Clinical Neurophysiology 125 (2014) 457–462

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Left posterior parietal theta burst stimulation affects gestural imitation regardless of semantic content

Tim Vanbellingen [a,b], Manuel Bertschi [a,b], Thomas Nyffeler [a,b,c], Dario Cazzoli [d], Roland Wiest [e], Claudio Bassetti [f], Alain Kaelin-Lang [g], René Müri [a,b], Stephan Bohlhalter [a,b,c,*]

[a] Perception and Eye Movement Laboratory, Department of Neurology, Inselspital, University Hospital Bern, Switzerland
[b] Perception and Eye Movement Laboratory, Department of Clinical Research, Inselspital, University Hospital Bern, Switzerland
[c] Neurology and Neurorehabilitation Center, Luzerner Kantonsspital, Switzerland
[d] Nuffield Department of Clinical Neurosciences, Clinical Neurology, University of Oxford, Oxford, United Kingdom
[e] Institute of Diagnostic and Interventional Neuroradiology, Inselspital, University Hospital Bern, Switzerland
[f] Department of Neurology, Inselspital, University Hospital Bern, Switzerland
[g] Movement Disorders Centre, Department of Neurology, Inselspital, University Hospital Bern, Switzerland

ARTICLE INFO

Article history:
Accepted 22 July 2013
Available online 17 September 2013

Keywords:
Imitation
Gestures
IPL
SPL
Theta burst stimulation

HIGHLIGHTS

- Continuous theta burst stimulation (cTBS) over left posterior parietal cortex affects gestural imitation.
- cTBS interfered with gestural imitation regardless of stimulation site (inferior or superior parietal lobe) and semantic content (meaningful versus meaningless).
- The increase of temporal–spatial errors under cTBS fits well with the concept that planning of visuomotor transformations including the appreciation of spatial relationships between body parts may be operative during imitation.

ABSTRACT

Objective: Neuro-imaging studies have suggested that the ability to imitate meaningless and meaningful gestures may differentially depend on superior (SPL) and inferior (IPL) parietal lobule. Therefore, we hypothesized that imaging-guided neuro-navigated continuous theta burst stimulation (cTBS) over left SPL mainly affects meaningless and over left IPL predominantly meaningful gestures.
Methods: Twelve healthy subjects participated in this study. High resolution structural MRI was used for imaging guided neuro-navigation cTBS. Participants were targeted with one train of cTBS in three experimental sessions: sham stimulation over vertex and real cTBS over left SPL and IPL, respectively. An imitation task, including 24 meaningless and 24 meaningful gestures, was performed 'offline'.
Results: cTBS over both left IPL and SPL significantly interfered with gestural imitation. There was no differential effect of SPL and IPL cTBS on gesture type (meaningless versus meaningful).
Conclusions: Our findings confirm that left posterior parietal cortex plays a predominant role in gestural imitation. However, the hypothesis based on the dual route model suggesting a differential role of SPL and IPL in the processing of meaningless and meaningful gestures could not be confirmed.
Significance: Left SPL and IPL play a common role within the posterior–parietal network in gestural imitation regardless of semantic content.

1. Introduction

Imitation, with its unique perfection in humans, plays a significant role in development and learning of motor, social, and communication skills (Hurley and Chater, 2005). Defective imitation of gestures, often observed in patients after left parietal brain damage, reflects a core deficit in apraxia (Goldenberg, 2008). Behavioral dissociations in disturbed gestural imitation have been described in the literature. Whereas some studies described the case of patients exhibiting exclusive difficulties in imitating meaningless gestures (Goldenberg and Hagmann, 1997; Mehler, 1987; Tessari et al., 2007; Buxbaum et al., 2000), other studies showed an impairment in the imitation of meaningful gestures only (Bartolo and Cubelli, 2001; Buxbaum et al., 2003).

* Corresponding author at: Neurology and Neurorehabilitation Center, Luzerner Kantonsspital, Switzerland. Tel.: +41 41 205 54 37; fax: +41 41 205 24 41.
E-mail address: stephan.bohlhalter@luks.ch (S. Bohlhalter).

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http://dx.doi.org/10.1016/j.clinph.2013.07.024

This suggests that the imitation of meaningful and meaningless gestures may have a distinct neural basis.

Several neuroimaging studies demonstrated the fundamental role of superior (SPL) and inferior parietal (IPL) lobules in gestural imitation. With respect to different gesture types (meaningless and meaningful), some studies suggested a common neural network demonstrating a similar involvement of SPL and IPL (Grezes, 1998; Decety et al., 2002; Lui et al., 2008). In contrast, other studies showed predominant activation of the left SPL for meaningless gesture imitation, whereas left IPL involvement seemed to be crucial for meaningful gesture imitation (Peigneux et al., 2004; Rumiati et al., 2005). These findings supported the influential dual route model. According to this account, meaningful gestures are processed through an indirect, semantic route, and meaningless gestures through a direct, non-lexical route (Rothi et al., 1991; Buxbaum, 2001; Rumiati and Tessari, 2002; Tessari et al., 2007). Specifically, after perceptual (auditory, visual) analysis, meaningful gestures are evaluated for action meaning based on semantic memory. Further processing towards the final motor output also involves the recruitment of temporal–spatial gesture engrams, thought to be stored in the IPL (Heilman et al., 1982; Buxbaum, 2001). The non-semantic route is primarily responsible for meaningless gestures and corresponds to a visuo-motor transformation, which enables the replication of the external shape of a seen gesture, possibly mediated by SPL (Rothi et al., 1991; Buxbaum, 2001; Rumiati and Tessari, 2002; Tessari et al., 2007). However, functional imaging studies do not allow concluding whether the different regional activations were actually mandatory for the imitation performance. Considering the redundant organization of the brain, the activations may have simply reflected some reserve capacity (de Graaf and Sack, 2011). Therefore, it still has to be revealed whether SPL and IPL play a distinct or common role within the posterior–parietal network in controlling meaningless and meaningful gestural imitation.

Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive method that can transiently interfere with cortical activity. In contrast to neuroimaging, behavioral changes associated with rTMS allow to infer on the functional relevance of the stimulated cortical regions (Sandrini et al., 2010). The advantage of the inhibitory continuous theta burst stimulation (cTBS) protocol (Huang et al., 2005; Nyffeler et al., 2006; Goldsworthy et al., 2012a,b) is that the application of one short single train produces behavioral effects outlasting the stimulation up to 30 min (Nyffeler et al., 2006; Cazzoli et al., 2009a,b). Furthermore, in a previous study we were able to show that gestural performance (predominantly pantomime) could be modulated by cTBS on the left inferior frontal cortex (Bohlhalter et al., 2011), thereby proving cTBS as a valid research tool to investigate the neural basis of gesturing.

In order to further investigate whether SPL and IPL play a distinct role in gestural imitation, we applied imaging-guided, neuro-navigated cTBS in healthy subjects. Based on the dual route model, we expect that the inhibition of the left IPL by cTBS would mainly interfere with the imitation of meaningful gestures, and the inhibition of the left SPL primarily with the imitation of meaningless gestures.

2. Material and methods

2.1. Subjects

Twelve healthy subjects (nine women, aged 23–63 years), all right-handed as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971), participated in this study. Informed written consent according to the latest version of the Declaration of Helsinki was obtained from each subject prior to the experiment. The study was approved by the local ethics committee of the state of Bern. All subjects had normal or corrected-to-normal vision and hearing, and were screened for exclusion criteria for TMS application, such as current pregnancy, personal or family history of epilepsy or epileptic fits, and any psychiatric, neurologic, or medical history. Furthermore, subjects with any contra-indications for MRI (such as brain surgery, metallic foreign bodies and pacemakers) were not included in this study.

2.2. Experimental protocol

First, all subjects underwent structural MRI acquisition to be used for the imaging-guided neuro-navigation. Second, three experimental cTBS sessions on three different stimulation sites (superior parietal lobe [SPL], inferior parietal lobe [IPL]), and sham stimulation over vertex) were conducted in weekly intervals. The exact target stimulations sites for the three conditions (SPL, IPL, sham) are specified in the next section.

The order of stimulations was counterbalanced across participants. Consequently, four subjects received sham, SPL or IPL as a first stimulation. The behavioral task immediately followed the stimulation application.

2.3. Neuro-navigation

High-resolution T1-weighted structural images with a 3D-modified driven equilibrium Fourier transform (MDEFT) sequence (176 contiguous slices with 1 mm thickness, 256 mm $\times$ 256 mm FOV, TR = 7.92 ms, TE = 2.84 ms, flip angle 16°, matrix size = 256 $\times$ 256) were obtained from each subject using a 3T Siemens Trio whole-body MR scanner (Erlangen, Germany) and a 12-channel head matrix coil, and were used for individual coil positioning.

A 3D reconstruction of the scalp and brain surfaces was produced based on the individual MRI scans, using the LOCALITE software (LOCALITE GmbH, Sankt Augustin, Germany). The LOCALITE software was combined with an infra-red tracking system which was used to co-register the 3D scalp reconstruction with the actual subjects' head, based on facial/cranial landmarks. Consequently, the target points (vertex, SPL, and IPL) could be located on the real head for cTBS application. The target points were defined as follows. The left SPL (Brodmann area 7) was defined as the posterior third of the connecting line from the postcentral sulcus to the

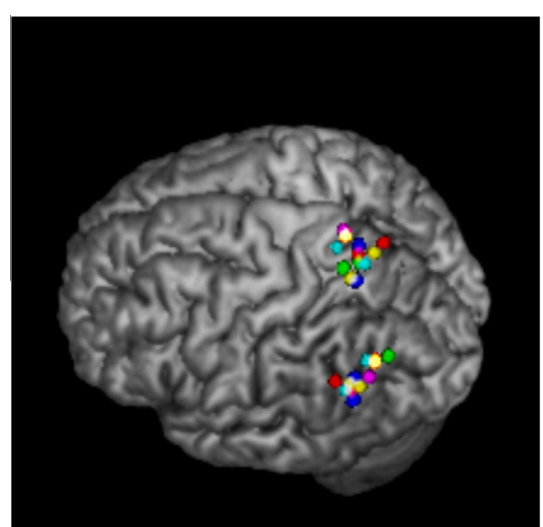

Fig. 1. Localization of TBS targets in the SPL and IPL for each subject projected on a normalized brain surface. Each color represents one subject.