



## Remodeling of cortical activity for motor control following upper limb loss



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### HIGHLIGHTS

- The neurophysiology of motor control in persons with upper limb amputation is not well known.
- Amputees show involvement of parieto-occipital areas during movement preparation and execution with the amputated limb.
- This may reflect increased visuospatial feedback for motor control involving the amputated limb.

### ABSTRACT

**Objective:** Upper extremity loss presents immediate and lasting challenges for motor control. While sensory and motor representations of the amputated limb undergo plasticity to adjacent areas of the sensorimotor homunculus, it remains unclear whether laterality of motor-related activity is affected by neural reorganization following amputation.

**Methods:** Using electroencephalography, we evaluated neural activation patterns of formerly right hand dominant persons with upper limb loss (amputees) performing a motor task with their residual right limb, then their sound left limb. We compared activation patterns with left- and right-handed persons performing the same task.

**Results:** Amputees have involvement of contralateral motor areas when using their sound limb and atypically increased activation of posterior parietal regions when using the affected limb. When using the non-amputated left arm, patterns of activation remains similar to right handed persons using their left arm.

**Conclusions:** A remodeling of activations from traditional contralateral motor areas into posterior parietal areas occurs for motor planning and execution when using the amputated limb. This may reflect an amputation-specific adaptation of heightened visuospatial feedback for motor control involving the amputated limb.

**Significance:** These results identify a neuroplastic mechanism for motor control in amputees, which may have great relevance to development of motor rehabilitation paradigms and prosthesis adaptation.

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## 1. Introduction

Reorganization of neural networks has been evaluated in various clinical populations; however, less is known about neuroplasticity in upper extremity amputees. Upper extremity amputees

have shown sensory reorganization (Cohen et al., 1991; Borsook et al., 1998; Chen et al., 1998), which tends to relate strongly to phantom sensations (Karl et al., 2001). While it is commonly thought that motor representations of the missing hand are occupied by the residual limb and lateral motor homunculus (Pascual-Leone et al., 1996), recent evidence suggests that the lateral shift may not always occur (Gagne et al., 2011). While most previous attempts to identify patterns of lateralization utilize transcranial magnetic stimulation (TMS), a criticism is that TMS only measures neural function related to the stimulation site. The use of

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whole-scalp electroencephalography (EEG) allows us to evaluate hemispheric laterality outcomes in motor areas for planning and execution, and identify novel patterns that may reveal unexpected and meaningful plasticity in amputees.

It remains unclear how hemispheric patterns of limb dominance change as a result of amputation. For persons with partial limb amputation, movements that involve proximal musculature of the residual limb may reduce confounds of type of prostheses when studying neuromotor control. Recent studies have sought to evaluate if proximal versus distal movements affect lateralization of motor planning. In a study on tool use movements that were more proximal (e.g., using a saw) compared to those that are more distal (using scissors) (Maki-Marttunen et al., 2014), findings showed that motor planning of proximal and distal gestures in right handed persons generally utilized left lateralized premotor and inferior parietal lobule areas that are known to be responsible for tool use tasks (Fridman et al., 2004; Wheaton et al., 2005a; Bohlhalter et al., 2009). We can also evaluate similar patterns with use of the left arm, as functional limb dominance may play a role in the hemispheric dominance of action planning (Kelly et al., 2015). In unilateral amputees that reject their prostheses, behavioral adaptation to the resulting one-handedness may present an opportunity for the proximal aspect of the non-dominant arm to display novel neural lateralization patterns.

