**Original Article in Cerebral Cortex**

## Supplementary Data

# Differential Contribution of the Supplementary Motor Area to Stabilization of a Procedural Motor Skill Acquired Through Different Practice Schedules

**Satoshi Tanaka [1,2], Manabu Honda [2,3], Takashi Hanakawa [2,4], Leonardo G Cohen[1]**

**[1]Human Cortical Physiology and Stroke Neurorehabilitation Section, National Institute of Neurological Disorder and Stroke, National Institute of Health, Bethesda, USA, [2]Department of Cortical Function Disorders, National Institute of Neuroscience, Kodaira, Japan, [3]Japan Science and Technology Corporation, SORST and [4]PRESTO, Kawaguchi, Japan**



## A. Supplemental Experimental Procedure

Control motor task: We also evaluated performance in an untrained non-sequential, simple visuomotor task (control motor task). The purpose was to determine if the hypothesized disruptive effects of rTMS were specific to the newly learned sequential skill or represented a less specific effect on motor function in general (newly learned or not). In this control task, subjects were instructed to respond to the presentation of a visual target (gray square) that appeared randomly at one of four peripheral locations (same visual stimuli and spatial locations used in Experiment 1, see Fig 1D) on the screen monitor by moving a cursor onto the target and clicking on it as quickly as possible (60 trials). Thus, the required visuo-motor response to the gray target was the same as that in the main experiment and only the sequential-movement link was removed. The endpoint measure of this control task was the mean RT in the 60 trials, before learning on Day 1 and after the recall time on Day 2.

The site of TMS: The site of stimulation for each cortical area was determined using previously described procedures (Matsunaga et al., 2005; Perez et al., 2007, 2008). SMA: First, we determined the optimal position for activation of the right tibialis anterior (TA) muscle by moving the coil in 1-cm steps along the mid-saggital line crossing Cz. The SMA location was defined as a position 1 cm in front of the most anterior location in the mid-sagittal line from where right TA MEPs could be evoked with mild background facilitation (Civardi et al., 2001; Matsunaga et al., 2005; Perez et al., 2007, 2008). Following these criteria, the site for the SMA stimulation was 3 cm anterior to the optimal position for activation of the TA muscle and 2–4 cm anterior to Cz in most subjects. In 17 subjects, a stereotactic frameless navigation system (eXimia, Nexstim Company, Helsinki, Finland) was also used to localize cortical positions in each individual's structural MRI. We determined the SMA position by projecting the location of each subject's anterior commissure (AC line) on his or her scalp (Picard and Strick., 2001). Both determinations of stimulated positions (with and without the stereotactic device) rendered comparable scalp locations in all subjects. Left M1: Optimum scalp position for activation of the right FDI muscle (Mills et al., 1992). PMd: For PMd, we determined the first 8% of the distance between the nasion and inion in each subject and defined the PMd location as this distance anterior to the M1 according to previously described procedures (Gerschlager et al., 2001; Picard and Strick, 2001; Tanaka et al., 2005; Perez et al., 2007). Sham stimulation: For sham stimulation, one coil was positioned in the same location described above for the SMA while a second coil located behind the subject's head discharged in air using the same parameters as those for real stimulation (Perez et al., 2007, 2008).

