-rank test; $p = 0.016$) and between A2 and A4 conditions (two-tailed Wilcoxon signed-rank test; $p = 0.039$), the difference was not significant between A3 and A2 conditions (two-tailed Wilcoxon signed-rank test; $p = 0.578$). Since the textures can be easily distinguished with an average accuracy of 90% or more in both conditions, the difference in discrimination accuracies between A3 and A2 conditions would not have been significant. By satisfying the following criterion, the subject was regarded as "Illusion−induced subject":

Accuracy in A3 condition ≥ Accuracy in A2 condition ≥ Accuracy in A4 condition

Subject 2 and Subject 8 did not satisfy the criterion. Based on the subjects' behavioral responses, we confirmed that illusion was induced as we intended, except for these two subjects.

3.2. Selected electrodes & HG activities during the stimulation periods

We selected electrodes that showed significant HG activity compared to the baseline, which were those on S1 of Subject 1 to Subject 6 and on S2 of Subject 7 and Subject 8 (Figure. 3A). The HG power in S1 peaked after 130ms based on the onset of stimulation, and before 100ms based on the offset of stimulation (Figure. 3B. Left). It was confirmed that the HG activity in S1 is maintained between the two peaks, and the difference in activity between the two textures appears during the maintenance period. Whereas the HG power in S2 has a delayed peak after 380ms based on the onset of stimulation, there was no notable peak around the offset (Figure. 3B. Right). These patterns of HG activity were constant regardless of the presence of friction sound, and were consistent with the features we saw in the previous study[16].

3.3. Difference in HG power according to the textures

First, we compared the HG power during the Rough and the

Smooth texture periods in trials where tactile information was presented without auditory information (A1 condition). The analysis was conducted separately for the data of correct trials (Figure. 3C. top) and incorrect trials (Figure. 3C. bottom). Among the subjects, the HG power of Subject 2 (with electrodes on S1) showed a significant difference between the two textures. Since the two textures were quite similar, there would have been no significant difference in the data of other subjects. Nevertheless, we confirmed that all subjects' HG power was greater during Rough texture periods than during Smooth texture periods ($p = 0.031$; two-tailed Wilcoxon signed-rank test for S1 subjects). However, no significant difference was found in the data of the incorrect trials, and there was no commonality between the subjects.

Second, we compared the HG power during the Rough and the Smooth texture periods in trials where tactile information was presented with Unmodulated friction sound (A2 condition). Again, the analysis was conducted separately for the data of correct trials (Figure. 3D. top) and incorrect trials (Figure. 3D. bottom). Among the subjects, the HG power of Subject 7 (with electrodes on S2) showed a significant difference between the two textures. We confirmed that all subjects' HG power was greater during Rough texture periods than during Smooth texture periods ($p = 0.031$; two-tailed Wilcoxon signed-rank test for S1 subjects). There was no significant difference in the data of the incorrect trials, and there was no commonality between the subjects.

These results show that the HG power in S1 and S2 represents the degree of roughness, regardless of the presence of auditory information. Although the two textures were quite similar, the HG patterns in S1 was replicated as we confirmed through the previous study[16]. However, the HG patterns in S2 was different from the results of the previous study, and this will be discussed in the latter section.

3.4. Difference in HG power according to the friction sound

In section 3.1, we confirmed that the subjects felt the roughness of textures differently according to the modulation method of the friction sound, except for Subject 2 and Subject 8. If the HG power in S1 or S2 represents the degree of roughness that a subject perceives, the power should also be different between two modulation methods (Amplified versus Attenuated). We compared the HG power during the Amplified sound and the Attenuated sound periods using the data from A3 and A4 conditions (Figure. 4A). We found significant difference only in the HG power of Subject 7 with electrodes on S2 between Amplified periods and Attenuated periods ($p = 0.013$; two−tailed Wilcoxon signed rank test; Figure. 4B; Figure. 4C). Interestingly, we found no significant difference in the data of Subject 8 (no illusion−induced) between Amplified periods and Attenuated periods, although the HG power was measured on S2 like Subject 7 (Figure. 4D). None of the HG power in S1 showed significant difference.

However, we could not rule out the possibility that the HG power of S2 changed due to the difference in sound intensity between the two auditory modulation methods, not due to the difference in roughness felt by the subject. To address this issue, we conducted additional experiments on the same subjects to confirm that the HG power measured on the S2 electrodes did not change simply due to the intensity of sound stimulation (Figure. S3A). In the additional experiments, only auditory stimulation (262 Hz pure tone) was presented without tactile stimulation. Large and small sound stimuli with a duration of 100ms were alternately presented. As a result, we confirmed that there was no significant HG response compared to the baseline when only auditory stimulation was presented, and that the HG power did not simply vary according to the sound intensity (Figure. S3C; Figure. S3F). On the other hand, significant HG responses were recorded on electrodes placed on the auditory cortex close to S2. We confirmed that the HG power in the auditory cortex changes with the intensity of the sound (Figure. S3D; Figure. S3G).

3.5. Predicting the subjects' behavioral responses

We checked whether the HG power data was classified according to the subjects' behavioral responses using data from A1 and A2 conditions (Figure. 5A; Figure. 5B). First, we checked the classification performance of the SVM when the HG power data in S1 was provided as input. The SVM classifier could classify the HG power data from A1 condition and A2 condition with an average accuracy of 73.53% and 77.37%, respectively. Subsequently, we checked the classification performance of the SVM when the HG power data in S2 was provided as input. When the HG data from A1 condition was used as input, the SVM classifier could classify the data with an average accuracy of 66.84%. Interestingly, however, the SVM classifier could classify data with an average classification accuracy of 93.65% when the HG power data from A2 condition was provided as input.

Finally, we checked whether the classifier used in the classification of data from A2 condition could predict the subjects' behavioral responses when data from A3 and A4 conditions were used as input. The average prediction accuracy was 56.08% when the HG data in S1 was provided as input. The prediction accuracy was quite low considering that the chance level was 50%. On the other hand, when the HG power data in S2 was provided as input, the average prediction accuracy was 78.01%.

4. Discussion

4.1. Summary

A classic method of confirming multisensory integration involved a passive presentation of sensory stimuli to subjects. However, since neural activity can vary depending on the degree of attention during stimulation periods[25,26], we used two alternative forced choice paradigm to capture and hold the subjects' attention on the stimulation. In addition, by checking the behavioral accuracy of the subjects, we could gather quantitative evidence on whether tactile illusion had occurred.

We confirmed that subjects felt texture stimulus to be rougher when presented with amplified friction sound and smoother when presented with attenuated friction sound. Tactile roughness information is known to be processed in the somatosensory cortices. If the integration of tactile information and auditory information occurred in the somatosensory cortices, the neural response in the according area would represent the degree of roughness the subject felt through audio-tactile integration. We confirmed that the HG power in S1 and S2 represent the roughness of texture when tactile information was presented without auditory information. In addition, it was verified that the HG power in S1 and S2 represent the roughness of the presented texture even when unmodulated sound was presented simultaneously.

Thereafter, we investigated whether the HG power varies when texture is felt to be rougher or smoother according to the method of sound modulation. The HG power in S1 did not change according to sound modulation. Interestingly, in S2 of the illusion-induced subject, the HG power changed according to the sound modulation, whereas in S2 of the subject in which illusion did not occur, the HG power did not change. This finding suggests that the HG power in S2 represents the degree of roughness felt by the subject, while the HG power in S1 represents the physical parameter of texture stimuli.

