Article

Title

Structured Movement Representations of a Phantom Limb Associated with Phantom Limb Pain

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Abstract

The relation between phantom limb pain (PLP) and the movement representation of a phantom limb remains controversial in several areas of neurorehabilitation, although there are a few studies in which the representation of phantom limb movement was precisely evaluated. We evaluated the structured movement representation of a phantom limb objectively using a bimanual circle–line coordination task. We then investigated the relation between PLP and the structured movement representation. Nine patients with a brachial plexus avulsion injury were enrolled who perceived a phantom limb and had neuropathic pain. While blindfolded, the participants repeatedly drew vertical lines using the intact hand and intended to draw circles using the phantom limb simultaneously. "Drawing of circles" by the phantom limb resulted in an oval transfiguration of the vertical lines ("bimanual coupling" effect). We used an arbitrary ovalization index (OI) to quantify the oval transfiguration. When the OI neared 100%, the trajectory changed toward becoming more circular. A significant negative correlation was observed between the intensity of PLP and the OI ($r=-0.66$, $p<0.05$). Our findings directly suggest that structured movement representations of the phantom limb are necessary for alleviating PLP.

Highlights

- We investigated the relationship between the phantom limb pain (PLP) and its movement representation.
- We used a bimanual coordination task to evaluate the movement representation.
- Negative correlation was observed between PLP and the bimanual coupling effect.
- Structured movement representations of a phantom limb is related with PLP.

Key word: phantom limb pain, movement representation, bimanual coordination

Abbreviations: PLP: phantom limb pain, BCT: bimanual circle–line coordination task

Introduction

Movement representations of our body are systemically structured through the cognitive process of sensorimotor integration interacting with the surrounding environment [1]. Deafferentation of a limb frequently leads to phantom limb awareness, and patients perceive vivid kinesthesia [2]. The majority of patients perceiving a phantom limb tend to experience decreased awareness of its kinesthesia, but the phantom limb is “recognized” as fixed in one or more peculiar positions [2]. Accompanying phantom limb awareness, patients with a deafferented limb frequently suffer from phantom limb pain (PLP) with maladaptation of central nervous system plasticity [3]. PLP is often resistant to pharmacotherapy, but it responds to some kinds of neurorehabilitation techniques such as mirror visual feedback in association with plastic change of brain [4,5,6,7]. Previous studies demonstrated that PLP patients who restored voluntary movement representation of their phantom limb described PLP alleviation after neurorehabilitation or use of a functional prosthesis [4,5,8,9]. One line of thinking about PLP neurorehabilitation that uses precise visual feedback of phantom limb movements is based on a working hypothesis that incoordination of movement representation of a limb causes pathological pain. However, few reports exist where the representation of a phantom limb’s precision of movement was evaluated in behavioral analysis. In the present study, we assessed structured movement representation of a phantom limb objectively using the bimanual circle–line coordination task (BCT) and validated the relation between phantom limb pain and structured movement representation.

Methods

Participants

Nine patients, who suffered from a brachial plexus avulsion injury and perceived a phantom limb and its pathological pain, participated in this study (Table 1). All participants were outpatients at our institute with a chief complaint of phantom limb pain. The Ethical Review Board of the Faculty of Medicine, The University of Tokyo approved this study. We explained the content of this study and the purpose to all subjects and obtained their written informed consent.

Quantitative evaluation of the movement representation

The bimanual circles–lines coordination task (BCT) used in the present study to assess movement representation of their phantom limb quantitatively has been used in previous studies of various neurological conditions [10-12]. In the BCT, spatial error occurs when drawing the vertical lines repeatedly by the intact hand with intending to draw circles by the affected side (termed the “bimanual coupling effect”). Take the case of phantom limb patients: a coupling effect on the intact hand (drawing straight lines) can be evaluated objectively and quantitatively during “non-visualized” but structured movement representations of the affected hand (drawing circles), even though the affected limb is missing. In a previous case report, Franz and Ramachandran demonstrated that such a bimanual coupling effect during the BCT was observed in an amputee patient with a vivid subjective experience of moving their phantom limb, but was not observed in another patient without the experience [12]. Conversely, straight lines drawn vertically by the intact hand can remain straight when drawing circles using the affected hand by patients with the motor neglect or chronic hemiplegia who have lost movement representations of their affected hand [10]. Based on these observations, we considered the BCT is a promising assessment tool for quantifying movement representations with high validity. The oval-shaped transfiguration when drawing straight lines using one limb indicates that the intermanual interference is induced by the movement representation of the other hand when drawing circles [13]. In addition, converging neuroimaging evidence has revealed that increased activity is observed in motor-related areas, such as the premotor cortex and supplementary motor area, during the BCT [14-16]. On the basis of this neuroimaging evidence, the internal movement representation itself should be sufficient to physically produce the bimanual coupling effect.

