Clinical Neurophysiology 126 (2015) 987–996

Contents lists available at ScienceDirect

Clinical Neurophysiology

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

Dynamics of functional and effective connectivity within human cortical motor control networks

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ARTICLE INFO

Article history:
Accepted 10 September 2014
Available online 18 September 2014

Keywords:
EEG
Effective connectivity
Efference copy
Praxis

HIGHLIGHTS

- The dynamics of causal interactions in the praxis network of normal adult humans is reported for the first time.
- Directionally specific propagation from parietal to frontal regions is seen only in the left hemisphere.
- Our observations may provide physiological evidence of corollary discharge in the human frontal–parietal praxis network.

ABSTRACT

Objective: Praxis, the performance of complex motor gestures, is crucial to the development of motor and social/communicative capacities. Praxis relies on a network consisting of inferior parietal and premotor regions, particularly on the left, and is thought to require transformation of spatio-temporal representations (parietal) into movement sequences (premotor).
Method: We examined praxis network dynamics by measuring EEG effective connectivity while healthy subjects performed a praxis task.
Results: Propagation from parietal to frontal regions was not statistically greater on the left than the right. However, propagation from left parietal regions to all other regions was significantly greater during gesture preparation than execution. Moreover, during gesture preparation only, propagation from the left parietal region to bilateral frontal regions was greater than reciprocal propagations to the left parietal region. This directional specificity was not observed for the right parietal region.
Conclusions: These findings represent direct electrophysiological evidence for directionally predominant propagation in left frontal–parietal networks during praxis behavior, which may reflect neural mechanisms by which representations in the human brain select appropriate motor sequences for subsequent execution.
Significance: In addition to bolstering the classic view of praxis network function, these results also demonstrate the relevance of additional information provided by directed connectivity measures.

1. Introduction

Praxis refers to the performance of skilled, complex motor gestures and is not only an important human capability in its own right but is also an excellent model for studying the performance and development of other human skills (Mostofsky and Ewen,

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http://dx.doi.org/10.1016/j.clinph.2014.09.006
1388-2457/

2011). The networks responsible for praxis skill learning and execution are of scientific interest for a number of reasons. Lesions of the praxis network are associated with the clinical syndrome of acquired apraxia, which is a clinical disorder that has attracted significant research (Wheaton and Hallett, 2007). Moreover, the anatomy of praxis network is relatively well characterized and therefore is a prime target for studying principles of neural circuit dynamics.

Since the early 1900s, the principal evidence for the understanding of the praxis network in the brain has been developed from lesion studies of adults with acquired apraxia. Acquired ideomotor apraxia manifests as the inability to perform or pantomime communicative gestures (e.g., waving good-bye) and tool-use gestures (e.g., brushing teeth), despite normal basic motor skills (including strength and coordination). Through systematic study of performance deficits in patients with a variety of anatomical lesions, a hierarchical model has been proposed which establishes putative information transformations at various anatomical regions within the praxis network (Heilman and Valenstein, 2003). Both visual and auditory regions may serve as input into praxis-specific regions of the network, which are typically lateralized to the left hemisphere and include left inferior parietal cortex, which is believed to contain a "praxicon" (analogous to a lexicon), in which sensori-motor representations of praxis gestures are stored. Lesions of this area result in deficits both in the production of praxis gestures and in the recognition of praxis gestures produced by others. During the production of gestures, sensori-motor representations or "programs" are believed to be transmitted from left inferior parietal to left premotor regions (Heilman and Valenstein, 2003), where they are transcoded into signals compatible with primary motor cortex, where the gesture is executed. Frontal lesions tend to result in deficits in production but not in recognition of gestures. The overall dynamics of information propagation in the brain during gesture production, as inferred from lesion studies, is thus understood to occur from parietal to frontal components of the praxis network.

While lesion studies have allowed investigators to infer the relationship between various regions, there has been relatively little direct physiological observation of the interactions between different cortical regions, using functional and effective connectivity techniques. Wheaton, Hallett and colleagues have demonstrated praxis-task-related activation of parietal and premotor regions as well as event-related functional connectivity between anatomical areas (specifically parietal and premotor) that constitute the network (Wheaton et al., 2005a,b, 2008, 2009).

