Fine manual dexterity is affected by transient inactivation of primary motor cortex using repetitive transcranial magnetic stimulation (rTMS)

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INTRODUCTION

The **primary motor cortex** (M1) plays an important role in the execution of complex behavioral tasks requiring coordinated movements of arm and hand muscles. The aim of the present study was to assess the role played by M1 hand area in the performance of a manual dexterity task involving a **synergistic action of proximal and distal muscles** called the **"reach and grasp" drawer task**, before and after a transient inactivation of M1 using repetitive transcranial magnetic stimulation (**rTMS**).

MATERIAL AND METHODS

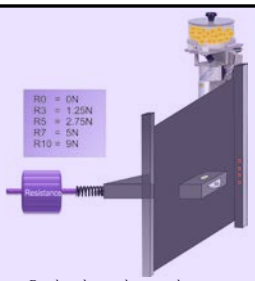
Reach and Grasp Drawer Task

We analysed several motor parameters in 2 human subjects:

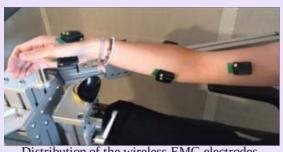
1) the temporal unfolding of the task, focusing on time intervals between key timepoints: from resting pad to knob touch (reaching time), from knob touch to start opening (onset time) and from start opening to full opening (opening time);

2) the continuous recordings of the force needed to grasp the button of the drawer (grip force) and the force needed to open the drawer against adjustable levels of resistance (load force);

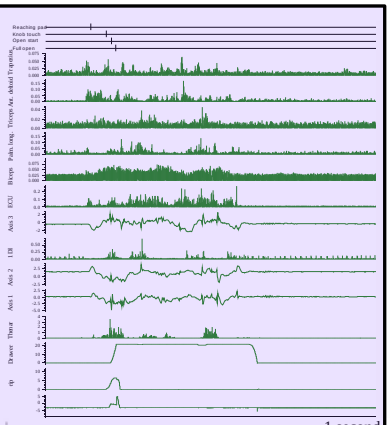
3) the electromyographic (EMG) activity of 8 arm and hand muscles.



Reach and grasp drawer task setup with adjustable resistances (N).



Distribution of the wireless EMG electrodes over the arm and hand muscles.



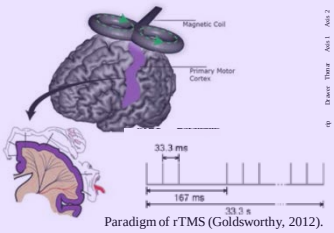
1 second

Simultaneous recordings of the motor parameters at the minimal level of resistance to the opening, showing the synergy between the EMG activity and the grip and load forces needed to perform the behavioral task, here before transient inactivation.

Repetitive Transcranial Magnetic Stimulation (rTMS)

To specifically inactivate the area of M1 involved in hand movements, we defined M1 hand region where single pulse of TMS stimulation elicited motor evoked potentials (MEPs) with the largest amplitude and the highest probability, and we applied series of bursts (3 pulses with 33.3 ms time interval) during 33.3 s, corresponding to the theta burst stimulation, at an intensity of 90% (subject 1), 80% (subject 2) and 0% (sham subject 1) of resting motor threshold.

Grid placed over the scalp to map M1.

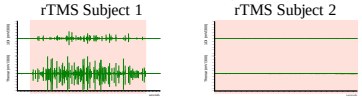


Paradigm of rTMS (Goldsworthy, 2012).

RESULTS

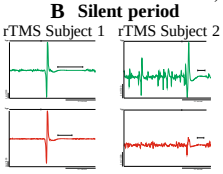
I. Effectiveness of rTMS application

A EMG during rTMS



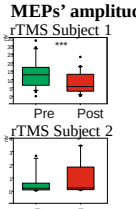
EMG recordings in intrinsic hand muscles during rTMS (stimulation intensity at 90% -S1- and 80% -S2- of resting motor threshold).

B Silent period



Decrease of the silent period induced by rTMS (stimulation intensity at 90% and 80% resting motor threshold).
To note that we cannot exclude an effect in S2, as his EMG baseline activity is different pre- and post- rTMS.

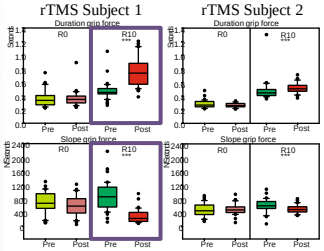
C MEPs' amplitude



Averaged MEPs recordings of intrinsic hand muscles activity elicited by single pulse TMS before (green) and after (red) rTMS.

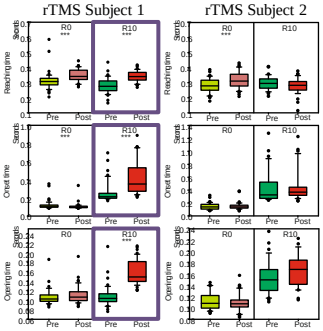
II. Effects of transient cortical inactivation by rTMS on the drawer task's performance

A Grip Forces



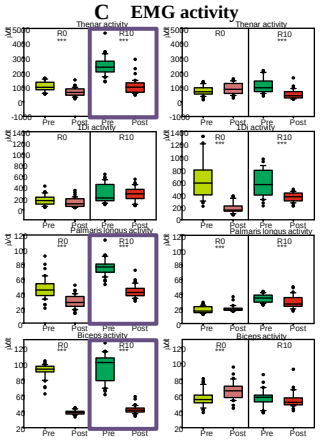
Boxplots showing averaging (40 purified trials aligned on knob touch) of grip duration and grip slope at two levels of resistance to the opening (R0=0N and R10=9N), before (green) and after (red) rTMS application in 2 subjects.