The patients sat comfortably in a chair and put their intact index finger on a tablet personal computer (PC) that was on a table in front of the patients. The patients were asked to draw the vertical lines back and forth with the intact hand not intentionally but spontaneously. The intact-hand line trajectories were automatically recorded by the tablet PC. While blindfolded, the patients were asked to perform repeatedly unimanual line drawing movements (drawing vertical lines back and forth on a tablet PC monitor using their intact index finger: unimanual condition: Unimanual Condition) or bimanual drawing movements (drawing the lines using the intact index finger and simultaneously intending to draw circles with the phantom index finger: bimanual condition: Bimanual Condition) at a comfortable speed for 20 s during each trial [Figure 1]. An oval-shaped transfiguration of the repeatedly drawn vertical lines by the intact hand when simultaneously intending to draw circles with the phantom limb indicated that voluntary movement representations of the phantom limb influenced the intact hand (termed the "bimanual coupling" effect [11]). There were two trials for each condition, resulting in a total of four trials.

To quantify the extent of the distortion of the intact-hand line trajectories, we obtained an ovalization index (OI, %) of the lines drawn with the intact hand, according to previous studies [10,11]. From the recorded trajectories in each trial, respective circular figures were extracted by identifying two apical endpoints of respective back-and-forth cycle trajectories. Long and short axes were established for the respective circular figures. An arbitrary variable was calculated from each cycle trajectory according to the following formula: variable = [standard deviation of long-axis data / standard deviation of short-axis data] × 100. Then, for each patient, the OI was defined as the mean value of the variables computed on all recorded cycle trajectories under the respective conditions. If the OI value was near 0, the trajectory did not become distorted toward a circular transfiguration. If the OI value was 100, the trajectory became a precise circle.

Subjective evaluation of the movement representation

Phantom limb patients generally describe movement representation of their phantom limb, but their perceptual contents are varied. For example, some describe movement representation as perception of phantom limb to be telescoped, while others describe involuntary motor imagery, or the others describe movement representation only when they perceive a vivid reality of voluntary motor imagery. We designed this study to reveal the intimate relationship between phantom limb pain and subjectively-described movement representation of it. We employed a virtual reality (VR) system to measure specifically the perceptual content of voluntary movement of the phantom limb as homogeneously as possible. The patients wore a head-mounted display (Oculus Rift;

Oculus VR, Menlo Park, CA USA) and a three-dimensional computer graphic (3D-CG) of an upper forearm and hand with five fingers presented on the display. The virtual forearm and hand appeared in the patients' correct orientation with respect to their body, and the patients perceived it as occupying the phantom limb. Motion of their intact arm and hand, which was detected by an infrared camera (Kinect; Microsoft Corp., Edmond, WA, USA) and a motion capture data glove (CyberGlove 2; CyberGlove Systems, San Jose, CA, USA), was horizontally flipped like a mirror-reversed image to create virtual limb motion. With this VR system, the patients were asked to exercise both the intact and phantom limbs symmetrically at their discretion (e.g., flexion-extension cycles, rotation of the limbs) for at least 5 min. Subsequently, using a 7-point Likert scale from 0 (none) to 6 (extremely strong), the following two statements were rated and summed: "I felt as if I could exercise my phantom limb voluntarily" and "The phantom limb was brought under control of my will and I could make the limb go where I wanted it to go." The patients conducted this test twice, and the mean score from two sessions constituted the subjective data regarding movement representation of their phantom limb.

Statistical analysis

To determine whether hand dominance affects the bimanual coupling effect, the coupling effects (bimanual OI scores minus unimanual OI scores) between patients with an impaired dominant hand (dominance group) and those with an impaired non-dominant hand (non-dominance group) were compared using the Mann–Whitney U test. The OI values under the unimanual and bimanual conditions were compared using the Wilcoxon signed-rank test. To determine the relation between structured movement representations of the affected hand and PLP, correlations were determined between the relative OI (i.e., bimanual OI scores minus unimanual OI scores) and pain intensity on an 11-point numerical rating scale (NRS) using Spearman's rank correlation analysis. Also, relations between subjective data on the movement representation of the phantom limb and PLP intensity and the OI were analyzed. In addition to these main analyses, to check the test–retest reliability of the subjective evaluation of movement representation, we compared the score of the first VR session and the second session using the Wilcoxon signed-rank test. Correlations were determined between the variability of participants' subjective phantom movement (the score of the second session minus that of the first session) and their OI or pain intensity (NRS) using the Spearman's rank correlation analysis to investigate the variability of their subjective phantom movement and whether it correlated with the OI or PLP. Statistical analysis was performed using SPSS version 17.0 (SPSS, Chicago, IL, USA). The level of significance was set at <5%.

