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);

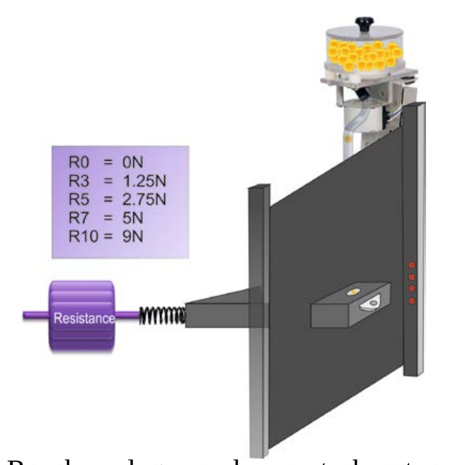
2) the continuous recordings of the force needed to grasp the button of the drawer (grip force) and the force needed to open the drawer against adjustable levels of resistance (load force);

3) the electromyographic (EMG) activity of 8 arm and hand muscles, as well as the accelerations in 3 dimensions of the movements of the hand and arm.

Repetitive Transcranial Magnetic Stimulation (rTMS)

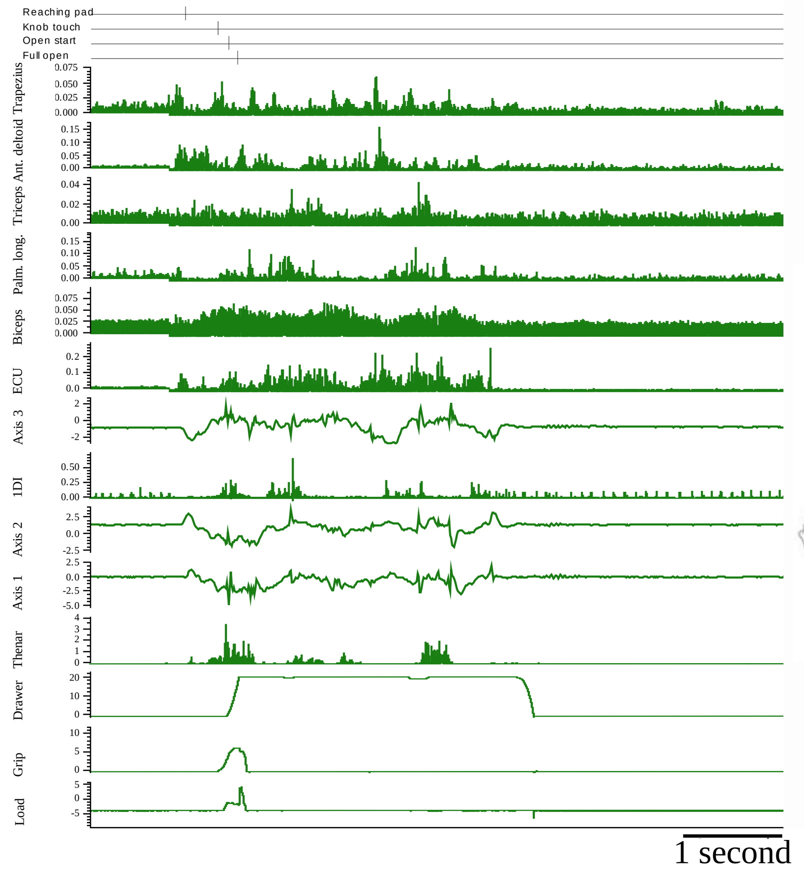
To specifically inactivate the area of M1 involved in hand movements, we defined M1 hand region where single pulse of TMS stimulation elicited motor evoked potentials (MEPs) with the largest amplitude and the highest probability, and we applied series of burst (3 pulses with 33.3 ms time interval) during 33.3 seconds 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.