## B. Supplemental Results

Error response: The error response (the total number of incorrect mouse clicks in each block) in Experiment 1 was analyzed (Supplemental Fig A). On Day 1, there was a significant main effect of TIME ($F_{(5,280)}$=18.88, $p < .001$) and interaction TIME x PRACTICE ($F_{(15,280)}$=4.16, $p < .001$) on accuracy. At block 1, subjects in the blocked-practice groups made fewer errors overall than those in the random-practice groups (one-way ANOVA, $F_{(3,56)}$=3.18, $p<.04$), whereas at the end of practice (block 6) the number of errors was comparable across all groups ($F_{(3,56)}$=.50, p=.68). On Day 2, the main effect of PRACTICE was significant ($F_{(1,56)}$=23.94, $p<.001$), indicating fewer errors in the random- than in the blocked-practice groups. However, the main effect of rTMS ($F_{(1,56)}$=1.39, p=.24) and PRACTICE x rTMS ($F_{(1,56)}$=.55, p=.82) interaction were not significant. Post-hoc comparisons between sham and rTMS conditions for each practice schedule also did not reveal significant differences (For blocked practice, $t_{(28)}$=.84, p=.41; For random practice, $t_{(28)}$=.87, p=.39). Overall, these results indicate that rTMS over SMA did not modify accuracy (reaction times) as it did RTs (response times).

Reaction Time: The reaction time (time between the onset of the visual color cue and the onset of only the first movement in the sequence) in Experiment 1 was analyzed. On Day 2, there was no significant effect of PRACTICE ($F_{(1,56)}$=.30, p=.59), rTMS ($F_{(1,56)}$=.37, p=.55), or their interaction ($F_{(1,56)}$=2.97, p=.09). Therefore, the effect of rTMS on RT was not simply accounted for by the time required to reach the first target in the sequence.

## C. Supplemental References


Civardi C, Cantello R, Asselman P, Rothwell JC. 2001. Transcranial magnetic stimulation can be used to test connections to primary motor areas from frontal and medial cortex in humans. Neuroimage 14:1444-1453

Gerschlager W, Siebner HR, Rothwell JC. 2001. Decreased corticospinal excitability after subthreshold 1 Hz rTMS over lateral premotor cortex. Neurology 57:449-455.

Matsunaga K, Maruyama A, Fujiwara T, Nakanishi R, Tsuji S, Rothwell JC. 2005. Increased corticospinal excitability after 5 Hz rTMS over the human supplementary motor area. J Physiol 562:295-306.

Mills KR, Boniface SJ, Schubert M. 1992. Magnetic brain stimulation with a double coil: the importance of coil orientation. Electroencephalogr Clin Neurophysiol 85:17-21.

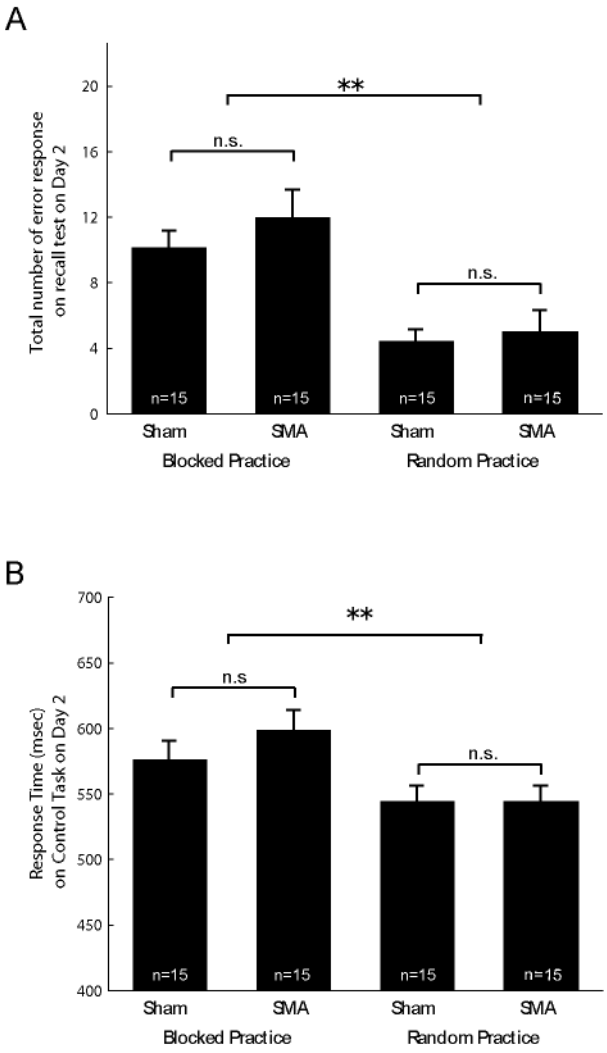
Perez MA, Tanaka S, Wise SP, Willingham DT, Cohen LG. 2008. Time-specific contribution of the supplementary motor area to intermanual transfer of procedural knowledge. J Neurosci 28:9664-9669.

