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Selective enhancement of motor cortical plasticity by observed mirror-matched actions

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ABSTRACT

Watching others learn a motor task can enhance an observer's own later performance when learning the same motor task. This is thought to be due to activation of the action observation (or mirror neuron) network. Here we show that the effectiveness of plasticity induced in human motor cortex (M1) is also significantly influenced by the nature of prior action observation. In separate sessions, 17 participants watched a video showing repeated goal-directed movements (action observation) involving either the right hand (congruent condition) or the same video mirror-reversed to simulate the left hand (incongruent condition). Participants then received pulses of transcranial magnetic stimulation over the hand area of left M1 paired with median nerve stimulation of the right hand (paired associative stimulation; PAS). The resting motor-evoked potential (MEP) in right abductor pollicis brevis (APB) increased significantly 20 minutes after PAS, but only when participants had previously watched the congruent video. In this condition, all participants showed an increase in MEP amplitude at 20 minutes post-PAS. There was no change in MEP amplitude following PAS when participants watched the incongruent video. We conclude that prior action observation is a potent modulator of subsequent PAS-induced neuroplasticity, which may have important therapeutic applications.

Introduction

Several experimental paradigms have recently been developed that induce plasticity within the human cortex using non-invasive stimulation (Huang et al., 2005; Pascual-Leone et al., 1994; Ridding et al., 2001; Stefan et al., 2000). Plasticity refers to a change in central nervous system structure and function, and is critical for learning and memory (Sanes and Donoghue, 2000), and recovery from nervous system injury (Nudo et al., 1996). Research has focussed on improving functional recovery after brain injury (particularly stroke), with studies demonstrating improvement in function in stroke patients with such stimulation paradigms used on their own (Kim et al., 2006), or in conjunction with physical therapy (McDonnell et al., 2007). Unfortunately, the functional gains reported have generally been modest. This is probably due in part to individual differences in responsiveness to stimulation.

Many factors appear important in mediating plasticity induction in humans (for review see Ridding and Ziemann (2010)). One such factor is the history of prior cortical activity (Iyer et al., 2003; Muller et al., 2007; Stefan et al., 2006). One way of modifying cortical activity in the motor system is by observing others perform a matching movement. It is now well established that a specific set of neurons is activated during both action observation and action execution. Originally found in monkeys (Rizzolatti et al., 1996a), but also thought to be present in humans (Chong et al., 2008; Kilner et al., 2009; Rizzolatti et al., 1996b), mirror neurons are active when individuals perform a goal-directed movement and also when they observe another individual performing a matching goal-directed movement. Prior activation of such a network has been suggested to influence subsequent motor learning (Mattar and Gribble, 2005).

An 'artificial' paradigm has been developed which mimics the use-dependent plasticity associated with motor learning (Stefan et al., 2000). This paired associative stimulation (PAS) paradigm pairs a peripheral electrical stimulus delivered to a nerve innervating a muscle in the hand, with a pulse of transcranial magnetic stimulation (TMS) to the corresponding motor representation in the contralateral motor cortex. The changes induced with PAS are thought to reflect long-term potentiation (LTP)-like changes in synaptic efficacy (Stefan et al., 2002). The circuits activated by PAS are the same as – or at least very similar to – the circuits activated by motor learning (Ziemann et al., 2004). Importantly, PAS requires no muscle activation to induce plasticity in motor cortex, and could potentially offer advantages in neurorehabilitation (compared with motor training), particularly when voluntary muscle activation is not possible (due to hemiplegia), or even deleterious (dystonia).

We therefore investigated whether PAS-induced plasticity could be enhanced by prior action observation. Specifically, we hypothesised that action observation should enhance the effects of subsequent PAS-induced plasticity, but only when the observed action activates the same circuits as those modified during PAS.

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Materials and methods

Participants

Seventeen participants (mean age, 26.29 ± 1.39 years; 9 females) took part in the study. All participants were right handed (median laterality quotient = 0.84, range 0.30-1.00) as assessed by the Oldfield handedness questionnaire (Oldfield, 1971). All participants gave written informed consent prior to participation in the study, which was approved by the University of Queensland Medical Research Ethics Committee.

Overview of experimental procedure

Participants attended two experimental sessions, separated by at least one week. In each session they were required to watch an action observation video (15 minutes), after which plasticity was induced in the motor cortex using TMS and concurrent stimulation of the median nerve (the PAS procedure). In order to activate the same neural circuits as those stimulated during action observation, participants performed a simple action execution task during the PAS procedure. The two sessions were identical except that in one, participants watched a video in which a model performed actions with the same (right) hand as the participant during the subsequent PAS procedure, whereas in the other session the video showed the same actions performed with the opposite (left) hand (via mirror-reversal of a common video source). Cortical excitability was probed before action observation, as well as before and after plasticity induction, to quantify changes in plasticity in the different sessions. An overview of the experimental set-up is shown in Fig. 1.