Reach and Grasp Drawer Task



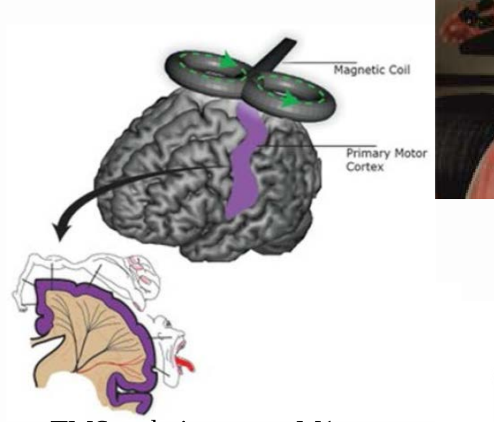
Reach and grasp drawer task setup with adjustable resistances (N).

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



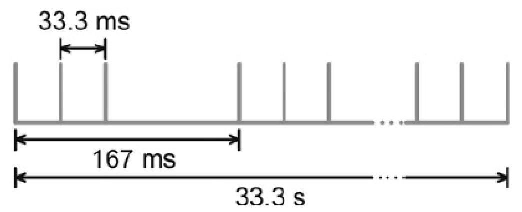
Simultaneous recordings of the motor parameters at the minimal level of resistance to the opening, showing the synergy between the EMG activity and the grip and load forces needed to perform the behavioral task, here before transient inactivation. <=

Repetitive Transcranial Magnetic Stimulation



TMS technique over M1.

Grid placed over the scalp to map M1.



Paradigm of rTMS (Goldsworthy, 2012).

RESULTS

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;

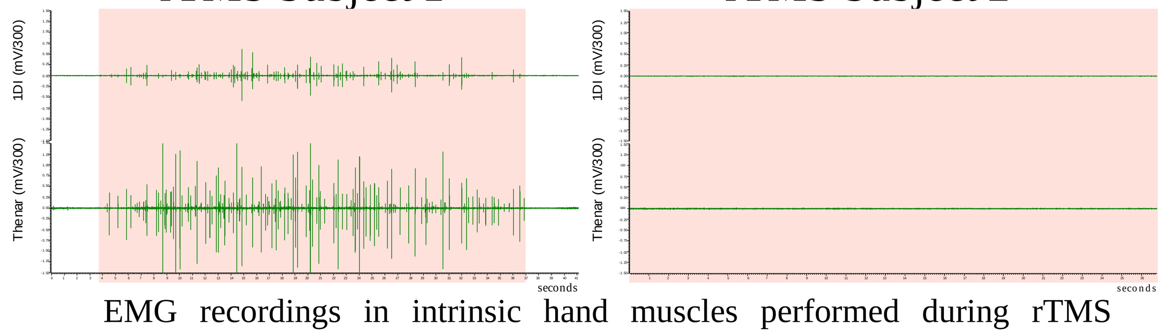
D) Changes of **accelerations** during the displacements of the hand to perform the task, expressed by waveforms modifications and increase of standard deviations;

E) Similar increased durations in monkey.

These greater effects of rTMS application in subject 1 should however be interpreted with caution, as they are moderated by statistical significances, and based on 2 subjects only.

