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RAPID PLASTICITY OF MOTOR CORTICOSPINAL SYSTEM WITH ROBOTIC REACH TRAINING

S. S. KANTAK, [a] **L. M. JONES-LUSH,** [a,b] **P. NARAYANAN,** [a,c]
T. N. JUDKINS [a†] **AND G. F. WITTENBERG** [a,c,d*]

[a] *Department of Physical Therapy and Rehabilitation Science, University of Maryland School of Medicine, 100 Penn Street, Baltimore, MD 21201, United States*

[b] *Department of Anatomy and Neurobiology, University of Maryland School of Medicine, Health Science Facility-2, Baltimore, MD 21201, United States*

[c] *Department of Neurology, University of Maryland School of Medicine, 110 South Paca Street, Baltimore, MD 21201, United States*

[d] *Geriatric Research, Education, and Clinical Center, VA Maryland Health Care System, 10 North Greene Street, Baltimore, MD 21201, United States*

Abstract—Goal-directed reaching is important for the activities of daily living. Populations of neurons in the primary motor cortex that project to spinal motor circuits are known to represent the kinematics of reaching movements. We investigated whether repetitive practice of goal-directed reaching movements induces use-dependent plasticity of those kinematic characteristics, in a manner similar to finger movements, as had been shown previously. Transcranial magnetic stimulation (TMS) was used to evoke upper extremity movements while the forearm was resting in a robotic cradle. Plasticity was measured by the change in kinematics of these evoked movements following goal-directed reaching practice. Baseline direction of TMS-evoked arm movements was determined for each subject. Subjects then practiced three blocks of 160 goal-directed reaching movements in a direction opposite to the baseline direction (14 cm reach 180° from baseline direction) against a 75-Nm spring field. Changes in TMS-evoked whole arm movements were assessed after each practice block and after 5 min following the end of practice. Direction and the position of the point of peak velocity of TMS-evoked movements were significantly altered following training and at a 5-min interval following training, while amplitude did not show significant changes. This was accompanied by changes in the motor-evoked potentials (MEPs) of the shoulder and elbow agonist muscles that partly explained the change in direction, mainly by increase in agonist MEP, without significant changes in antagonists. These findings demonstrate that the arm representation accessible by motor cortical stimulation under goes rapid plasticity induced by goal-directed robotic reach training in healthy subjects. Published by Elsevier Ltd. on behalf of IBRO.

Key words: reaching, plasticity, robotics, transcranial magnetic stimulation.

INTRODUCTION

Goal-directed reaching is a movement that is fundamental for many human endeavors, and for the performance of many activities of daily living. The kinematic parameters of reaching movements, such as direction, are determined through activity in the primary motor cortex (M1) (Graziano et al., 2002; Paninski et al., 2004; Hatsopoulos et al., 2007; Matsuzaka et al., 2007; Rickert et al., 2009). Previous research in our laboratory employed transcranial magnetic stimulation (TMS) applied over M1 to map TMS-evoked movement representation, using a robotic device to measure movement kinematics. These M1 movement maps varied between subjects and stimulus locations, but within a given location, the direction and extent of the evoked movements were remarkably consistent over time (Jones-Lush et al., 2010). The stability of TMS-evoked movements in the controlled environment of the rehabilitation robot therefore allows practice-related changes in motor representation to be characterized.

Kinematic and kinetic parameters of goal-directed movements such as direction and force can be deduced from M1 activity. Multiple studies have investigated how kinematic parameters of movements represented in corticospinal projections are modified during the adaptation of reaching movements in a setting of a systematic force or visual perturbation (Gandolfo et al., 2000; Arce et al., 2010; Orban de Xivry et al., 2011). However, little is known about how kinematic parameters of movements represented in M1, with its projections to distal motor networks, are altered with repetitive practice of goal-directed reaching movements in the absence of a perturbation. Such typical goal-directed reaching movements are practiced in rehabilitation settings and are a distinct form of practice from adaptation to force fields or visuomotor transformations (Huang et al., 2011; Krakauer and Mazzoni, 2011).

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*Correspondence to: G. F. Wittenberg, Geriatric Research, Education, and Clinical Center, VA Maryland Health Care System, 10 North Greene Street, Baltimore, MD 21201-1524, United States. Tel: +1-410-637-3216; fax: +1-410-637-1417.

E-mail addresses: kantaksh@einstein.edu (S. S. Kantak), jlush@som.umaryland.edu (L. M. Jones-Lush), PNarayanan@som.umaryland.edu (P. Narayanan), tjudkins@i-a-i.com (T. N. Judkins), gwittenb@grecc.umaryland.edu (G. F. Wittenberg).

[†] Present address: Intelligent Automation Inc., Rockville, MD, United States.

Abbreviations: AD, anterior deltoid; BB, biceps brachii; EMG, electromyography; M1, primary motor cortex; MEPs, motor-evoked potentials; MT, movement time; PD, posterior deltoid; TB, triceps brachii; TMS, transcranial magnetic stimulation.

