



## Mirror-neuron system recruitment by action observation: Effects of focal brain damage on mu suppression

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### ABSTRACT

Mu suppression is the attenuation of EEG power in the alpha frequency range (8–12 Hz), recorded over the sensorimotor cortex during execution and observation of motor actions. Based on this dual characteristic mu suppression is thought to signalize activation of a human analogue of the mirror neuron system (MNS) found in macaque monkeys. However, much uncertainty remains concerning its specificity and full significance. To further explore the hypothesized relationship between mu suppression and MNS activation, we investigated how it is affected by damage to cortical regions, including areas where the MNS is thought to reside. EEG was recorded in 33 first-event stroke patients during observation of video clips showing reaching and grasping hand movements. We examined the modulation of EEG oscillations at central and occipital sites, and analyzed separately the lower (8–10 Hz) and higher (10–12 Hz) segments of the alpha/mu range. Suppression was determined relative to observation of a non-biological movement. Normalized lesion data were used to investigate how damage to regions of the fronto-parietal cortex affects the pattern of suppression. The magnitude of mu suppression during action observation was significantly reduced in the affected hemisphere compared to the unaffected hemisphere. Differences between the hemispheres were significant at central (sensorimotor) sites but not at occipital (visual) sites. Total hemispheric volume loss did not correlate with mu suppression. Suppression in the lower mu range in the unaffected hemisphere (C3) correlated with lesion extent within the right inferior parietal cortex. Our lesion study supports the role of mu suppression as a marker of MNS activation, confirming previous studies in normal subjects.

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### Introduction

Execution of a motor act and observation of that act performed by others, have been found to activate a common neural substrate. This was first demonstrated in cortical neurons of macaque monkeys, hence termed “mirror neurons” (for a review see Rizzolatti and Sinigaglia, 2010). Neurons with mirror-like properties were found primarily in the ventral premotor cortex (F5) and around the anterior intra-parietal sulcus (aIPS) of the macaque (di Pellegrino et al., 1992; Fogassi et al., 2005). More recently, studies suggested the existence of such neurons in humans based on functional brain imaging (fMRI; Buccino et al., 2004; for reviews see Fabbri-Destro and Rizzolatti, 2008; Morin and Grezes, 2008), Transcranial Magnetic Stimulation (TMS; Fadiga et al., 1995), single-unit recording (Mukamel et al., 2010), magneto-encephalography (MEG; for

a review see Hari, 2006) and electroencephalography (EEG; Cochin et al., 1999; Muthukumaraswamy et al., 2004; Perry and Bentin, 2009; for a review see Pineda, 2005). The human MNS (hMNS) is thought to reside in a network comprised of the inferior frontal gyrus (IFG), the anterior part of the inferior parietal lobule (aIPL) and the ventral premotor cortex, with the possible addition of cortical regions such as the superior parietal lobule (SPL) (e.g., Caspers et al., 2010; Filimon et al., 2007; Gazzola and Keysers, 2009; Gazzola et al., 2007; Grezes et al., 2003; Keuken et al., 2011; Molenberghs et al., 2012). The extensive hMNS research in the last two decades has been motivated by the alleged importance of this system in action understanding (Rizzolatti and Craighero, 2004; Rizzolatti and Sinigaglia, 2010), imitation (Iacoboni, 2005; Iacoboni et al., 1999), motor learning (Stefan et al., 2008), speech perception (Rizzolatti and Arbib, 1998), language development (Arbib, 2005; Corballis, 2010; Gallese, 2008), and formation of key social skills such as understanding the intentions (Blakemore and Decety, 2001; Iacoboni et al., 2005) and the emotional state of others (Dapretto et al., 2006; Gallese, 2007; Schulte-Ruther et al., 2007).

EEG research typically quantifies the assumed hMNS activity by focusing on mu rhythms, which are EEG oscillations within the alpha

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range (8–12 Hz), measured over the sensorimotor regions. The EEG power in this range is reduced during the execution of a motor action (Pfurtscheller and Berghold, 1989) and also during observation of a similar action performed by another person (Muthukumaraswamy et al., 2004; Perry and Bentin, 2009; for a review see Pineda, 2005; Woodruff and Maaske, 2010). This characteristic led researchers to assume that mu suppression represents the recruitment of a hMNS, since this dual activation mode reflects the basic property of the monkeys' mirror neurons (for a review see Pineda, 2005). However, the specificity of the suppression phenomenon (i.e., being related to a mirror mechanism) is far from being clear in light of the difficulty to pinpoint EEG sources and the difficulty to dissociate between the alpha and mu suppression phenomena during action observation.

Alpha and mu suppression are measured in the same EEG frequency range (8–12 Hz). Alpha rhythms are desynchronized in association with visual stimulation and during processing that involves attention and memory, especially over the occipital cortex (Khulman, 1978; Klimesch, 1997; Klimesch et al., 2007). In contrast, mu rhythms are desynchronized typically during execution of movement, most prominently over the sensorimotor cortex (Andrew and Pfurtscheller, 1997; Khulman, 1978; Perry et al., 2011; for a review see Pineda, 2005). In the case of action observation (a visual processing activity related to viewing biological movement) the suggested distinction between alpha and mu is not trivial, and the cortical distribution of suppression patterns showed inconsistencies. Several recent studies found a widespread suppression across the scalp and even greater suppression at occipital sites than at central sites (Perry and Bentin, 2010; Perry et al., 2010, 2011), whereas other studies found suppression to manifest predominantly at central sites (Frenkel-Toledo et al., 2013; Oberman et al., 2005, 2008). Perry and Bentin (2010) suggested that the suppression seen in anterior sites might also reflect the recruitment of attention resources needed for task performance rather than a 'simulation mechanism'. It is clear that suppression patterns depend, to a large extent, on the exact definition of the task subjects are required to perform with respect to the observed movements. Given this inconsistency in earlier research, the fact that both alpha and mu suppression phenomena are measured in the same frequency range and the low spatial resolution of EEG recording, additional evidence is needed to corroborate the notion that mu suppression denotes activation specific to a hMNS.