We thought that if the HG power in S2 represents the roughness felt by the subjects, subjects' behavioral responses could be predicted through the HG power data. Specifically, we expected that the behavioral response could be predicted through the data when the modulated sound was presented, regardless of whether illusion occurred or not. The HG power data from trials under A3 and A4 conditions was entered into a SVM classifier, trained with data from A2 condition. Then, the SVM classifier predicted the subjects' behavioral responses in these trials.

We thought that if the HG power in S1 or S2 represents the roughness felt by the subjects, subjects' behavioral responses can be predicted through the HG power data. The HG power data from trials under A3 and A4 conditions was entered into the SVM classifier, which was trained with data from A2 condition. Then, the SVM classifier predicted the subjects' behavioral responses in these trials. As a result, behavioral response could be predicted with high accuracy through the HG power data in S2 regardless of whether illusion occurrence in subjects. Nonetheless, behavioral response of subjects could not be predicted through the HG power data in S1. Thus, we reconfirmed that the degree of roughness, i.e., the audio–tactile integrated information, can be represented by HG power in S2, rather than in S1.

4.2. Tactile illusion during roughness perception

A previous study also confirmed that subjects judged texture to feel rougher or smoother when friction sound was amplified or attenuated within a frequency range of 2 to 20kHz[5]. However, the reason behind the phenomenon is yet to be clarified. Guest suggested that the amplified sound may have led to the illusion of stronger friction based on "a phenomenon in which stronger touches produce stronger sounds[27]." On the other hand, Yau argued that the frequency of sound may be the cause of varying perceptions of tactile stimuli[6], based on the fact that texture information and sound information share a sensory dimension of 'frequency.' Through carefully conducted experiments, he confirmed the phenomenon where vibrotactile stimulation is felt to be of higher frequency when a higher frequency sound is presented. Meanwhile, he reported that the change in sound frequency does not affect the evaluation of vibro–tactile stimulus intensity.

However, there is a contradiction between Yau' s results and that of Guest' s. The distance between surface particles is farther apart in rougher texture rougher textures, resulting in lower frequency vibrations when rubbed. To bring Yau' s results in line with Guest's claim, it would make more sense to perceive the vibrotactile stimulation frequency to be lower when presented with a higher frequency sound. Furthermore, it has not been reported whether tactile stimulation intensity is felt differently when various sound intensities are provided. Above all, since rubbing texture creates spatial codes and complex vibration that consists of a wide range of frequency components, the process of perceiving texture and the process of perceiving sinusoidal vibration are different[28,29].

We performed spectrum analysis with the friction sound presented to subjects (Figure S2. A). Since the two textures used in the experiment were quite similar, the friction sound generated when rubbing the two textures was also similar (Figure S2. D). It was confirmed that the friction sound of the two textures consisted mostly of 2 kHz to 20 kHz (modulated frequency band). Since we modulated and presented the volume of the sound in the according frequency band (2 kHz - 20 kHz), the subjects would have perceived the magnitude of friction sound differently. Based on these results, it is highly possible that the change in sound intensity, rather than frequency-shift of sound, caused the illusion.

4.3. The process of roughness perception in human somatosensory system

It is known that the tactile roughness information propagated from mechanoreceptors in the skin is processed in S1 and S2 sequentially and then transmitted to IPL known as the sensory association area[15,30]. The degree of roughness of texture is determined by various physical parameters of texture surface. The spatial and temporal features of the complex vibration, generated by rubbing between the finger pad and the texture, play an important role[16,31–34]. In general, the vibration generated when perceiving a rougher texture has a lower median frequency and a greater magnitude in spectrum, while the vibration generated when perceiving a smoother texture has a higher median frequency and a smaller magnitude[34]. Various textural information is coded by Merkel cells (SA1), Meissner corpuscles (RA1), and Pacinian corpuscle (PC)[28,35]. The sandpapers used in this experiment were fine textures with particle size of less than 30 μm, so it would have been coded mainly by RA1 and PC neurons[23,33].

The coded information transmitted through the sensory nerves reaches the somatosensory cortices of the brain. The tactile information is processed sequentially in S1 and S2 for further high-order elaborations[14,36,37]. In our earlier study, we confirmed that the HG power in S1 and S2 varies depending on the roughness of the texture and suggested that texture information is processed sequentially in both areas[16]. In the previous studies, we confirmed that the HG power in S2 was stronger when smooth texture was presented. However, the result is contrary to the HG pattern of S2 found in our current research, which could be contributed to two reasons: The difference in particle size of textures and the intensity of stimulation.

First, the difference in particle size between two textures was greater than that in the present study. 2mm grid texture was used as rough stimulus, which is mainly texture coded by RA1. For smooth stimulus, fine texture with an average particle size of less than 50 μm, which is mainly coded by PC, was used in our earlier study. In S1, the proportion of RA1 neuron is higher than that of PC neuron, whereas in S2, the proportion of PC neuron is higher than that of RA1 neurons[32,38]. Therefore, since PC neurons were greatly activated in the process of coding the fine texture, it is possible that the HG power in S2 was stronger when the fine texture were presented. In contrast, the two textures used in this experiment were quite similar to each other, and the particle size of the two textures we used in this experiment (<30 μm) was smaller than that of smooth texture used in our earlier experiment (<50 μm). According to previous studies using sandpapers similar to the one used in the current study confirmed that the PC neurons' activity patterns were similar when sandpaper roughness was different. Instead, it was confirmed that the rougher the stimulus, the greater the activity of RA1[28,35]. For this reason, it is possible that this experiment obtained the result that HG power is larger in S2 as well as in S1 when perceiving the rough texture.

Second, the reason can be considered from the perspective of stimulus intensity. Previous studies showed that neural activity of somatosensory cortices increased as tactile stimulus intensity increased[39–41]. It is possible that the HG power increased in both S1 and S2 because high intensity vibrations occurred between the texture and the finger when a rougher texture was presented.

Roughness is perceived by combining various surface factors, and neural activity may appear in various aspects depending on the type of texture. The neural activities in S1 when touching various textures have been revealed to some extent through primate studies[23]. Although, previous studies have indicated that S2 is most likely involved in texture perception, these studies mainly used textures with large particle sizes. Considering that preprocessed information in S1 is delivered to S2, it is not yet clear how the neural activities in S2 will appear when perceiving various types of textures. Our study used only two stimuli due to safety and time constraints, S2 response to more diverse texture stimuli should be further revealed in the future.

4.4. Audio-tactile integration in human S2

In the past, it was believed that each modality of sensory information was processed in each sensory cortex and then combined in high-order areas such as the posterior parietal cortex (PPC) and the prefrontal cortex (PFC). However, recent studies have shown that neural response related to multisensory integration appears in the sensory cortices, indicating that sensory association takes place in the sensory cortices. In this study, we thought that if multisensory integration were to occur in the sensory cortex, the neural response in the sensory cortex would represent integrated sensory information.

We confirmed that the HG power in S2 represents the degree of roughness perceived through audio-tactile integration. In the past, somatosensory cortices were known to process only tactile information. However, recent human fMRI studies have reported that S2 is activated even when only auditory stimulation is presented, and the degree of the activation varies depending on the frequency of the presented auditory stimulation[18,42,43]. These results may indicate that neurons that code auditory information and neurons that code tactile information both exist in human S2. Indeed, at the single−cell level, a previous study found that both touch selective neurons and sound selective neurons coexist in S2 of mice, and the degree of neuronal activity of each sensory modality is affected by the other[19]. By measuring neuronal activities in human S2 with higher spatial resolution, it will be possible to confirm whether neuronal response to each sensory modality can be jointly identified as roughness information in S2.