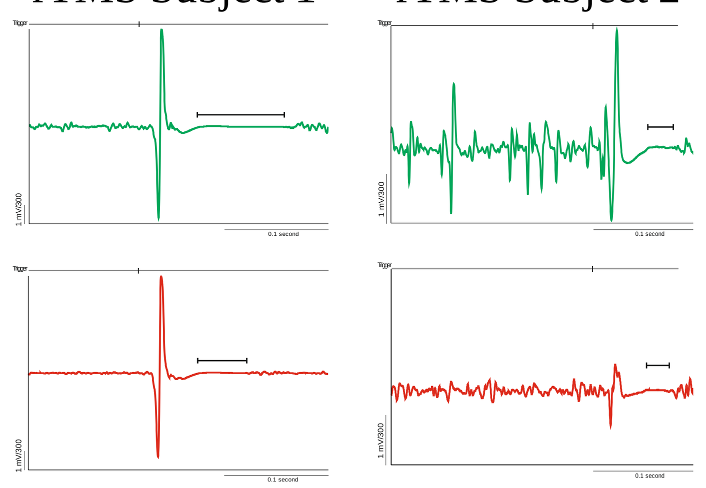
I. Effectiveness of rTMS application

A EMG during rTMS



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

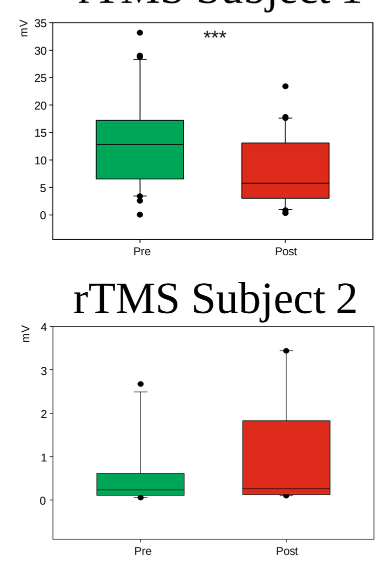
B Silent period



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.

