

## Is BA 44 part of the human Mirror Neuron System? A fMRI Study.

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### Introduction

Mirror neurons (MNs) are a class of visuo-motor neurons, firing during both action execution and action observation, discovered in the primate's ventral premotor cortex (F5) and in inferior parietal cortex (PF-PFG) (1). Neurophysiological and neuroimaging studies in humans demonstrated that watching actions performed by others induces in the observer the subliminal activation of motor pathways sustaining the observed action (*Motor Resonance*) and the activation of a fronto-parietal cortical network, so called Mirror Neuron System (MNS) (1). Given their properties, MNs are suggested to be involved in higher motor/cognitive processes such as the recognition/understanding of observed actions, motor imitation and learning. These neurons have been hypothesized to be at the origin of language acquisition/evolution, based on the involvement of BA44 (Broca's area) within the areas activated for observation of hand actions and thus referred to be part of the MNS (1). The underlying hypothesis refers to a functional link between hand gesture and speech in the course of language evolution. However the actual involvement of BA44 as part of the MNS is matter of debate. A recent work (2), aimed at studying the Motor resonance during observation/execution of hand grasping actions, failed to find BA 44 within the activated MNS areas. Given the implications of the presence/absence of BA44 in the MNS for language theories, aim of this study was to explore the activation of the MNS in response of observation/execution of the action performed by the 2 crucial effectors, the hand and the mouth, both supposed to be mapped within the BA44 (1). Actions selected as test are supposed to be the most powerful in activating mirror neurons given their specificity in activating these neurons in monkeys. The involvement of Broca's cortex in the MNS has been investigated by identifying this area with a with a phonological fluency task and then by matching the areas activated with the functional test with those revealed by the conjunction analysis as part of the MNS.

### Materials and methods

Twenty-two healthy right-handed subjects (10 M, mean age 32.4 yrs, range 20-52) underwent a fMRI study. Brain MRI scans were obtained using a 3.0 Tesla Scanner (Intera, Philips Medical System, Best, The Netherlands) using an Echo-Planar Imaging sequence (EPI) (TE 30 msec, TR 3000 msec, FOV 240 mm, 40 slices). Every subject underwent 5 fMRI runs, all block-designed and fully randomised. Subjects were asked to 1) perform a covert fluency task on acoustical phonological cue (**FLU**) 2) observe short movies of an hand (left or right) grasping different objects (**OHG**), 3) execute hand grasping actions (left or right hand) (**EGH**), 4) Observe short movies of a mouth grasping objects (**OMG**), 5) Execute mouth grasping actions (**EMG**). During the EHG and EMG runs, subjects viewed images of objects on a screen and were asked to execute iteratively the grasping movement as the objects would be close to their hand/mouth. fMRI data were analyzed using SPM5 ([www.fil.ion.ucl.ac.uk/spm](http://www.fil.ion.ucl.ac.uk/spm)). We defined 5 contrasts for every subject: 1) Fluency (**FLU**), 2) Observe hand grasp (**OHG**), 3) Execute hand grasp (**EHG**), 4) Observe mouth grasp (**OMG**), 5) Execute mouth grasp (**EMG**). In the second-level analyses we performed a one-sample T-test ( $p < 0.05$  FWE) to compute areas active during **FLU** condition. We also performed two conjunction analyses to discover areas active both during execution and observation of grasping actions, and thus possibly part of the MNS. We performed a conjunction analysis between **OHG** and **EHG** (*Hand grasp MNS*) and a conjunction analysis between **OMG** and **EMG** (*Mouth grasp MNS*) ( $p < 0.05$  FWE, inclusive masking threshold  $p < 0.05$ ).

### Results

The Fluency task (Fig. 1a) activated a left frontal area involving both BA44/45 and BA6, along with the right cerebellum. The conjunction analysis for *Hand grasp MNS* (Fig. 1b) showed the activation of a left-dominant fronto-parietal network involving premotor cortex (BA6), inferior parietal lobule (BA40), postcentral cortices (BA2-3, primary sensorymotor area), posterior parietal (BA7), extrastriate cortex (BA37) and prefrontal cortex (BA9). The conjunction analysis for *Mouth grasp MNS* (Fig. 1c) revealed a pattern very similar to the Hand Grasp MNS, although more caudal in the frontal and parietal components, with a more prominent activation of the very caudal part of BA6 until the rostral border of BA44.

### Discussion

In our study, we identified brain areas active both in observation and execution of actions, and thus involved in motor resonance for hand and mouth actions. The two identified circuits were very similar (Fig. 1d) but with a clear somatotopy involving premotor and parietal cortices. The observed somatotopy fits the motor and sensory *homunculi*. Moreover, with the fluency task we identified brain areas involved in speech production: the left inferior frontal gyrus (BA44) and the mouth component of the premotor cortex (BA6). We then compared the areas active in speech production with those involved in *Hand* and in *Mouth grasp MNS*. A considerable overlap was found in the BA6 for both conditions, and a minimal, if any, overlap in the BA44 was found only for *Mouth grasp MNS*.

Given the absence of BA 44 in *Hand grasp MNS*, the virtually no involvement of this area in *Mouth grasp MNS*, and the clear somatotopy of the premotor cortex activation, our results challenge the hypothesis that BA44 is part of the MNS and drive the necessity to reconsider the theory of the MNS involvement in language evolution.

(1) G. Rizzolatti, L. Craighero, *Annu. Rev. Neurosci.* **27**, 169 (2004).

(2) M. Cabinio *et al.*, *Neuroimage* **51**, 313 (2010).

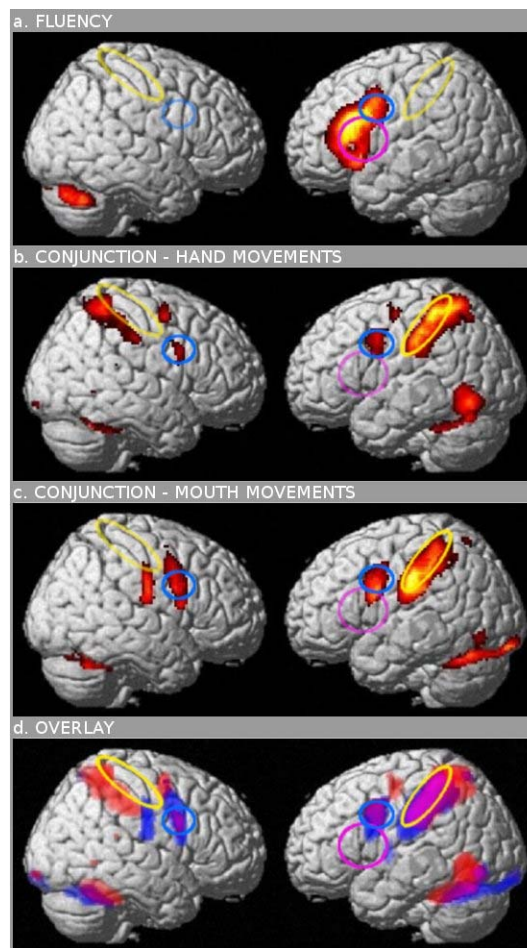


FIG. 1  
Voxels active in: a) FLUENCY task; b) CONJUNCTION analysis for HAND movements; c) CONJUNCTION analysis for MOUTH movements; d) OVERLAY of the activations of panel b (red) and panel c (blue). Yellow circles: somatosensory cortex; blue circles: premotor cortex; Pink circles: inferior frontal gyrus (BA44)