ABSTRACT
This report describes the brain responses to acupuncture in an upper limb amputee patient. A 62-year-old male had previously undergone a lower left arm amputation following an electrical accident. Using functional MRI, we investigated brain responses to acupuncture stimulation in the aforementioned amputee under three conditions: (a) intact hand, (b) prosthetic hand (used by the patient), and (c) fake fabric hand. The patient described greater de qi sensation when he received acupuncture stimulation in his prosthetic hand compared to a fake hand, with both stimulations performed in a similar manner. We found enhanced brain activation in the insula and sensorimotor cortex in response to acupuncture stimulation in the amputee’s prosthetic hand, while there was only minimal activation in the visual cortex in response to acupuncture stimulation in a fake hand. The enhanced brain responses to acupuncture stimulation of the patient’s prosthetic hand might be derived from cortical reorganisation, as he has been using his prosthetic hand for over 40 years. Our findings suggest the possible use of acupuncture stimulation in a prosthetic hand as an enhanced sensory feedback mechanism, which may represent a new treatment approach for phantom limb pain.

INTRODUCTION
Following arm amputation, many individuals experience sensations associated with the area where the absent limb was located. To address these phantom sensations, a simple approach has been proposed as an alternative treatment: mirror box therapy. Mirror box therapy allows some patients to perceive illusions of movement or touch in a phantom limb by inducing somatosensory and motor pathway coupling between the phantom and real limb. Upon viewing the reflection of their intact hand in a mirror, many amputees perceive the illusion as having two hands, with some patients experiencing tactile sensation on the phantom limb when the intact arm was touched. This process has been proven in previous study to reverse cortical reorganisation.

From a neurological perspective, acupuncture therapy consists of various sets of stimuli, including visual, tactile and bodily sensations. The study of body schema using multisensory modalities is an emerging field of research that may provide insights into the mechanisms underlying acupuncture therapy. Previously, we used the rubber hand illusion (RHI) to show that modification of bodily self-awareness resulted in different physiological responses to the same acupuncture stimulation in healthy volunteers. This study led to a new research question: what would the brain responses be if an upper limb amputee received acupuncture on his prosthetic hand? If a patient were to perceive his prosthetic hand as his own, acupuncture therapy may produce de qi sensations and brain responses similar to those of his intact hand.

Here, we conducted functional MRI (fMRI) of an upper limb amputee, investigating brain responses to acupuncture stimulation under three conditions: (a) intact hand (visual, tactile and bodily sensation components), (b) prosthetic hand (used by the patient; visual and bodily sensation components), and (c) fake fabric hand (new to the patient; visual component).

Presentation and history
A 62-year-old man underwent a lower left (non-dominant) arm amputation in 1972 following an electrical accident that
had resulted in serious burns to the left wrist requiring numerous operations including skin grafts. The current length of the patient’s intact right arm is 40.5 cm, while his left arm is only 26 cm long (figure 1A). Immediately after amputation, the patient was fitted with a prosthetic hand which he has been wearing ever since for up to 16 h per day, removing the limb only when sleeping due to his concerns over poor blood circulation. The patient was initially hesitant to discuss issues regarding phantom limb pain (PLP) and other painful sensations; however, in time, he discussed phantom pain issues, describing painful sensations whenever he attempted to stretch, move or fight with his missing arm. These sensations were strongest shortly after the amputation, but have diminished over time. Apart from pain, he reported no other issues with phantom limb sensation (PLS). At the time of presentation he had received no prior treatments for PLP, but was receiving medication for both diabetes and hypertension. All the procedures were performed with the approval of the Institutional Review Board of Korea University in Seoul, Republic of Korea.

**fMRI experiment procedure**

The patient was placed in the scanner and instructed to keep his eyes on the acupuncture stimulation site during each session (session 1: acupuncture stimulation on intact right hand and left prosthetic hand; session 2: acupuncture stimulation on the intact right hand and fake left hand). He was told to rest both arms on his abdomen in a comfortable position. A mirror attached to the head coil was installed to ensure a clear view of both hands.