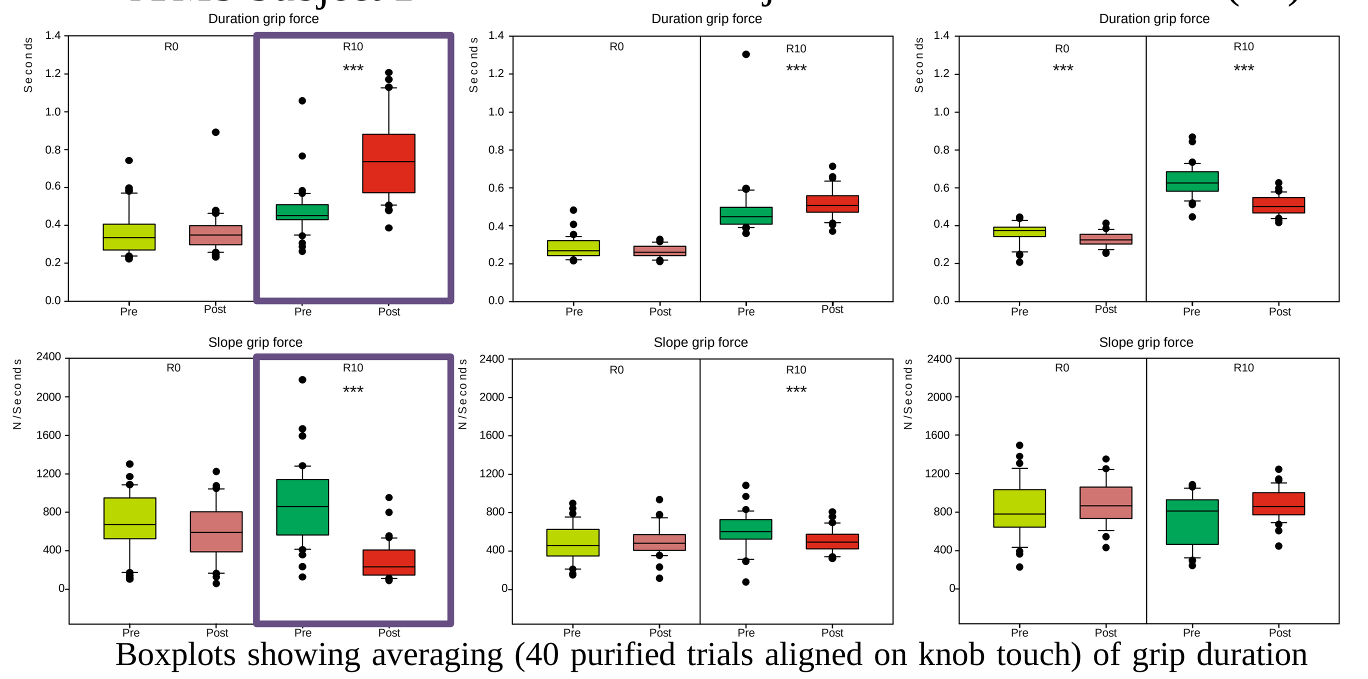
C Amplitude of the MEPs



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

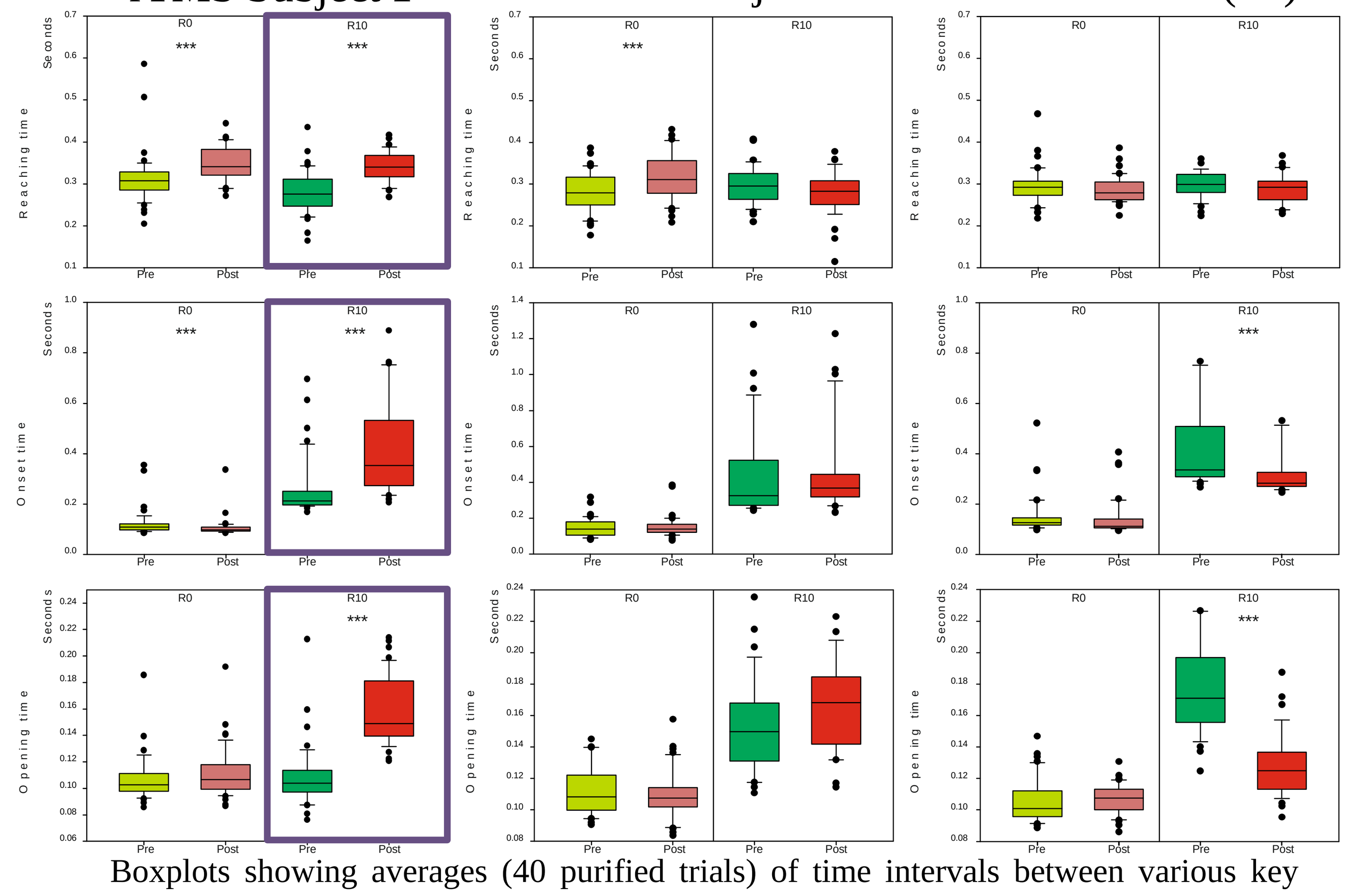
II. Effects of transient cortical inactivation by rTMS on the reach and grasp drawer task's performance