Neuroanatomically, in order to increase efficiency of brain function, the length of connection for intercortical communication should be minimized[44]. Previous anatomical studies found out that the ipsilateral auditory cortex and S2 are linked in the monkey brain[45,46]. Moreover, a previous DTI study showed that there are extensive ipsilateral connections between the auditory cortex and S2 in the human brain[47]. These neuroanatomical results provide evidence to our hypothesis that audio−tactile integration occurs in S2. Furthermore, it will be possible to further the understanding of the neural mechanism underlying audio−tactile integration by investigating the functional connectivity between the auditory cortex and S2 while tactile illusion occurs.

4.5. Limitation of ECoG analysis

ECoG has the advantage of being able to measure the neuronal population activity in the brain at high temporal and spatial resolution without brain penetration. Using ECoG has a great advantage in this study, since various neural processes related to multi−sensory integration are represented by neural oscillations in distinct frequency bands.

During multisensory integration, it is known that the bottom−up process from low−level sensory area to high−level association area and the top−down process that flows backward occur simultaneously. We wanted to investigate where the intervention of auditory information occurs in the sequential bottom−up processing of tactile information. The HG activity is known to reflect cognitive processes, and recently it has been suggested that the HG activity is associated with bottom−up neural processes[8,48]. Previous studies that analyzed the functional connectivity between the human brain areas during sensory perception tasks show that the connectivity from low−level areas to high−level areas is strong in the higher frequency bands (>30 Hz), while the connectivity from high−level areas to low−level areas is strong in lower frequency bands (<30 Hz)[49,50]. Another study researched the connectivity between layers of the macaque primary visual cortex (V1) was studied. In the study, the Granger causality in the gamma range (30–90 Hz) was directed from layer 4 to layer 3 and 5 and from layer 6 to layer 5, which indicates that the gamma−rhythm originates from the V1 layers that receive feedforward input from the lateral geniculate nucleus[51]. These results demonstrate that the HG activity reflects bottom-up process. Thus, it can be said that the HG activity that we analyzed in this study is suitable for our research on multi-sensory integration.

However, since an ECoG electrode measures the local field potential around itself, there is a possibility that signals generated in other regions are measured conjointly. In this study, despite the S2 electrodes being placed on the parietal lobe, it was likely that signal generated in other areas was involved. Although the S2 electrodes of the two subjects were located in quite similar brain regions, the HG power differs depending on the friction sound only in S2 of the illusion induced subject. In addition, when only auditory stimulation was presented, it was confirmed that the difference in the HG power of the S2 electrodes according to the intensity of sound was not significant. These results may indicate that the HG power we recorded on S2 does not simply affected by the auditory evoked responses. As discussed in the former section, further consideration will be possible if a method that can simultaneously measure the individual activity of neurons in S2 were to be used.

4.6. Conclusion

Roughness of the texture can be perceived by using tactile information without the presentation of auditory stimulus. However, it is evident that auditory information affects roughness judgment through the process of audio-tactile integration. That is, a model in which the intervention of auditory information occurs during the process of transmitting tactile information to the PPC through S1 may be constructed. In this study, we discovered that audio-tactile integrated information is represented by the HG power in S2, rather than in S1. Considering that the HG activity is largely related to the bottom-up process of brain function, it is possible that the neural information transmitted from S1 and the auditory cortex is integrated in S2. Given these points, we suggest that auditory information is integrated in S2 in the sequential processing of tactile information in human somatosensory cortices.

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List of Figures

<Figure 1>

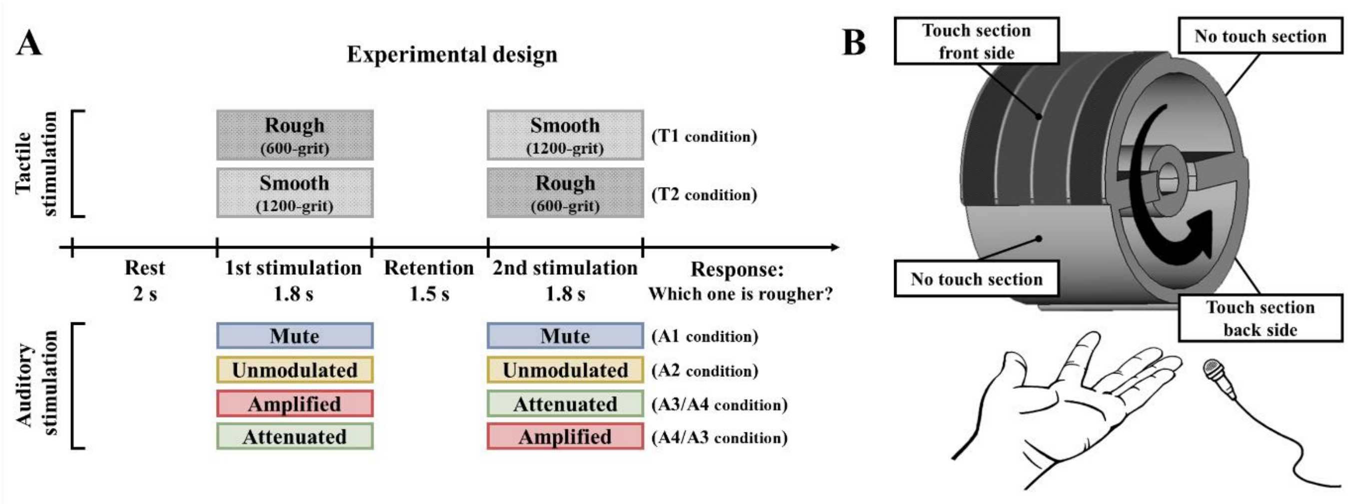

Figure 1. The experimental design used in this study. **(A)** Experimental paradigm. One of the two types of tactile stimulation conditions and one of the four types of auditory stimulation conditions were presented simultaneously. After the second stimulation period, the subjects chose the one that felt rougher between the two stimuli by pressing the button. **(B)** A schematic illustration of the Texture drum. While the subject's index finger is fixed, the drum rotates once, providing two texture stimuli. The finger pad and drum touch each other only at the Touch sections, and the friction sound generated from the touch is recorded in real time and presented as an auditory stimulus after going through one of the various modulation processes.