Experimental arrangement

Participants were seated comfortably in an experimental chair with their arms comfortably resting on a table. Surface electromyographic (EMG) recordings from the abductor pollicis brevis (APB) muscle of the right hand were obtained using bipolar Ag-AgCl electrodes in a belly-tendon montage. EMG signals were amplified 1000 times, filtered (5 Hz – 500 Hz via a NeuroLog system (Digitimer, UK), digitized online (2 kHz/channel) with a data acquisition interface (BNC-2110; National Instruments, USA) and custom MatLab software (Mathworks, USA) and stored on computer for offline analysis. The EMG signal from APB muscle was displayed on an oscilloscope to help participants maintain EMG silence when required.

Transcranial magnetic stimulation (TMS)

All participants completed a TMS safety screen (Keel et al., 2001), and were excluded if there was a family history of epilepsy, they were taking any neuroactive drugs or had undergone neurosurgery. Monophasic TMS was applied through a figure-of-eight coil (outer diameter of each wing 70 mm) connected to a Magstim 200 magnetic stimulator (Magstim, Whitland, Dyfed, UK). The coil was held tangentially to the skull with the handle pointing backwards and laterally at an angle of 45° to the sagittal plane at the optimal scalp site to evoke an MEP in the relaxed APB muscle of the right hand. With this coil placement, current flow was induced in a posterior to anterior direction in the brain. The optimal scalp position was marked with a pen, and the coil was held throughout the experiment by hand, with the position continually checked throughout the experiment.

TMS measures of motor cortex excitability

Motor cortex excitability was assessed at several time points during each experimental session (see Fig. 1B for time-line of experimental assessments).

Mean peak-to-peak amplitude of the APB MEP at rest was calculated by averaging the individual peak-to-peak amplitudes of MEPs elicited by 20 separate TMS pulses (~0.2 s^{-1}). The stimulus intensity was expressed as a percentage of maximum stimulator output (% MSO). MEPs were evoked prior to action observation, following action observation (immediately prior to PAS) and 5 minutes following PAS.

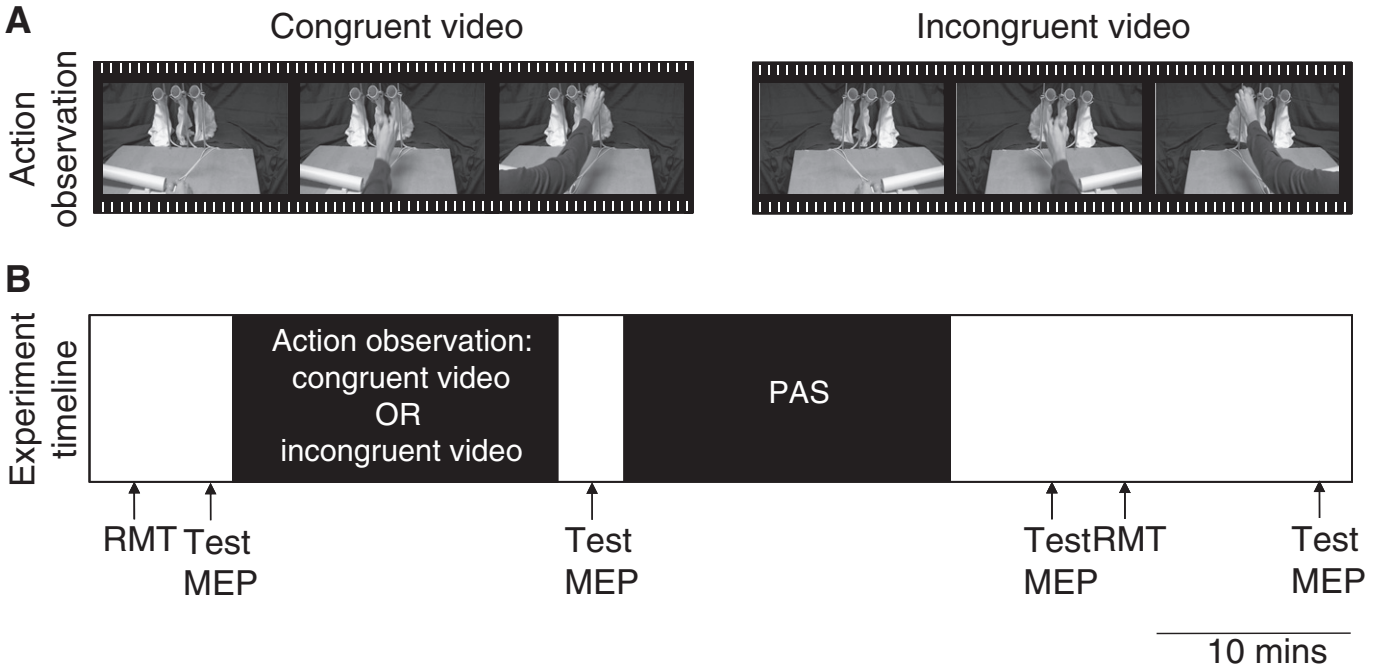

Fig. 1. Schematic representation of the experimental protocol. **(A)** Participants observed one of two action videos in each session showing repeated goal-directed movements, involving either the "congruent" hand or the "incongruent" hand (mirror-reverse of congruent hand). **(B)** Overview of the testing protocol, indicating the approximate timings for assessment of neurophysiological parameters and their relation to action observation and action execution with PAS. MEP – motor evoked potential; RMT – resting motor threshold.