Results

Comparing the bimanual coupling effect between the dominance group and non-dominance group, there were no significant differences [p = 0.64: dominance group, 2.23 ± 1.41 (mean ± SD); non-dominance group, 1.89 ± 1.88]; hand dominance did not seem to influence the bimanual coupling effect. There NRS of pain intensity were 4.78 ± 1.92 (mean ± SD) and the OI scores in each condition were as follows: Unimanual condition, 6.01 ± 1.92; Bimanual condition, 8.05 ± 1.85. The bimanual circle-lines coupling showed a significant oval-shaped transfiguration (i.e., high OI scores) compared with unimanual coupling ($p < 0.01$). The oval-shaped transfiguration elicited by bimanual coupling negatively correlated with pain intensity ($r=-0.66$, $p<0.05$) (Fig. 1B). Examples of trajectories under unimanual and bimanual conditions are shown in Figure 1C,D. The subjective data for movement representation were not associated with the oval transfiguration elicited by bimanual coupling (r=0.11, p=0.38) or pain intensity (r=0.11, p=0.39) (Fig. 2A,B). Comparing the score of participants' subjective movement representation in the first session and the second session, there were no differences between sessions (p = 0.26: first session, 6.44 ± 2.92; second session, 7.22 ± 2.59). Further, there were no correlations between the variability of their subjective phantom movement and the OI (r=−0.39, p=0.15) and pain intensity (r=−0.06, p=0.44).

Discussion

The present study was the first attempt to verify the relationship between PLP and its structured movement representation, which is quantitatively evaluated with the BCT. In the present study, the ovalization index in the bimanual condition was higher than that in the unimanual condition [Unimanual: 6.01 ± 1.92, Bimanual: 8.05 ± 1.85]. This result suggests that the movement representation of a phantom limb remains to some degree, despite patients' long-term deafferentation. Further, it was revealed that the higher ovalization index the PLP patients show, the more decreased pain intensity they feel (Fig. 1B). Thus, structured movement representations, evaluated here in a quantitative way, have an intimate relationship with PLP intensity. Previous studies have demonstrated that the movement representation of a phantom limb induced by mirror visual feedback or virtual reality treatments alleviate PLP [4,5]. Considering these previous [4,5,6,7] and our present findings, we can conclude that the underlying mechanism of PLP is directly connected to its movement representation. Observing the clinical features of the two outlier patients (Patients A and B), who both demonstrated a higher OI, would indicate the characteristics of patients with a structured movement representation of their phantom limb. From these observations, both patients frequently used their affected limb as much as possible on a daily basis despite it being paralyzed (for example, pressing on the paper using the affected arm during writing with the intact hand). From these patients' characteristics, using the affected limb as a functionally-useful limb in a limited way might be an important way to maintain the structured movement representation of their phantom limb.

In upper-limb amputee patients who perceive a phantom limb and its neuropathic pain, the primary motor cortex contralateral to the phantom limb is not activated when they intend to move their phantom limb [6]. In amputee patients who restored the structured movement representation of their phantom limb and whose PLP decreased, the primary motor cortex becomes activated more strongly compared with the activation before amelioration of PLP [17]. Further, reorganization of the somatotopy in the sensorimotor cortex is observed in amputee patients, and a greater reorganization of the cortex reportedly correlates with greater pain intensity of the phantom limb [18,19]. However, a succession of functional brain imaging studies does not support the relationship between reorganization of the sensorimotor cortex and PLP intensity [20,21]. Considering these, the relationship between PLP and its movement representation and the sensorimotor cortex might be plausible, but is still controversial. Not only the primary motor cortex but also other motor-related cortices such as supplementary motor area, premotor area and the cerebellum also become activated when moving a phantom limb. The entirety of the motor system in the central nervous system (CNS) might be involved in the relationship between PLP intensity and its movement representation.

