In vivo definition of parieto-motor pathways during movement planning using twin-coil TMS and DT-MRI based tractography

M. Cercignani[1], G. Koch[2,3], C. Caltagirone[2,3], and M. Bozzali[1]

[1]Neuroimaging Laboratory, Fondazione Santa Lucia, Roma, Italy, [2]Dept of Clinical and Behavioural Neurology, Fondazione Santa Lucia, Roma, Italy, [3]Dept of Neuroscience, University of Rome 'Tor Vergata', Roma, Italy

Introduction

Transcranial magnetic stimulation (TMS) not only changes neural activity at the site of stimulation, but also affects interconnected cortical and sub-cortical areas [1]. Recently, a new method which uses a twin-coil or 'paired-pulse' TMS paradigm has been proposed for studying functional 'connections' between posterior parietal cortex (PPC) and ipsilateral motor cortex (M1) non-invasively in humans [2]. A conditioning TMS pulse is applied over PPC, shortly prior to a test pulse over the hand area of M1. The latter pulse evokes a small twitch in contralateral hand muscles, measurable with surface electro-myography (EMG). When the interval between the PPC and M1 pulses is around 4-6 ms, the EMG response triggered by the M1 pulse is enhanced, indicating that the PPC pulse has altered excitability of M1. Depending on the task, this excitability of functional connections may vary with the motor state [3-5]. Despite these evidence of functional connectivity, the pathways involved in these neurophysiological interactions remain unknown. A recent paper investigated the relationship between TMS measures of functional connectivity during decision making and structural connectivity (measured by diffusion tensor [DT] MRI and fractional anisotropy [FA]) [5]. In the current study, we use probabilistic DT tractography to define the anatomo-functional pathway originating from a key sub-region of the PPC that lays over the caudal intraparietal sulcus (cIPS), presumably involved in reaching and grasping. To this aim, we examined the causal changes induced by cIPS TMS on the ipsilateral M1 excitability when subjects were planning either a whole hand grasp (WHG) or a precision grip (PG) of an ecological object positioned either in front or lateral in respect with subjects' body midline and correlated the output with indices derived from DT MRI.

Methods

Ten subjects (F/M=5/5, median age [range]= 28 [22-34] yrs) took part in the study. During TMS recording, the task was to reach and grasp a cup positioned at either a central or right position, as signalled by an auditory tone that indicated symbolically how the subject should grasp on that particular trial. Depending on the tone, subjects were required either to pinch the handle of the cup (PG) or to grasp the whole cup from the top (WHG). The M1 area was defined as the point where stimulation evoked the largest motor evoked potential (MEP) from the contralateral first dorsal interosseous (FDI) muscle. The coil position for left PPC TMS was defined relative to the P3 position of the 10-20 electro-encefalographic (EEG) system. According to previous investigations this site is situated close to a posterior part of the adjoining cIPS [2,6]. In all subjects MRI guided frameless stereotaxy was used to verify the trajectory of the induced magnetic field and the distance from the underlying portion of cortex in respect to P3 position. TMS was delivered over M1 of the left hemisphere at different delays (25, 50, 75, 100, 125, 150 ms) after the cue sound. The intensity of the M1 pulse was adjusted to evoke an MEP of approximately 1 mV, peak to peak, in the relaxed left FDI. In half of the trials, M1 TMS was preceded by a conditioning pulse delivered 4 ms earlier, over the ipsilateral PPC at an intensity of 90% of the resting motor threshold (RMT). DT MRI was obtained at 3T using a twice-refocused spin echo EPI (TE/TR=90/8500ms, bmax=1000smm^{-2}, 27 directions, repeated 3 times, 9 b_0s, voxel size 2.3mm^3). All DT MRI data were transformed to MNI coordinates using the preservation of principal direction (PPD) algorithm [7]. All subjects had also a T1-weighetd 3D scan, which was registered to the DT MRI data using an affine transformation [8]. The cIPS and the anterior intraparietal sulcus (aIPS), another area implicated in these kind of tasks, were manually drawn on the T1 volume for every subject, and mapped to the space of DT MRI. The seed mask for reconstructing the superior longitudinal fasciculus (SLF) was defined on color-coded anisotropy maps, dorso-lateral to the putamen, on 4 contiguous coronal slices [9]. Probabilistic tractography [10], implemented in Camino (www.cs.ucl.ac.uk/research/medic/camino/), was used to segment the seed mask according to the probability of connection to either the cIPS or the aIPS [11]. For each subject, two portions of the SLF were reconstructed using the regions resulting from the segmentation as seeds, and the average FA of both portions was computed. The correlation between the percentage increase in MEP during cIPS-M1 TMS at peak (relative to M1 only TMS) and mean tract FA was investigated.

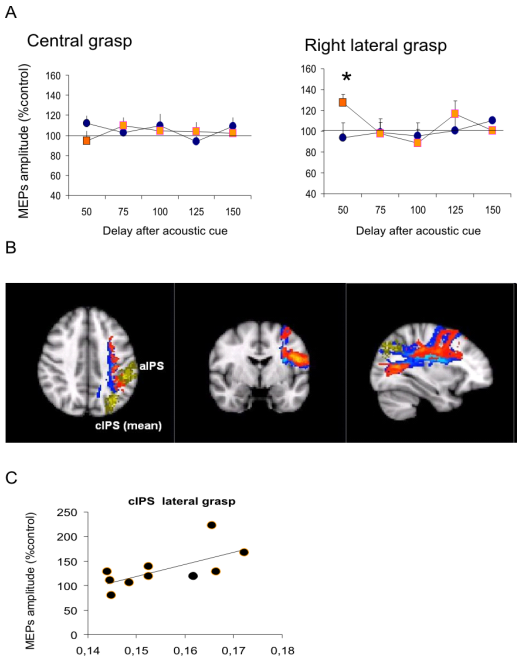

Fig 1. TMS and tractography results. A) Percentage facilitation of MEPs due to cIPS stimulation relative to the M1-only baseline. B) Mean reconstructed portions of the SLF (averaged across subjects), overlaid onto a T1-weighted tempalte image: in blue, portion connecting to the cIPS, in red, portion connecting to the aIPS. In Yellow, the cortical masks averaged across subjects. C) Scatterplot of percentage MEPs at peak against mean tract FA (obtained from cIPS portion).

Results

Fig 1A plots percentage facilitation of these MEPs due to the cIPS conditioning pulse (relative to the M1-only baseline), at intervals from 25-150 ms after onset of the imperative auditory signal. Facilitation due to the cortical stimulation over cIPS became evident specifically when subjects planned a lateralized WHG but not PG, as indicated by ANOVA showing a significant interaction between GRASP and TIME main factors ($F(1,9)=4.34$; $p<0.05$). Post hoc analysis using Bonferroni corrected t-tests showed that the cIPS-M1 grasp-specific facilitation arose selectively at an early delay of 50 ms after the auditory signal (WHG vs. PG; $p<0.05$ for both muscles). Fig 1B shows the results of tractography, averaged across subjects. A significant correlation between peak MEPs and tract specific FA was found for both the SLF portion connecting to the cIPS ($R=0.65$, $p=0.02$; See Fig 1C) and that connecting to the aIPS ($R=0.68$, $p=0.01$).

Discussion

Our findings reveal that cIPS-M1 connectivty is specifically activated during planning of lateral whole hand grasping movements. Moreover these measures directly correlated with FA of the underlying SFL, suggesting that this information is effectively mediated by this white matter pathway.

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