<Figure 2>

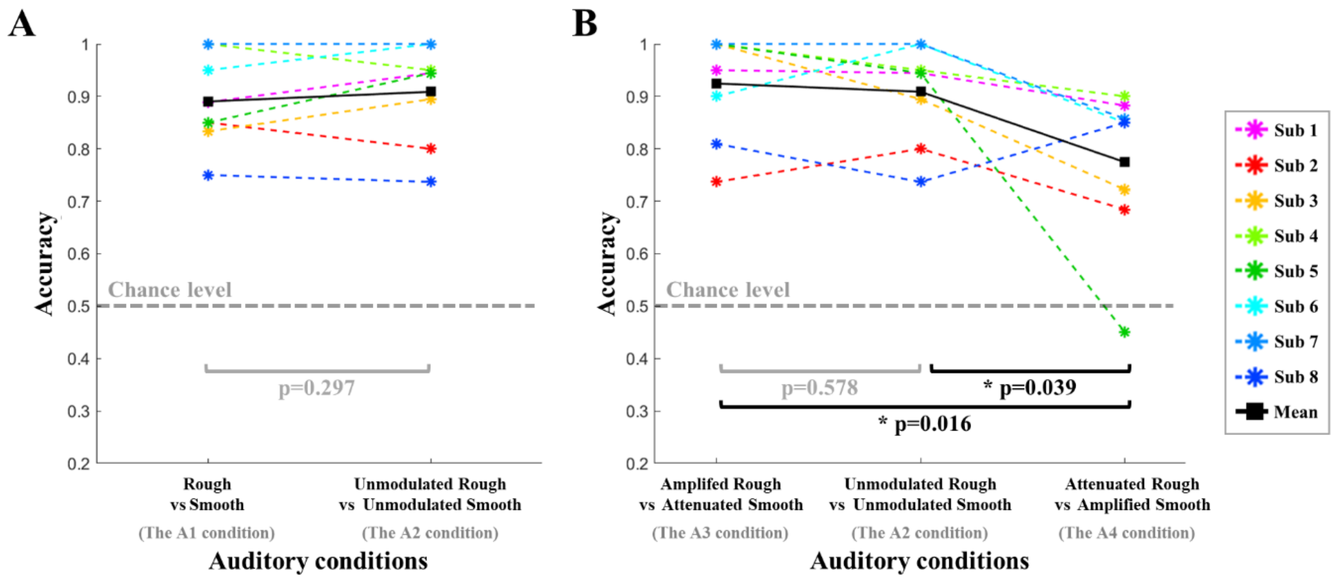

Figure 2. The discrimination accuracy of each subject. Each colored point corresponds to the discrimination accuracy of each subject. The discrimination accuracy averaged across the subjects is shown on the graph by the black-colored square. **(A)** Changes in the discrimination accuracy of each subject according to the presence of friction sound. **(B)** Changes in the discrimination accuracy of each subject according to modulation of friction sound. P-values of the Wilcoxon signed-rank test between the auditory conditions are shown together on the graph.

<Figure 3-1>

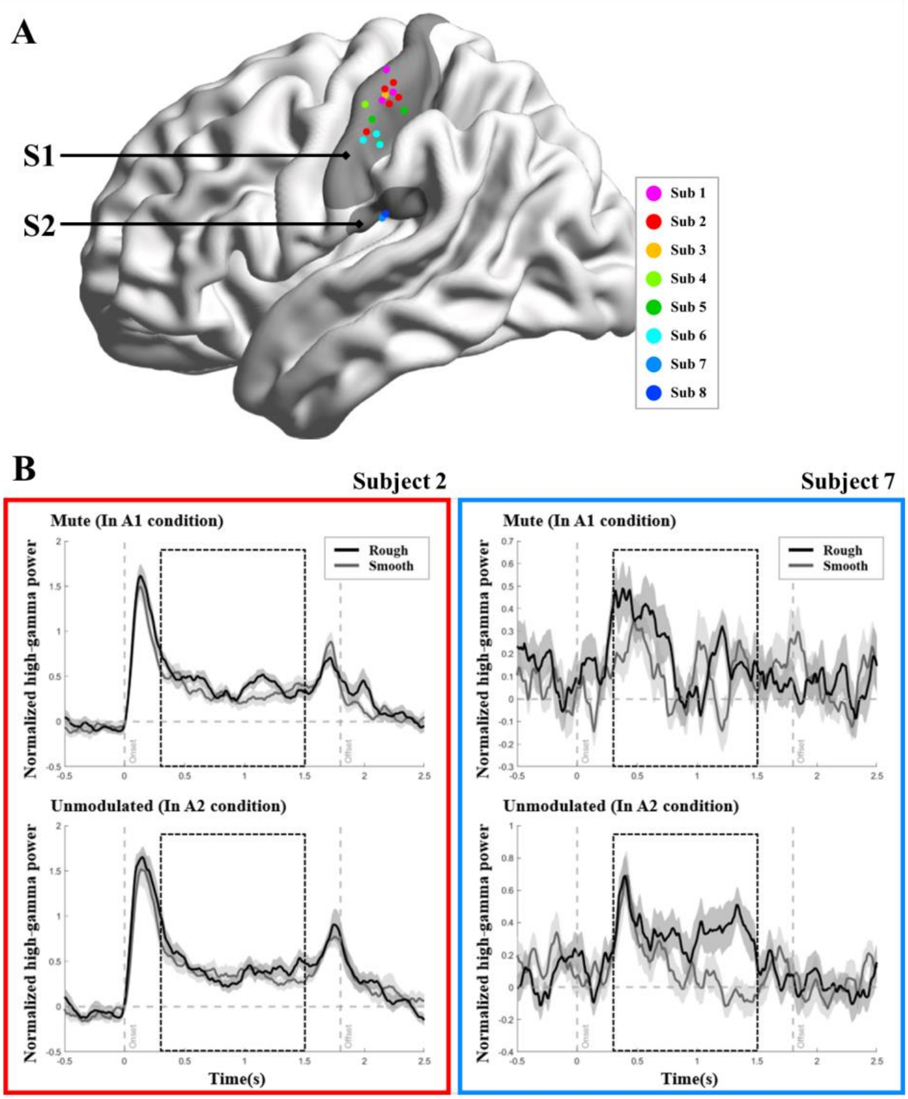

Figure 3. The difference in HG power between Rough texture periods and Smooth texture periods. **(A)** Electrodes on S1 and S2 that showed significant HG activity during the first and second stimulation periods. The MNI coordinates of the electrodes placed on the subjects' brain were marked with dots on the ICBM 152 template. Each colored dot corresponds to the electrode implanted in each subject. **(B)** The HG power time series (solid line: averaged HG power; shaded area: SE) during the Rough texture periods and Smooth texture periods that is recorded on S1 (in the red box) and S2 (in the blue box). For visualization, data were temporally smoothed with a window of 100ms.