The prosthetic hand was manufactured by the Korean Prosthetic Limbs Research Institute (and had been used for 3 years); the fake hand was made of cotton and fabric (figure 1B). A qualified physician performed acupuncture stimulation using non-magnetic titanium sterile acupuncture needles (40 mm in length, 0.20 mm in diameter; DongBang Acupuncture, Boryeoung, Republic of Korea), with stimulations administered according to the beat of a 1-Hz metronome transmitted via earphones. Acupuncture stimulation was delivered eight times in total at LI4 for 20 s (four times on the intact hand and four times on the prosthetic hand). Both sessions were performed in a similar manner, and the prosthetic hand was replaced with a fake hand between sessions 1 and 2. After each session, the patient was asked to evaluate the de qi sensation by completing a questionnaire using a 10-point Likert scale ranging from ‘strongly disagree’ (0) to ‘strongly agree’ (10).

**fMRI data acquisition and analysis**

Brain imaging was performed with a three-axis gradient head coil in a MAGNETOM Trio 3T scanner (Siemens, Erlangen, Germany). BOLD functional imaging was conducted using echo planar imaging (EPI) with a T2*-weighted sequence (echo time (TE) 30 ms, repetition time (TR) 2000 ms). To minimise movement artefacts, the head of the subject was held in place with a brace. Each scan session contained 260 volumes of the whole brain that was done in 37 axial slice acquisitions (TR=2000 ms, TE=30 ms, flip angle=90°, field of view=240×240 mm², voxel size=3.8×3.8×4.0 mm³). Image collection was preceded by four dummy scans to allow for equilibration of the MRI signal. For anatomical images, a three-dimensional gradient-echo T1-weighted sequence was used (TR=2000 ms, TE=2.37 ms, flip angle=9°, field of view=240×240 mm², voxel size=0.9×0.9×1.0 mm³, 192 slices).

Functional imaging data were preprocessed and analysed using Nipype, a software pipeline bridging three analytical programmes, SPM8 (Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk/spm/), Freesurfer (http://surfer.nmr.mgh.harvard.edu/) and FSL (http://www.fmrib.ox.ac.uk/fsl/index.html), into one workflow. In the preprocessing stage, a rigid-body transformation was used to realign functional images to the mean EPI image, correcting for subject head movement and slice timing. Outlier images exhibiting >1 mm of movement or with an intensity Z-threshold >3 SDs from the mean were removed from the analysis using an artefact detection algorithm (http://www.nitrc.org/projects/artifact_detect/). Freesurfer was used to segment each anatomical volume into grey and white matter structures, and to perform cortical surface reconstruction. The mean functional image generated by realignment was registered to the participant’s reconstructed structural MRI data. Finally, the images were smoothed on the cortical surface with a Gaussian filter (4-mm full width at half maximum).

For each stimulation, a box-car function was created to represent the event block. This time series was then convolved with a canonical haemodynamic response function (HRF), generating a simulated BOLD response. The statistical evaluation was based on a least-squares estimation using the general linear model for serially auto-correlated observations, and was performed separately on each voxel in the participant’s space. Each contrast image was thresholded at a false discovery rate of p<0.05 topologically corrected for multiple comparisons on the cluster level. Finally, Freesurfer was used to project the thresholded contrast image from the volume to the reconstructed subject’s surface.

**Behavioural responses to acupuncture stimulation**

In session 1, the patient perceived similar de qi sensation in the prosthetic hand compared to the intact hand (6 vs 7). In contrast, in session 2, the patient
described markedly less de qi sensation in the fake hand compared to the intact hand (1 vs 7). Therefore, acupuncture produced similar de qi sensation in the amputated limb and intact hand only when the prosthesis hand was placed next to his body.

Brain responses to acupuncture stimulation

Brain activation in response to acupuncture stimulation of the intact right hand was observed in the bilateral dorsolateral prefrontal cortex (dLPFC), ventrolateral prefrontal cortex (vLPFC), primary motor cortex (MI), primary and secondary somatosensory cortex (SI, SII), middle temporal gyrus, insula, and medial temporal (MT) visual area (figure 2A).