Perez MA, Tanaka S, Wise SP, Sadato N, Tanabe HC, Willingham DT, Cohen LG. 2007. Neural substrates of intermanual transfer of a newly acquired motor skill. Curr Biol 17:1896-1902.

Picard N, Strick PL. 2001. Imaging the premotor areas. Curr Opin Neurobiol 11:663-672.

Tanaka S, Honda M, Sadato N. 2005. Modality-specific cognitive function of medial and lateral human Brodmann area 6. J Neurosci 25:496-501.

## D. Supplemental Figure




**Supplemental Figure**:

**A.** Effects of practice and SMA stimulation applied shortly after training on total number of errors on Day 2. rTMS over the SMA did not affect number of errors on Day 2 significantly in either random- or blocked-practice groups.

**B.** Effects of practice and SMA stimulation applied shortly after training on response times in control task (see Methods section) on Day 2. In the control-motor task, rTMS over the SMA did not affect response times significantly in either random- or blocked-practice groups. The bars depict mean+S.E.M. **=p<.01.

## E. Supplemental Table

**Descriptions of nine experimental groups.**

| Group | Condition | No. of subjects (females) | Age | rMT | Sleep before recall | | Computer mouse use | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Time (hours) | Quality | Total Year (years) | Weekly (days) |
| Experiment 1 | | | | | | | | |
| A | Blocked, Sham | 15(6) | 28.7±2.0 | 54.2±3.5 | 7.2±.3 | 7.1±.6 | 11.5±1.2 | 7.0±.0 |
| B | Blocked, SMA | 15(6) | 30.1±1.9 | 57.5±3.8 | 7.4±.2 | 7.5±.4 | 13.5±1.4 | 6.9±.1 |
| C | Random, Sham | 15(7) | 28.0±2.1 | 55.1±2.5 | 7.2±.3 | 7.0±.4 | 10.7±1.0 | 6.7±.2 |
| D | Random, SMA | 15(6) | 24.0±.7 | 56.9±3.0 | 7.2±.2 | 7.1±.4 | 11.8±1.1 | 7.0±.0 |
| Experiment 2 | | | | | | | | |
| E | Blocked, Cz+2cm | 12(5) | 27.4±1.6 | 54.2±2.5 | 7.5±.2 | 7.7±.3 | 14.9±1.0 | 6.9±.1 |
| F | Blocked,SMA+6h | 12(4) | 26.1±1.1 | 49.1±1.5 | 7.2±.3 | 7.8±.3 | 14.5±1.2 | 6.9±.1 |
| G | Blocked, L.M1 | 13(5) | 22.6±1.3 | 65.0±3.7 | 7.3±.5 | 7.2±.4 | 8.2±.9 | 7.0±.0 |
| H | Random, L.M1 | 13(6) | 23.1±.6 | 61.2±2.6 | 7.0±.6 | 7.9±.4 | 11.6±1.2 | 7.0±.0 |
| I | Random,L.PMd | 13(4) | 23.3±.8 | 59.4±2.8 | 7.0±.3 | 7.5±.4 | 12.1±1.2 | 7.0±.0 |

**Note:** Mean $\pm$ S.E.M. of age, resting motor threshold (rMT), total time (hours) and quality (visual analog scale ranging from 1: poor to 10: good) of sleep time on nights before recall testing, and experience in (total years) and frequency of use of computer mouse (days per week),