<Figure 3-2>

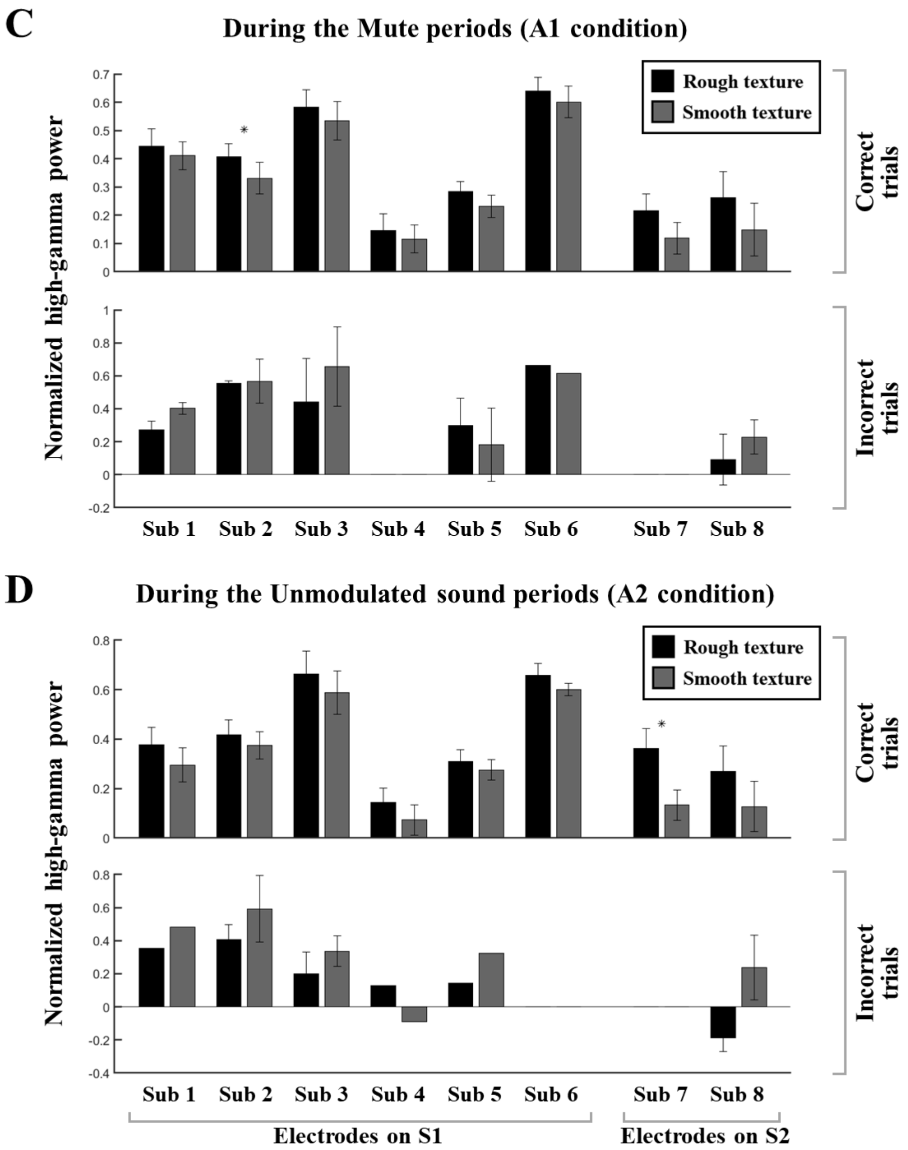

Figure 3. The difference in HG power between Rough texture periods and Smooth texture periods. **(C), (D)** Temporally-averaged (within the dashed box of B) HG power during the Rough texture periods and Smooth texture periods in A1 condition and A2 condition, respectively. Error bars indicate the SE. It was marked with an asterisk when the subject' s HG power is significantly different ($p<0.05$). If the subject answered correctly in all trials, it was not shown in the "Incorrect trials" graph.

<Figure 4>

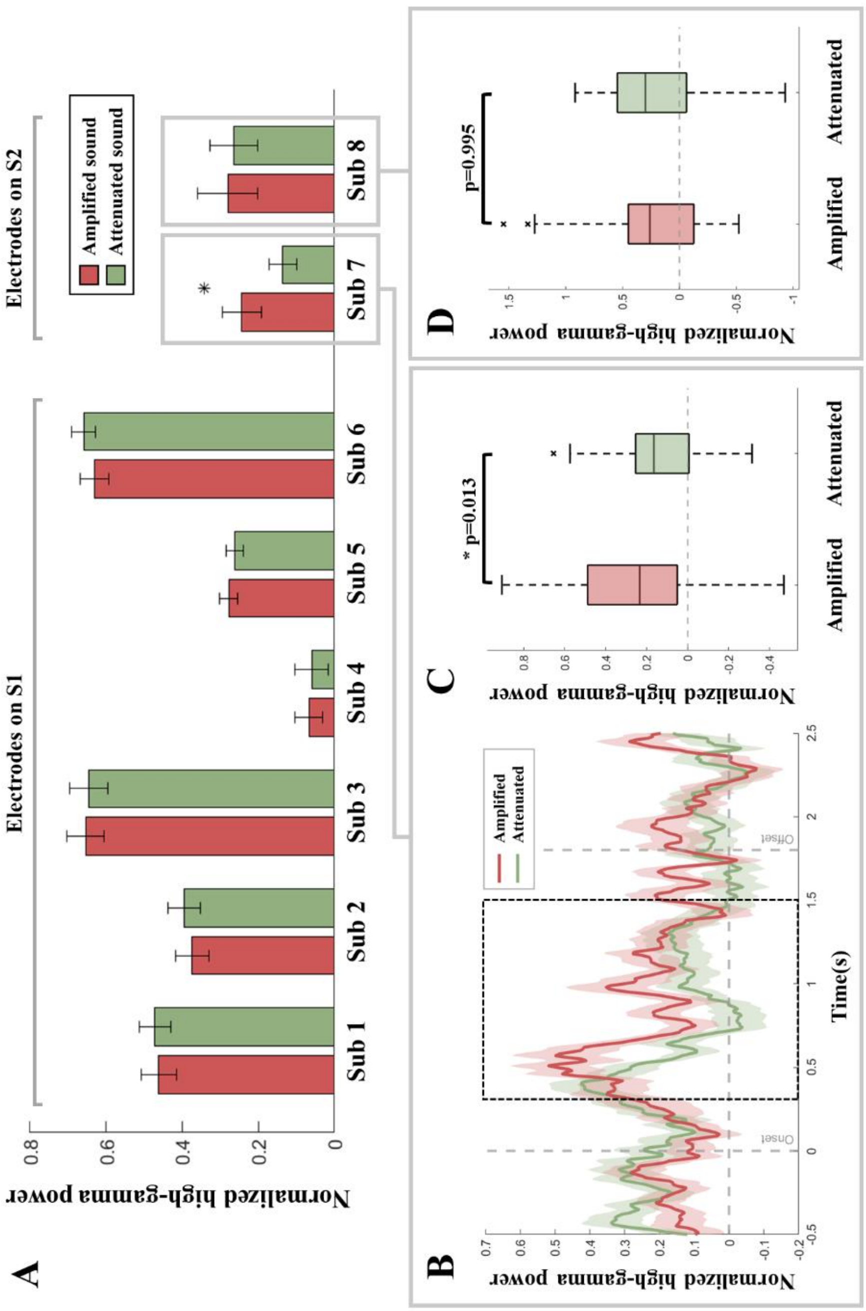
A
Electrodes on S1
Electrodes on S2
Amplified sound
Attenuated sound
Normalized high-gamma power
Sub 1
Sub 2
Sub 3
Sub 4
Sub 5
Sub 6
Sub 7
Sub 8
B
Amplified
Attenuated
Onset
Offset
Time(s)
C
* p=0.013
Amplified
Attenuated
D
p=0.995

Figure 4. The difference in HG power between Amplified friction sound periods and Attenuated friction sound periods. **(A)** Temporally−averaged (within the dashed box of B) HG power during the Amplified friction sound periods and Attenuated friction sound periods in A3 and A4 conditions. Error bars indicate the SE. It was marked with an asterisk when the subject' s HG power is significantly different between the two stimulation periods. **(B)** The HG power time series (solid line: averaged HG power; shaded area: SE) during the Amplified sound periods and Attenuated sound periods that is recorded on S2 of Subject 7 (Illusion−induced subject). **(C), (D)** Temporally−averaged (within the dashed box of B) HG power during each sound periods of Subject 7 and Subject 8, respectively.