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Repetitive practice of motor tasks induces changes in movement characteristics of those tasks and associated neurophysiology that likely form the neural basis for the recovery of motor deficits after CNS injury (Butefisch et al., 2000; Muellbacher et al., 2001). One paradigm that demonstrates this physiological plasticity is TMS-evoked thumb movements (Classen et al., 1998). Stereotyped thumb movements are evoked in a consistent direction by TMS. Subsequent practice of movements in the direction opposite to the evoked movements results in a reversal in the direction of post-practice TMS-evoked finger movement for several minutes (Classen et al., 1998). While highly repetitive practice of simple single-joint finger movements demonstrates clear neural plasticity, such practice is very different from the multi-joint goal-directed reaching movements that characterize clinical rehabilitation, and evidence for plasticity related to proximal upper extremity movements is scarce. Further, it is not known which kinematic parameters of movements represented in corticospinal system (by which we mean M1 and the subcortical and spinal networks to which it projects) are amenable to change with repetitive practice of goal-directed unperturbed reaching movements.

Here, we investigate the temporal evolution of practice-induced changes in the kinematic characteristics of the reaching movements evoked by TMS applied over M1. First, baseline stability of the kinematic features of TMS-evoked arm movements was assessed over time. Then, changes in those features were assessed as participants practiced goal-directed reach movements in a direction opposite to the one evoked at the baseline. We hypothesized that repetitive goal-directed reaching practice would trigger use-dependent plasticity that would enhance representation of the practiced reaching movements accessible by transcranial stimulation of the motor cortex. We further explored the relationship between kinematic characteristics of TMS-evoked reach-like movements and motor-evoked potentials (MEPs) to begin to relate the changes in movement representation to changes in muscle activity.

EXPERIMENTAL PROCEDURES

Participants

Twenty-two healthy volunteers (seven females, mean age ± standard deviation (SD): 27 ± 3.15 years, one left-handed) with no history of neurological disease participated in the study. All participants met the TMS safety criteria (Wassermann, 1998). All provided informed consent and were evaluated per a protocol approved by the University of Maryland Institutional Review Board and the local Veterans Administration Research Committee.

Data collection

Participants were seated comfortably in front of a two degree-of-freedom planar robot (Interactive Motion Technologies, Cambridge, MA, USA) with their dominant arm in the robotic arm cradle. The forearm was secured to the robot's molded arm cradle with two straps (Jones-Lush et al., 2010) that maintained the participant's elbow just below the horizontal plane as compared to the hand and shoulder (Fig. 1A). Subjects were instructed to remain relaxed with their hand resting around the handle at the end of the cradle. A center-acting spring-like force (75 N m) was applied by the robot to prevent the arm from drifting and to return it to the initial configuration after movements were made, without any subject effort. The robot encoders recorded the position and velocity of all movements in the horizontal X, Y plane. Data were digitized at 200 Hz and stored for offline analysis. Surface electromyography (EMG) from the right arm muscles of four principal shoulder/elbow contributors (anterior deltoid, AD; posterior deltoid, PD; biceps brachii, BB and triceps brachii, TB) was visually and auditorily monitored to ensure that the subjects were at rest prior to TMS stimulation. In 11 of 22 participants, EMG was recorded for offline analysis. In the other 11 participants, these proximal muscle recordings had a long-lasting TMS-induced artifact that contaminated many MEPs, limiting the ability to analyze MEP plasticity in these participants (despite using standard Ag/AgCl disk electrodes and a TMS-specific amplifier from James Long, Caroga Lake, NY, USA). In the remaining 11 participants, we used microamplifiers with integrated dry metal electrodes (B&L Engineering, Santa Ana, CA, USA) that effectively eliminated the TMS artifact. EMG was digitized at 2 kHz using a Dell computer equipped with an A/D board (National Instruments, Austin, TX, USA), and was time-synchronized with the position data. A 100-ms period after stimulus was examined.

TMS

Single-pulse stimulation of the dominant (contralateral to the practice arm) motor cortex was performed using a MagStim 200 (MagStim Ltd., Wales, UK) with a 90-mm loop-diameter figure-of-8 coil. Coil and head positions were recorded by a frameless sterotaxic system (BrainSight, Rogue Research, Montréal, QC, Canada), and coregistered with an anatomical MRI of the standard brain template to allow for precise localization of stimulation location throughout the course of the experiment. During stimulation the coil was held tangential to the scalp with the handle pointing backward and laterally at a 45° angle to the sagittal plane.

Baseline measurements

Arm movements were elicited by methodically stimulating the area over the dominant M1, guided by a 5 × 5 cm grid centered over the anatomical landmark of the hand knob and aligned with the anterior–posterior and medial–lateral axes of the head (Jones-Lush et al., 2010). Movement hotspots were located for each subject, defined as the location that, when stimulated, produced the largest movement recorded by the planar robot. Movement thresholds were then determined at the hotspot for each subject, defined as the lowest stimulation level that