B Time Intervals



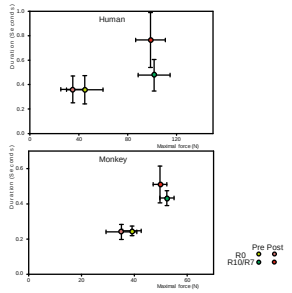
Boxplots showing averages (40 purified trials) of time intervals between various key timepoints (reaching time, onset time and opening time) in the course of the drawer task's execution at two levels of resistance to the opening (R0=0N and R10=9N), before (green) and after (red) rTMS application in 2 subjects.

C EMG activity

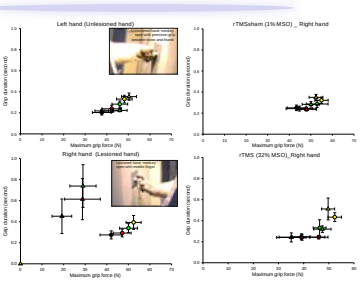


Boxplots showing averages (40 purified and rectified trials, aligned on knob touch (Thenar, 1DI and Palmaris longus) or on start openig (Biceps)) of EMG activity of hand and arm muscles before (green) and after (red) rTMS application in 2 subjects performing the drawer task at two levels of resistance to the opening (R0=0N and R10=9N).

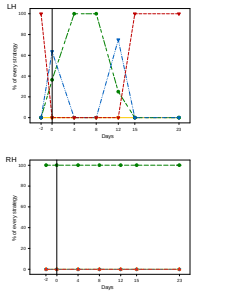
D Comparison Human-Monkey



Mean and standard deviation on bi-directional error bar plots showing a covariation between maximal and duration of grip force.
Similar pattern is observed between 1 human (upper panel) and 1 monkey (lower panel): After rTMS, at higher resistance to the opening, there is an increase of grip duration to open the drawer with a comparable maximal grip force.



Measure of duration and maximum grip force applied by monkeys on the knob to open the drawer against four increasing levels of resistances, represented by mean and standard deviation on bi-directional error bar plots.
Left panels: permanent inactivation (5 sessions pre-ibotenic acid lesion and 5 sessions of the acute post-lesion period).
Right panels: reversible inactivation (one daily session before and after rTMS, performed before permanent lesion).



Effect of muscimol injection in the intact hemisphere:
Percentage of different strategies used at R0 for the left (affected by muscimol) and right (previously affected by ibotenic acid) hands.

I. Preliminary results show a **direct effect of rTMS application** in 1 of the 2 subjects.

II. In the manual dexterity task, a more pronounced effect of rTMS could generally be observed in this same subject, especially at **higher level of resistance** to the opening :

A) Increase of **grip duration** associated with a decrease of **grip slope**;

B) Increase in **time intervals** between various key timepoints in the course of the task's execution;

C) Decreased **EMG activity** of hand and arm muscles;

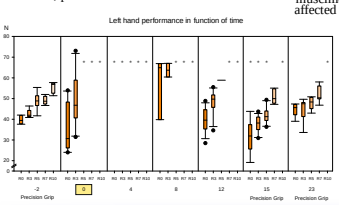
D) Similar increased durations in monkey.

These effects of rTMS application should however be interpreted with caution, as they are moderated by statistical significances, and based on 2 subjects only.

DISCUSSION AND PERSPECTIVES

These preliminary results in 2 human subjects showed motor changes after rTMS application that were more pronounced in subject 1 than in subject 2. Various parameters can explain these observations, such as the positioning and the orientation of the coil, which can either induce an activation or an inactivation of the target brain region, as well as the stimulation intensity at which rTMS is applied.

In a similar procedure experiment with a monkey, the same type of behavioral pattern changes were observed; further experiments should complete these observations. The inactivation of other cortical areas also involved in the motor control, such as the premotor cortex and the supplementary motor area, should assess the exact implication of those areas in manual dexterity. Furthermore, in complement to behavioral observations, a combination with EEG recordings could bring to light the electrophysiological impacts of lesions with various effects durations: rTMS application, muscimol injection and ibotenic acid injection.



Maximal grip forces at the various levels of resistance, one session before and six sessions after unilateral muscimol injection (reversible inactivation).

Grant sponsors: Swiss National Science Foundation, Grants No. 31-61857.00, 310000-110005, 3100JA- 132465 (EMR), PZ00P3_142258 (ES), the National Centre of Competence in Research (NCCR) on "Neural plasticity and repair", Novartis Foundation, The Christopher Reeves Foundation (Springfield, NJ, USA); The Swiss Primate Competence Centre for Research (SPCCR).