<Figure 5>

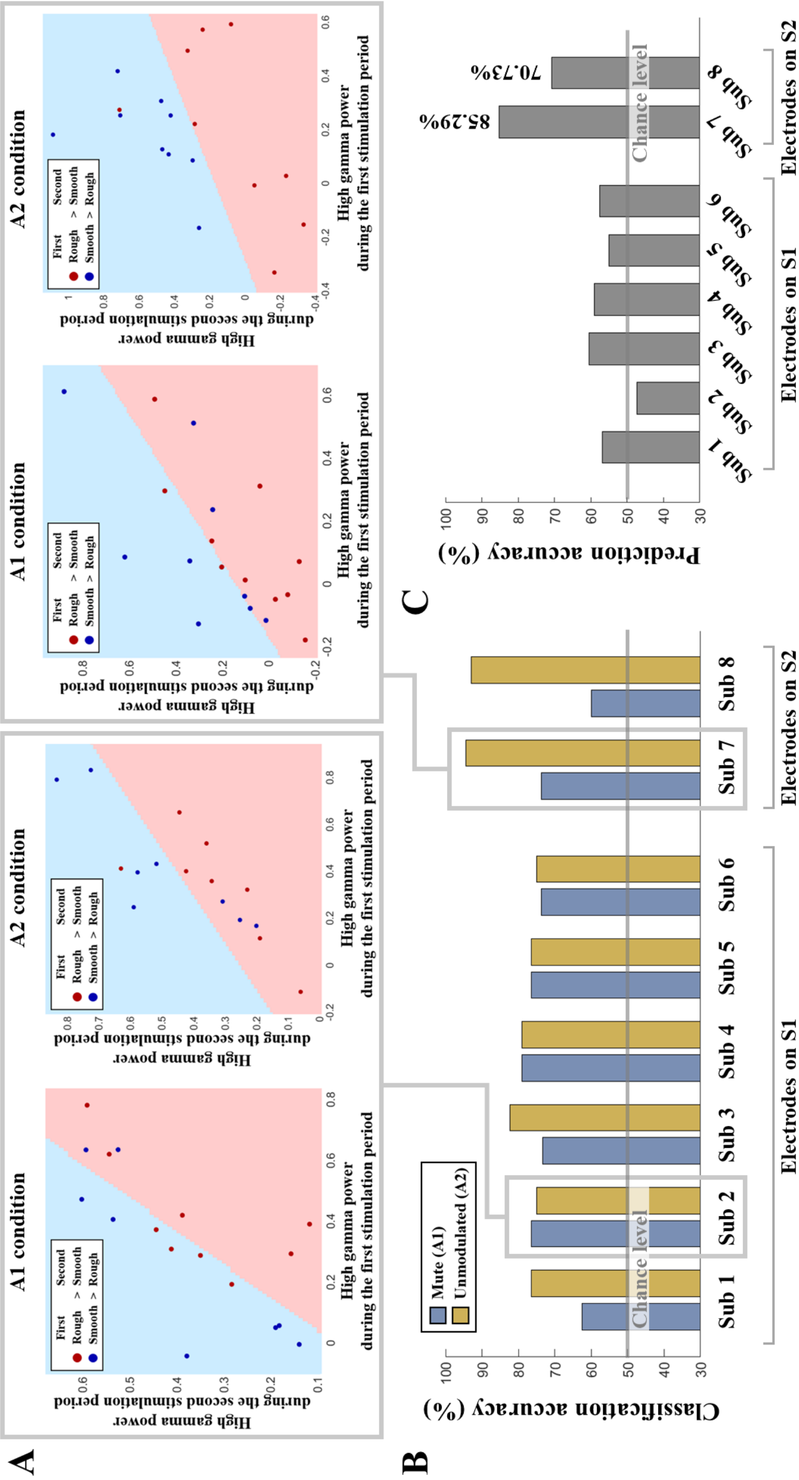
A
A1 condition
A2 condition
First Second
Rough > Smooth
Smooth > Rough
High gamma power during the second stimulation period
High gamma power during the first stimulation period
B
Classification accuracy (%)
Mute (A1)
Unmodulated (A2)
Chance level
Sub 1
Sub 2
Sub 3
Sub 4
Sub 5
Sub 6
Sub 7
Sub 8
Electrodes on S1
Electrodes on S2
C
Prediction accuracy (%)
85.29%
70.73%

Figure 5. Classification of HG power data and prediction of behavioral response using SVM. **(A)** Classification of HG power data in A1 and A2 conditions using SVM. Each colored dot corresponds to HG power data of a single trial. The red dots are the data when the subject responds that the first stimulus was rougher, while the blue dots are the data when the subject responds that the second stimulus was rougher. The areas classified by the SVM classifier were shaded in different colors. **(B)** Classification accuracy of SVM classifier for each subject. The chance level was 50% because the subject had to choose either response. **(C)** The Accuracies of predicting the behavioral response of single−trial data for each subject.

Supplementary information

<Table S1>

Subject number	Sex	Age	Diagnosis	Implant hemisphere	The number of total electrodes	The number of selected electrodes	Recording system
1	F	29	Temporal lobe epilepsy	Right	54	3	Neuvo
2	M	24	Parietal lobe epilepsy	Left	62	5	Neuroscan
3	F	32	Temporal lobe epilepsy	Left	48	1	Neuroscan
4	F	27	Frontotemporal lobe epilepsy	Left	26	1	Neuroscan
5	F	37	Temporal lobe epilepsy	Left	46	3	Neuvo
6	M	58	Temporal lobe epilepsy	Left	52	3	Neuvo
7	F	23	Temporal lobe epilepsy	Right	36	1	Neuvo
8	F	22	Temporal lobe epilepsy	Left	64	1	Neuroscan

Table S1. Subject information. Demographic, clinical, and electrode information are included in the table.

<Figure S1>

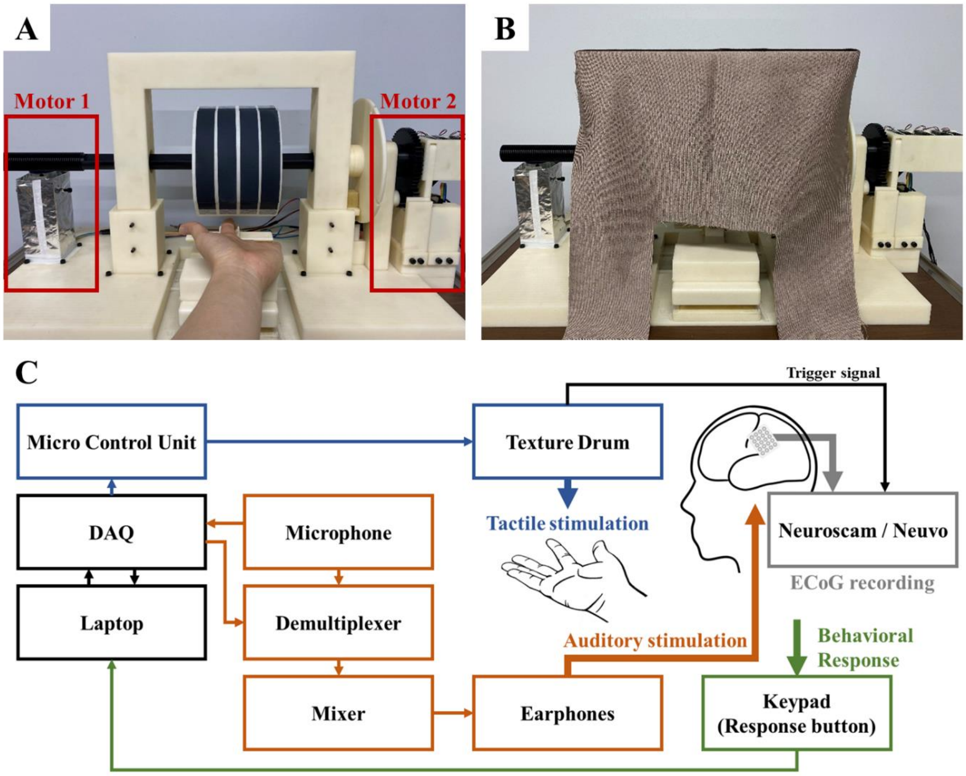

Figure S1. Texture drum equipment and schematic diagram of the experimental setup. **(A)** Texture drum equipment. The subjects' hands were fixed as shown in the picture during the experiment. The equipment includes two motors: Motor 1 moves the drum side to side, Motor 2 rotates the drum. **(B)** Texture drum equipment with a curtain attached. The curtain was attached during the experiment to prevent subjects from acquiring visual information about the textures. **(C)** Schematic diagram of the experimental setup.