In session 1, brain activation in response to acupuncture stimulation of the left prosthetic hand was observed in the contralateral insula, dLPFC, vLPFC, SI, MT and primary visual cortex (VI) (figure 2B). Activation was significantly reduced during session 2, in which brain activation in response to acupuncture stimulation of the fake left hand was observed only in the MT and VI (figure 2C). All peaks were significant to p<0.05, with a minimum cluster extent threshold 20 continuous voxels after false discovery rate correction for multiple comparison. All coordinates are in MNI space.

DISCUSSION

In this study of body ownership in an upper limb amputee, we demonstrated enhanced brain activation in the insula and sensorimotor cortex in response to acupuncture stimulation of the amputee’s prosthetic hand (figure 2B). However, when acupuncture was performed on a fake hand instead, we observed only minimal activation in the visual cortex (figure 2C). These findings are consistent with our previous studies in which experimental assessment of body ownership using the RHI produced similar brain responses to acupuncture stimulation in healthy volunteers. In contrast, during RHI tests, acupuncture stimulation of the real hand resulted in significantly lower brain responses in the insula, indicating that the insula plays an important role in modulating the interoceptive system. These data show that the RHI approach can induce rapid reorganisation of the body schema over a timescale of seconds. In this experiment, it is assumed that the enhanced brain responses to acupuncture stimulation in the patient’s prosthetic hand are derived from cortical reorganisation, as he has been using his prosthetic hand for over 40 years.

In the present study, the patient reported greater de qi sensation when he received acupuncture stimulation in his prosthetic hand relative to an equivalent fake hand.
Certain components ascribed to the de qi sensation share general aspects of ‘bodily self-awareness’, as both physical sensation and the perception of oneself are crucial components of this perception. Acupuncture treatment of the intact limb has previously been shown to be beneficial in patients with PLP and PLS; our study expands upon these previous efforts to show that acupuncture stimulation may enhance bodily self-awareness in the prosthetic hand of an amputee. Procedures, such as extended viewing of movement of the intact hand in a mirror or motor imagery, have been shown to reduce the incidence of phantom pain by resolving a conflict between motor intention and sensory feedback. Regularly practiced mental imagery reduced phantom sensation in the missing limb, resulting in significant pain relief, with a corresponding reduction in cortical reorganisation. Our findings suggest the possible clinical use of acupuncture stimulation, even in a prosthetic hand, as an enhanced sensory feedback mechanism that may represent a new treatment approach for PLP. These findings also reflect recent efforts in medicine, which have sought to expand upon this method by creating artificial limbs that feel and act similar to real limbs. This provides evidence in clinical practice for using prosthetic devices for all amputee patients as part of their rehabilitative care. The data presented here are insufficient to draw firm conclusions as regards pain reduction at this stage; further clinical studies are necessary to validate the usefulness of these sensory feedback methods.

In summary, our findings show that a patient with a unilateral arm amputation perceived greater de qi sensation and experiences brain activation in the insula and sensorimotor cortex during acupuncture stimulation in his incorporated prosthetic hand, but not during acupuncture stimulation on a fake hand performed in a similar manner. It is suggested that the brain responses to acupuncture stimulation reflect both sensory-discriminative and also cognitive and affective dimensions of pain. Given the contribution of the painful sensation-associated component during acupuncture stimulation in a block-designed fMRI, we cannot fully claim that brain responses to acupuncture in the amputee patient are distinct from brain responses to other painful stimuli in the current study.

Contributors YC conceived the study; YC and CW designed the study; I-SL and W-MJ conducted the experiment, analysed the data and drafted relevant sections of the paper; YC drafted the article; and CW and Y-SL revised the article.

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Competing interests None declared.

Ethics approval All procedures were performed with the approval of the Institutional Review Board of Korea University in Seoul, Republic of Korea.

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REFERENCES


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