Conversely, there was no relationship between PLP and subjectively-reported movement representation of a phantom limb in the present study. In addition, there were no significant correlations among the variabilities of subjectively-reported phantom limb movement, PLP intensity and their OI. Our methodological reliability can be confirmed because the subjective evaluations of movement representations of participants' phantom limbs were consistent through multiple sessions with the VR system. As a previous report demonstrated, subjective introspections about phantom limbs are sometimes gigantic confabulations [22]. There were individual differences in introspection in the situation of sensorimotor incongruence, which is one of the underlying mechanisms of PLP [23,24]. Particularly, among patients with chronic pain, their body perception of the affected limb, which is explained to clinicians by the patients themselves, generally does not match objective signs of the affected limb because it is affected by pain and their strong negative emotion with regard to the affected limb [25]. There was a mismatch between subjective and objective evaluations of movement representations of patients' phantom limbs. Considering this finding, evaluating the phantom limb in a quantitative way is important. Clinicians and researchers have tried to develop methods of quantitative evaluation for phantom limb, for example, the template matching task [26] and the pointing task [27], and have succeeded in evaluating the body schema of a phantom limb quantitatively [26,27]. However, there are few studies in which movement representations of a phantom limb are evaluated in a quantitative way. For example, the hand laterality task is commonly used to quantitatively evaluate the movement representations of some kinds of neurological patients [28,29]. The hand laterality task, as already reported, shows difficulties in its application to patients with deafferentation of one limb, because of their incorrect cognitive processes during the task [30,31]. In the present study, dissociation between the subjective descriptions of moving a phantom limb and objective movement representations, which are measured as bimanual interference, was certainly observed. Consequently, there was an intimate correlation only between structured movement representations and PLP, but not between its subjective description and PLP, suggesting that structured movement representations of a phantom limb are essential for disentangling PLP. The structured movement representations of a phantom limb should be focused on, even in the absence of introspection regarding their origins. Evaluating the movement representation in a quantitative manner might reveal the analgesic mechanisms of neurorehabilitation for PLP.

The following future perspectives of our study should be considered. We did not compare between the data of patients with and without PLP, because of the difficulty of recruiting patients who perceive a phantom limb but do not feel pain. To more strongly demonstrate the intimate relationship between PLP and its structured movement representation more clearly, we need to compare data between the two sets of phantom limb patients. Also, in the present study, we could not directly connect the CNS with the structured movement representation of a phantom limb and PLP. Measurements of the CNS function using fMRI or EEG might disentangle the underlying mechanism(s) of phantom limb pain more clearly.

Conclusions

In conclusion, we found an intimate relationship only between the structured movement representations of a phantom limb and its pain. We suggest the importance of evaluating the movement representations in a quantitative way, and that structured movement representations of the phantom limb are necessary for alleviating PLP.

Conflict of interest

The authors report and confirm that there are no conflicts of interest. We alone are responsible for the contents and writing up of our study.

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Table 1: Patient data

Subject	Sex	Age	Affected	Handedness	Disease Duration (year)	Type of BPI	Intercostal nerve transfer	Part of PLP
Patient A	Male	53	Left	Right	36	incomplete	-	Hand
Patient B	Male	54	Right	Right	20	complete	+	Hand
Patient C	Male	46	Right	Right	21	complete	+	Hand
Patient D	Male	56	Right	Right	6	complete	-	Arm
Patient E	Male	47	Right	Right	14	complete	+	Hand
Patient F	Female	64	Left	Right	8	complete	+	Arm, Hand
Patient G	Male	51	Right	Right	13	complete	+	Shoulder, Arm, Hand
Patient H	Male	49	Left	Right	26	complete	+	Hand
Patient I	Male	42	Left	Right	8	incomplete	+	Forearm, Hand