<Figure S2−1>

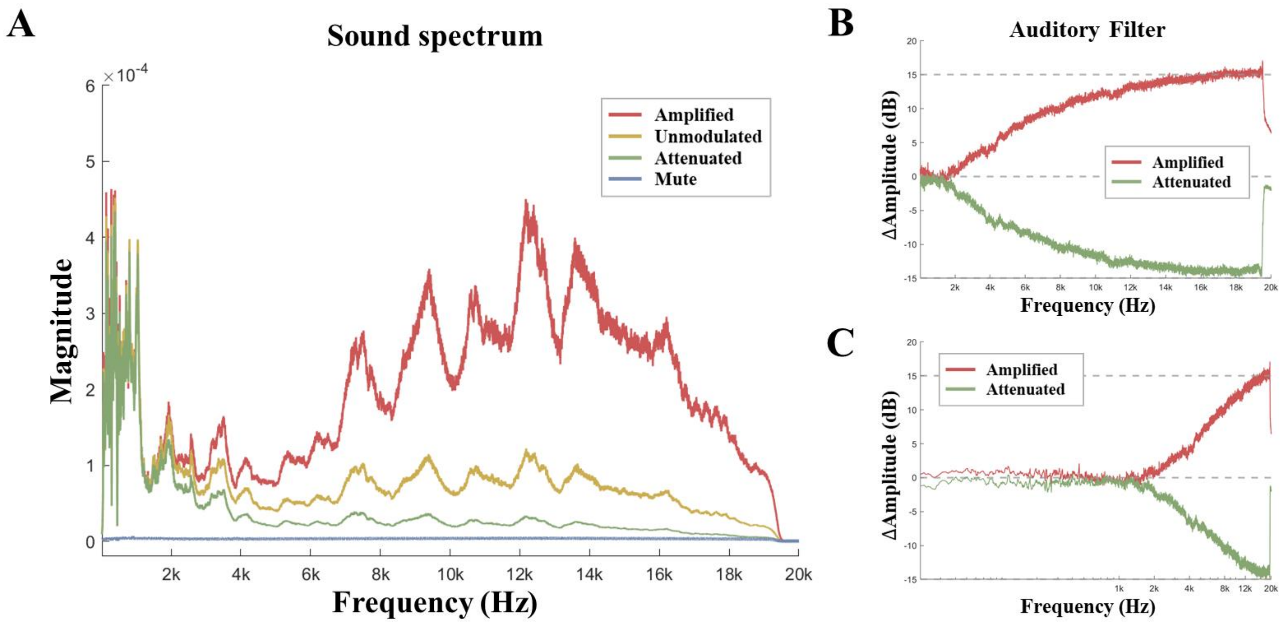

Figure S2. Spectra of friction sound presented for auditory stimulation. **(A)** Spectral analysis results of four types of modulated sounds presented to the subjects during the stimulation periods. Sound recorded in a quiet environment was used for accurate spectral analysis. **(B)**, **(C)** Auditory filters used for modulation. The audio filter was reproduced by dividing the spectrum of unmodulated sound from the spectrum of modulated sound. The x−axis was expressed as linear scale and as logarithmic scale in B and C, respectively.

<Figure S2-1>

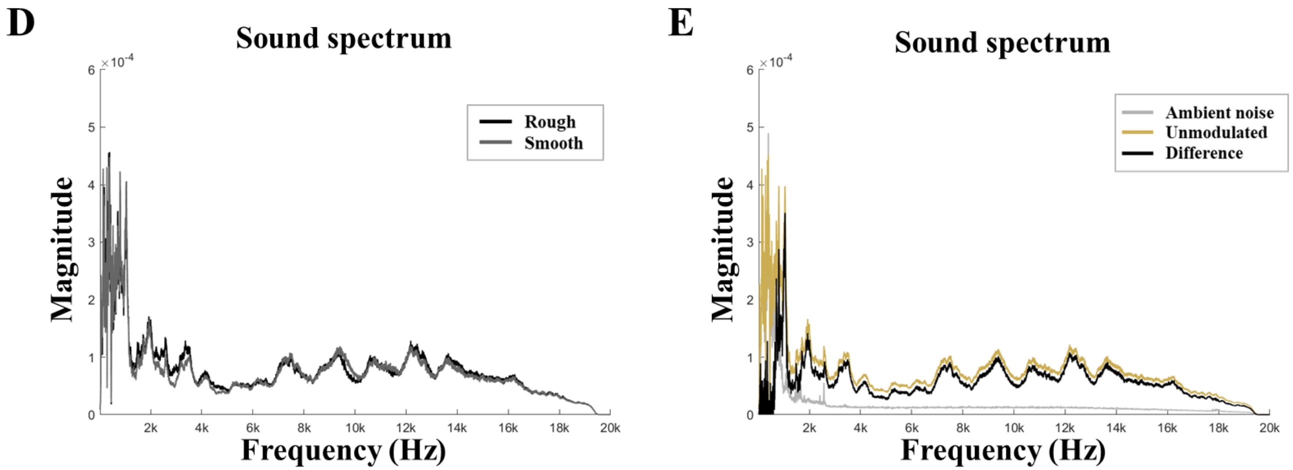

Figure S2. Spectra of friction sound presented for auditory stimulation. (D) Spectral analysis results of unmodulated friction sound during Rough texture periods and Smooth texture periods. (E) Comparison of friction sound spectrum and ambient noise spectrum.

<Figure S3-1>

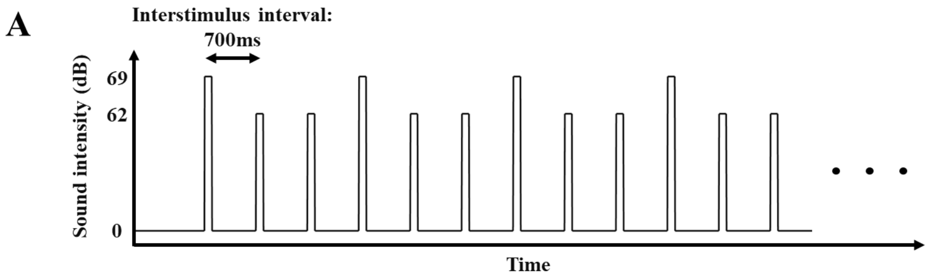

Figure S3. The HG responses when only auditory stimulation is presented. **(A)** The design of additional experiments in which only auditory stimulation was passively presented. Auditory stimuli were pure tones of 262 Hz with a 100ms duration. The auditory stimulation was a sequence of pure tone sounds (262Hz) with a duration of 100ms. One large sound (69dB) and two small sounds (62dB) were alternately presented at intervals of 700ms.