The relation between mu event-related desynchronization (ERD) and manual motor activity is supported also by a small number of studies conducted in stroke patients. Pfurtscheller et al. (1980) found in two of five stroke patients with mild hemiparesis reduced alpha ERD over the affected hemisphere during voluntary movement of both the paretic and the non-paretic hand, compared to the ERD recorded over the unaffected hemisphere. In a different study, the same research group described a reduced response of the alpha/mu ERD over the affected hemisphere not only during hand movement but also during speech (Pfurtscheller et al., 1984). Platz et al. (2000) found in three patients with somatosensory deficits (without overt paresis) reduced alpha/mu ERD at central sites during both preparation and execution of movements with the affected upper limb. Pfurtscheller et al. (1981) and recently Stepien et al. (2011) found that patients with cortical stroke show an inter-hemispheric central alpha ERD asymmetry during both the paretic and non-paretic hand movement, with attenuation of the ERD over the affected hemisphere, whereas patients with subcortical stroke tend to show a symmetric alpha/mu ERD.

The aforementioned findings in stroke patients corroborate the notion that alpha/mu ERD marks the recruitment of cortical neurons involved in movement execution. Demonstration that ERD in the 8–12 Hz range is affected by cortical lesions also during action observation would support a more specific linkage between mu suppression and activation of a hMNS. Thus, we examined here the degree to which the 8–12 Hz frequency range is modulated during observation of movement in stroke patients with damage to different parts of the brain. Our

hypothesis was that if mu suppression during action observation reflects hMNS activity, its magnitude in the affected hemisphere (recorded from electrodes placed over the sensorimotor areas) will be lower relative to the unaffected hemisphere, similarly to the effect of unilateral cortical stroke on execution-related suppression (Pfurtscheller et al., 1980, 1981, 1984; Platz et al., 2000; Stepien et al., 2011). Moreover, based on earlier research concerning the cortical location of the putative hMNS (Arnstein et al., 2011; Caspers et al., 2010; Gazzola and Keysers, 2009; Gazzola et al., 2007; Keuken et al., 2011; Molenberghs et al., 2012; for a review see Rizzolatti and Sinigaglia, 2010), we assumed that the extent of damage within the posterior parietal cortex (IPL, SPL), the inferior frontal gyrus (IFG) and the ventral premotor cortex would correlate with the magnitude of mu-suppression in patients with stroke (the greater the damage is, the less suppression is expected). Based on previous (Marshall et al., 2009; Perry et al., 2010) and on our recent findings (Frenkel-Toledo et al., 2013) that showed that action observation affects the lower mu range (8–10 Hz) more than the upper range (10–12 Hz), we expected the above effect of cortical damage to be shown mainly in the lower range.

## Methods

### Participants

Thirty-eight first-incident stroke patients (22 males) ranging in age from 24 to 76 years (mean and standard deviation:  $55.4 \pm 13.7$  years) participated in this study. The patients were recruited during their hospitalization at the Loewenstein Rehabilitation Hospital (LRH), Ra'anana, Israel. Time after stroke onset till admission to the study ranged between 23 and 132 days (mean and standard deviation:  $58.7 \pm 29.7$  days). Patients were included in the study only if they did not suffer from psychiatric or prior neurological disorders, had normal or corrected-to-normal visual acuity and their language and cognitive status enabled comprehension of the task requirements. All but one subject were right-handed. The patients signed an informed consent approved by the institutional Ethics Review Board of the LRH and the Tel-Aviv University. Three patients had to be excluded from the analysis due to excessive amount of artifacts in their EEG (one male aged 60, and two females aged 65 and 63), and two additional patients were excluded due to refusal to participate in the entire experiment (two males aged 73 and 67). Hence, the reported results are based on 33 subjects (right hemisphere damage (RHD);  $n = 14$ , left hemisphere damage (LHD);  $n = 19$ ). The demographic and clinical data of the stroke group are described in Table 1.

### Clinical examination

For the evaluation of the motor ability of the hemiparetic upper limb, standard clinical scales: Fugl Meyer (FM; Fugl-Meyer et al., 1975; Gladstone et al., 2002) as well as apraxia test (van Heugten et al., 1999) were used. All tests were delivered by the same physical therapist.

### Stimuli and experimental conditions

The subjects were examined in the following experimental conditions: a) *rest* - eyes closed and blindfolded (to assure minimal eye muscle contraction and complete darkness), b) *baseline* - observing a non-biological movement - a video clip showing a rolling ball on a table, c) *right egocentric* - observing a video clip showing reaching and grasping an object with the right hand observed from an egocentric viewpoint (the subject sees the actor from behind), d) *left egocentric* - observing a video clip showing reaching and grasping an object with the left hand observed from an egocentric viewpoint, e) *right allocentric* - observing a video clip showing reaching and grasping an object with the right hand observed from an allocentric viewpoint (the subject faces the actor), f) *left allocentric* - observing a video clip showing reaching and grasping an

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