To study the interactions among the various regions of the human praxis network, we used measures of effective connectivity to examine causal interactions between nodes in the network at behaviorally relevant time scales. "Effective connectivity" measures show directed ("causal") interactions between brain regions, derived from physiological time-series data, such as EEG (Friston, 1994; Behrens and Sporns, 2012).

We recorded scalp EEG in neuro-typical adults during the performance of a praxis task and tested two basic predictions from the classical hierarchical model of the human praxis network. First, this model predicts that the magnitude of activation and information propagation is greater in the left hemisphere than in the right. With few exceptions (Wheaton and Hallett, 2007), left-hemisphere lesions are responsible for acquired apraxia, and although physiological studies using fMRI and EEG have demonstrated bilateral activation, many of these studies demonstrate greater activation in the left (dominant) hemisphere (Moll et al., 2000; Wheaton et al., 2005a,b; Bohlhalter et al., 2009). Second, as discussed above, the model predicts that the directionality of information propagation is primarily posterior-to-anterior, i.e., from parietal to premotor regions.

Based on the classical model, we therefore hypothesized that neural activation and propagation accompanying praxis task would be greater in magnitude in the left hemisphere than the right, and that propagation would be directed from posterior to anterior regions.

2. Materials and methods

2.1. Participants

Seventeen right-handed (based on self-report) adult subjects (10 male, 7 female) at least 18 years of age (mean age = 26.18, SD = 4.17) participated in the study. Volunteers were screened to exclude individuals with neurological or psychiatric disorders. Each session lasted 1–1.5 h. Informed consent was obtained, and participants were compensated with a $25 gift card for their participation. The protocol was approved by Johns Hopkins Medicine Institutional Review Board.

2.2. Task

The task was largely based on the paradigm from Wheaton et al. (2005) and consisted of the pantomime of using 10 common tools (scissors, spoon [to stir coffee], ice cream scoop, doorknob, pencil, screwdriver, hammer, paintbrush, key, chalkboard eraser). These tools were selected because the pantomime of their use would allow the participant to keep his or her elbow on the chair's armrest, thus minimizing movement artifact in the EEG recording. Prior to the recording, the participants were asked to demonstrate the correct use of each of the tools. During the EEG recording, the stimuli were presented using eevoke software (ANT, the Netherlands). During the pre-stimulus portion of each trial, subjects first fixated on a cross at the center of the computer monitor; this stimulus lasted 4 s (Fig. 1). The fixation cross was replaced by the photograph of one of the ten tools, each with a size on the monitor that intersected 9° of visual angle; participants were instructed not to make any movements during this time. We refer to this first stimulus as the "*Prepare*" stimulus. After this *Prepare* stimulus remained on the screen for 3 s, a green box appeared around the photograph of the tool ("*Go*" stimulus). During the presentation of the *Go* stimulus (which lasted 3.5 s), subjects pantomimed the use of the tool with their right hand until the word "Rest" appeared. "Rest" lasted 2 s and was replaced by the fixation cross for the next trial. 100–160 trials were recorded in each subject, with the experimenter continuously observing performance. Accuracy in the performance of praxis movements approached 100% for

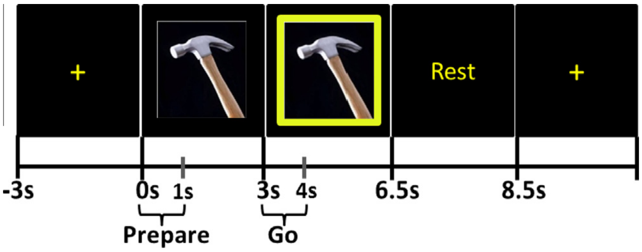

Fig. 1. Tool-use task. The photograph immediately after the fixation cross is the *Prepare* stimulus, during the presentation of which subjects were instructed not to move. When the green frame appears around the photograph (*Go* stimulus), subjects pantomimed the use of the tool. Each trial was epoched from −1.2 s (relative to the onset of *Prepare*; during the fixation cross) to +6.8 s (after the onset of the *Rest* stimulus). The periods from 0–1 s (relative to the onset of *Prepare*) and from 3–4 s were used for subsequent analyses, based on results of Matching Pursuit analyses (described in Section 3.1). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)