<Figure S3-2>

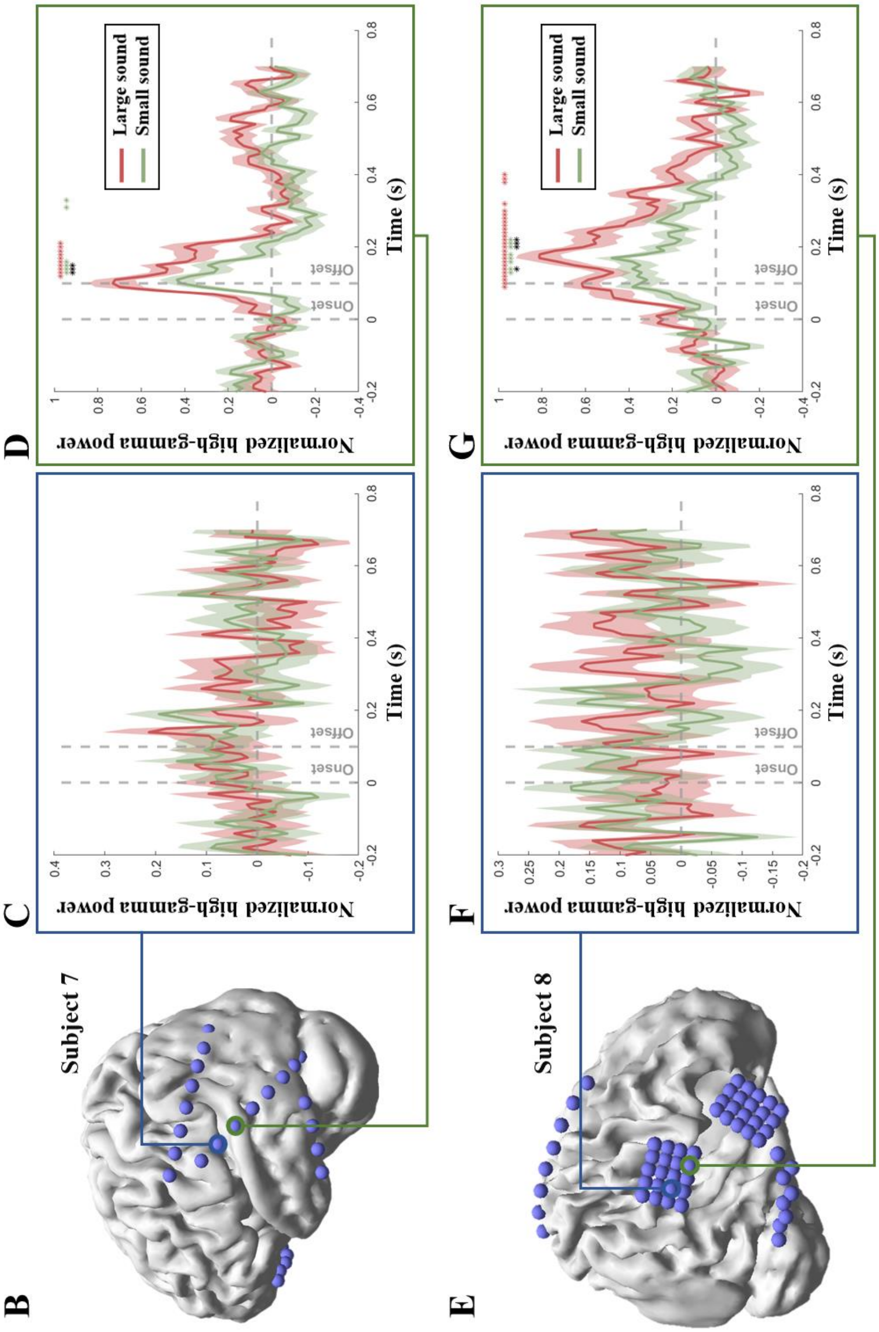
B
C
D
E
F
G
Subject 7
Subject 8
Normalized high-gamma power
Time (s)
Onset
Offset
Large sound
Small sound

Figure S3. The HG responses when only auditory stimulation is presented. **(B), (E)** Location of the ECoG electrodes inserted to Subject 7 and Subject 8, respectively. The electrode marked with the blue edge is the previously selected S2 electrode, and the electrode marked with the green edge is the electrode placed on the auditory cortex. **(C), (F)** The HG power of S2 electrode according to sound intensity (solid line: averaged HG power; shaded area: SE). **(D), (G)** The HG power of the electrode on the auditory cortex according to sound intensity. The time bins with significant HG responses are asterisked at the top of the C, D, F, and G graphs. **Red asterisk:** Significant HG response compared to baseline ($p<0.001$; Wilcoxon signed−rank test) when large sound stimulation is presented. **Green asterisk:** Significant HG response compared to baseline ($p<0.001$; Wilcoxon signed−rank test) when small sound stimulation is presented. **Black asterisk:** Significant HG response in both conditions, and the HG power between the two conditions have a significant difference ($p<0.05$; Wilcoxon signed−rank test).

초 록

인간 체성감각 피질에서의 청각-촉각 연합 신경 메커니즘

인간은 촉각 정보를 통해 질감의 거칠기를 지각하지만, 촉각 정보와 함께 제시되는 소리 정보의 영향을 받아 질감의 거칠기를 다르게 판단하기도 한다. 하지만 거칠기 지각을 위해 두 감각 정보가 어떻게 연합되는지에 대한 신경학적 메커니즘은 밝혀지지 않았다. 본 연구에서는, 인간의 일차 체성감각 피질(S1)과 이차 체성감각 피질(S2)의 하이-감마(high-gamma, 60-150Hz) 활성이 촉각과 청각이 연합된 정보를 표상하는지를 조사하였다.

진단을 목적으로 경막하 전극이 삽입된 뇌전증 환자를 대상으로 실험을 진행하였으며, 피험자에게 질감을 제시하는 동시에 변조된 마찰음을 제시해줌으로써, 피험자가 소리의 영향을 받아 질감의 거칠기를 다르게 지각하는 착각 현상을 유도하였다.

착각이 일어났을 때, S2의 하이-감마 활성도는 질감의 종류뿐만 아니라 마찰음의 변조 방식에 따라서도 달라지는 것을 확인하였다. 이와 달리, S1의 하이-감마 활성도는 질감의 종류에 따라서만 달라지는 것을 확인하였다. 나아가, 선형 서포트 벡터 머신(SVM)이 S2의 하이-감마 활성도를 입력으로 하여 피험자의 응답을 성공적으로 예측하는 것을 확인하였다.

이로써 S1의 하이-감마 활성은 질감의 물리적 특징만 표상하는 반면 S2의 하이-감마 활성은 피험자가 감각 연합을 통해 실제로 지각한 거칠기 정도를 표상한다는 것을 확인하였다. 따라서 우리는

인간의 체성감각 시스템을 따라서 촉각 정보가 처리되는 과정에서 S2에서부터 청각 정보의 개입이 일어난다는 다 감각 연합 모델을 제안한다.

주요어 : 다감각 연합, 이차 체성감각 피질, 하이-감마 활성, 거칠기, 뇌피질뇌파, 인간 뇌 기능

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