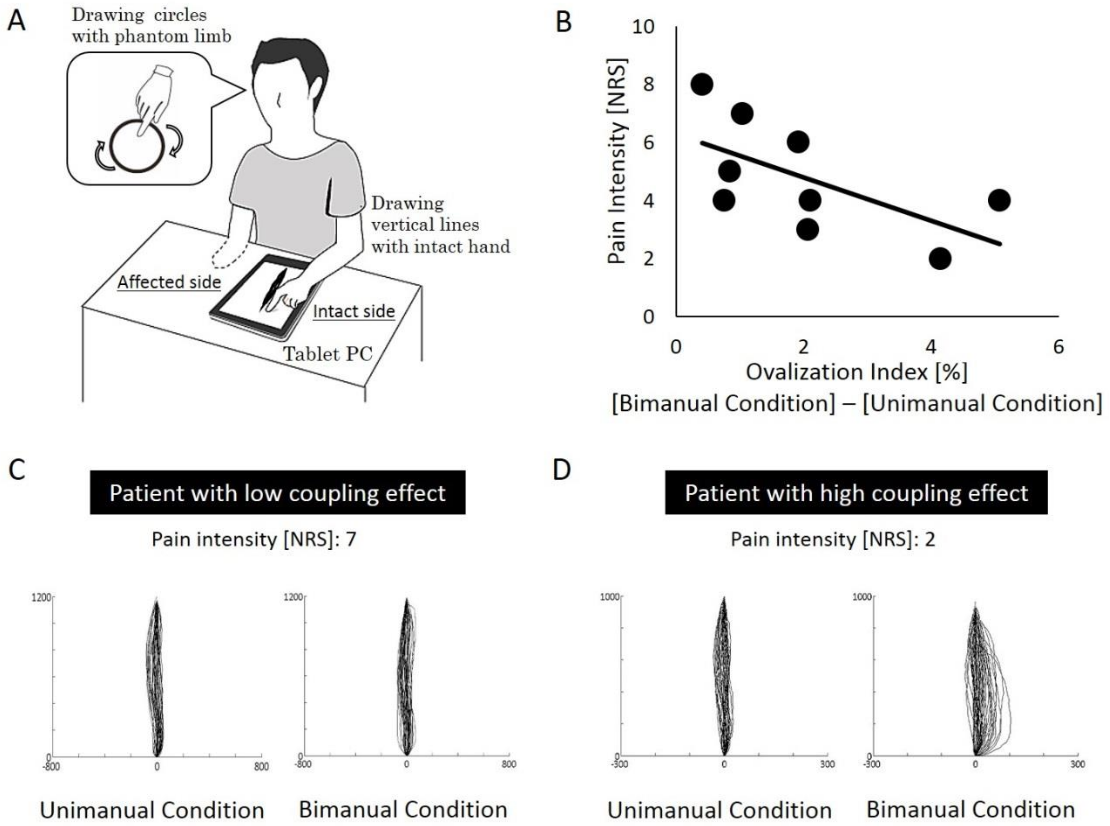

Figure 1: The relationship between the result of bimanual circle-line coordination task and phantom limb pain.

Figure 1A: The experiment image of bimanual circle-line coordination task. The patients sat comfortably in a chair and put their intact index finger on a tablet PC that was on a table in front of the patients. Patients intend to draw circles with their phantom limb while drawing vertical lines with intact hand in the bimanual condition.

Figure1B: Relationship between PLP and movement representation of phantom limb. A significant negative correlation was observed between pain intensity and OI ($r = -0.66$, $p < 0.05$).

Figure 1C,D: Examples of trajectories in the bimanual circle-lines coupling task. In a patient, the OI value comparable between unimanual and bimanual conditions. This result indicated low bimanual coupling effect (Figure 1C). In contrast, a patient demonstrated more circular transfiguration (i.e., high OI value) under the bimanual condition, compared with trajectories under the unimanual condition, indicating a high coupling effect (Figure 1D).

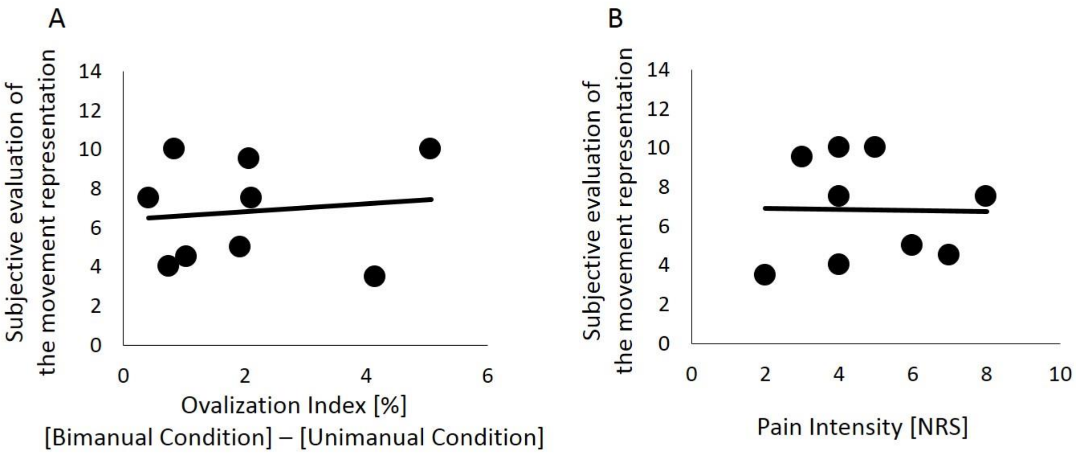

Figure 2: Relationship between subjective evaluation of the movement representation of the phantom limb, structured movement representations of the phantom limb, and phantom limb pain intensity.

Figure 2A, 2B: There were no significant correlations between the subjective evaluation of the movement representation and the ovalization index (r = 0.11, p = 0.38) or pain intensity (r = 0.11, p = 0.39).