The goal of this work was to understand if contralateral motor activation for left and right limbs are affected in persons with partial limb loss. We had formerly right hand dominant (right affected) amputees performed a simple, gross proximal arm movement task using the sound (left) and the amputated (right) limbs. By focusing on movement of the proximal upper extremity (i.e., residual limb on the amputated side), we constrained device-specific differences in performing the task. This allowed us to identify whether unique patterns of activation are seen in amputees when using their left (“non-dominant”) limb without the confound of functional dexterity of the prosthesis. Neural function while performing motor tasks has been extensively addressed in the neurosciences and can be evaluated using EEG. In particular, beta band (18–22 Hz) modulation has been shown to reflect motor planning and execution, primarily with activation localization over motor areas contralateral to the limb performing the task (Shibasaki and Hallett, 2006). Recent evidence further refines the role of beta modulation, demonstrating that beta oscillations correlate with the excitability of spinal motoneurons (Takemi et al., 2015). Further, it is suggested that decreases in beta power relate to an active disinhibition of brain areas that determine parameters of movement (Brinkman et al., 2014). This evidence for beta band involvement in motor processes reinforces the predictability of laterality measures in left and right-handed persons, where movement tends to yield contralateral sensorimotor cortical activations (Stancak and Pfurtscheller, 1997, Solodkin et al., 2001). Previous studies have identified strong outcomes in assessment of motor laterality (Formaggio et al., 2008; Nam et al., 2011) and effector-specific motor planning (Wheaton et al., 2008) when assessing beta band laterality. Beta band activation has been seen in brain areas related to motor preparation, even in tasks involving anticipatory visuospatial attention (Gould et al., 2011). For amputees, it is possible that motor lateralization remains either contralateral, shifted laterally (Pascual-Leone et al., 1996), or involves a completely novel pattern. We will assess this by focusing on power changes (activations) over sensorimotor areas including current source density modeling. As current source density allows us to evaluate the spatial extent of neural activations, we will additionally evaluate current source density of alpha (10–12 Hz) rhythms to identify the intrinsic relationship of these rhythms within their cortical generators compared to beta band activity (Pfurtscheller and Andrew, 1999).

As well, we will also identify whether any unique patterns are seen for amputees when using their left (“non-dominant”) limb after chronic (>6 months post injury) amputation. We compared the patterns of amputees to left and right dominant persons performing the same task. This allowed us to compare the motor outcomes in amputees with the lateralization patterns in persons with sound limbs. It was hypothesized that formerly right hand dominant amputees would show patterns of neural activation consistent with maintained contralateral motor activation (similar activations to intact right hand dominant individuals).

## 2. Methods

### 2.1. Participants

Twenty-five subjects participated in this study. Before participating in the study, all subjects were consented according to guidelines of the Georgia Institute of Technology Institutional Review Board. Twenty of the subjects were healthy intact individuals. Ten were right hand dominant (6 males, mean age 27.7) and the other ten were left hand dominant (4 males, mean age 23.4) based on the Edinburgh Handedness Inventory (Oldfield, 1971). The remaining five subjects were formerly right hand dominant individuals with a right upper limb amputation (Table 1). Amputees were asked their hand dominance prior to amputation using the Edinburgh Handedness Inventory. All persons were free of phantom sensations or lingering pain from surgeries, and had completed all physical therapy. At the time of visit, all participants had active range of motion of the right shoulder (residual limb) within normal limits in all degrees of motion. Manual muscle testing revealed 5/5 muscle strength in all degrees of motion.

### 2.2. Setup

All participants (amputees or intact subjects) wore a prosthetic device on their right arm. Persons with intact limbs wore the Fictive Amputee Modeling System (FAMS, (Cusack et al., 2014)), which simulates transradial amputation by constraining the arm in a prosthetic device and eliminating forearm rotation, wrist flexion/extension, and hand movement forcing the user to perform tasks with a split hook terminal device (Cusack et al., 2012, 2014, 2016). Amputees wore their own prosthesis on the right arm (Table 1 indicates level of amputation and type of device). Surface electromyography (EMG) was placed on the anterior and posterior deltoid of the right and left arm, and served as a surrogate marker of movement onset. Subjects were fitted with a standard tin 58-channel EEG cap (Electrocap, Eaton, OH) to record neural activity using Synamps 2 (Neuroscan, Charlotte, NC). Electrooculography was also recorded to monitor for eye movements, and was later used for artifact rejection using autoregressive modeling (Cerutti et al., 1988). Data acquisition was performed using a right ear reference at a sampling rate of 1000 Hz and filtered to DC–100 Hz. The left ear was also recorded and used to create (offline) a linked ear reference.

### 2.3. Tasks

Each participant performed two tasks for approximately 12 min each. From a seated position with the arm on an armrest, the first task was to “raise and rotate the left arm”, followed by “raise and rotate the right arm” in separate blocks. Specifically, the participant was to lift the arm from the armrest, elevate their arm (to approximately 90 degrees horizontal flexion) with the elbow fully extended, then rotate at the shoulder. After performing the task one time, participants returned to rest. All intact subjects

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