A Grip Forces



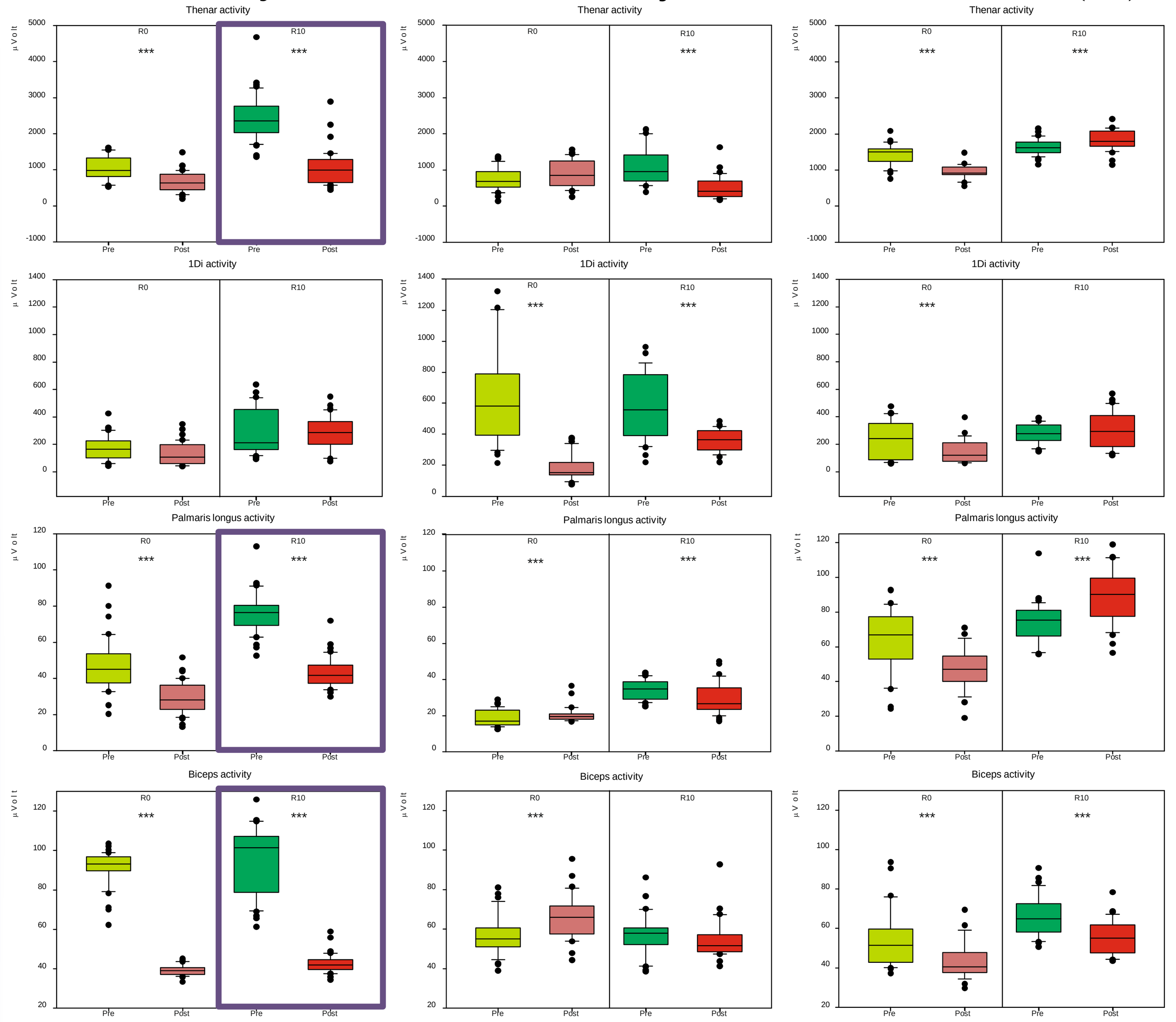
Boxplots showing averaging (40 purified trials aligned on knob touch) of grip duration and grip slope at two levels of resistance to the opening (R0=0N and R10=9N), before (green) and after (red) rTMS application in 2 subjects and sham rTMS in 1 subject.

B Time Intervals



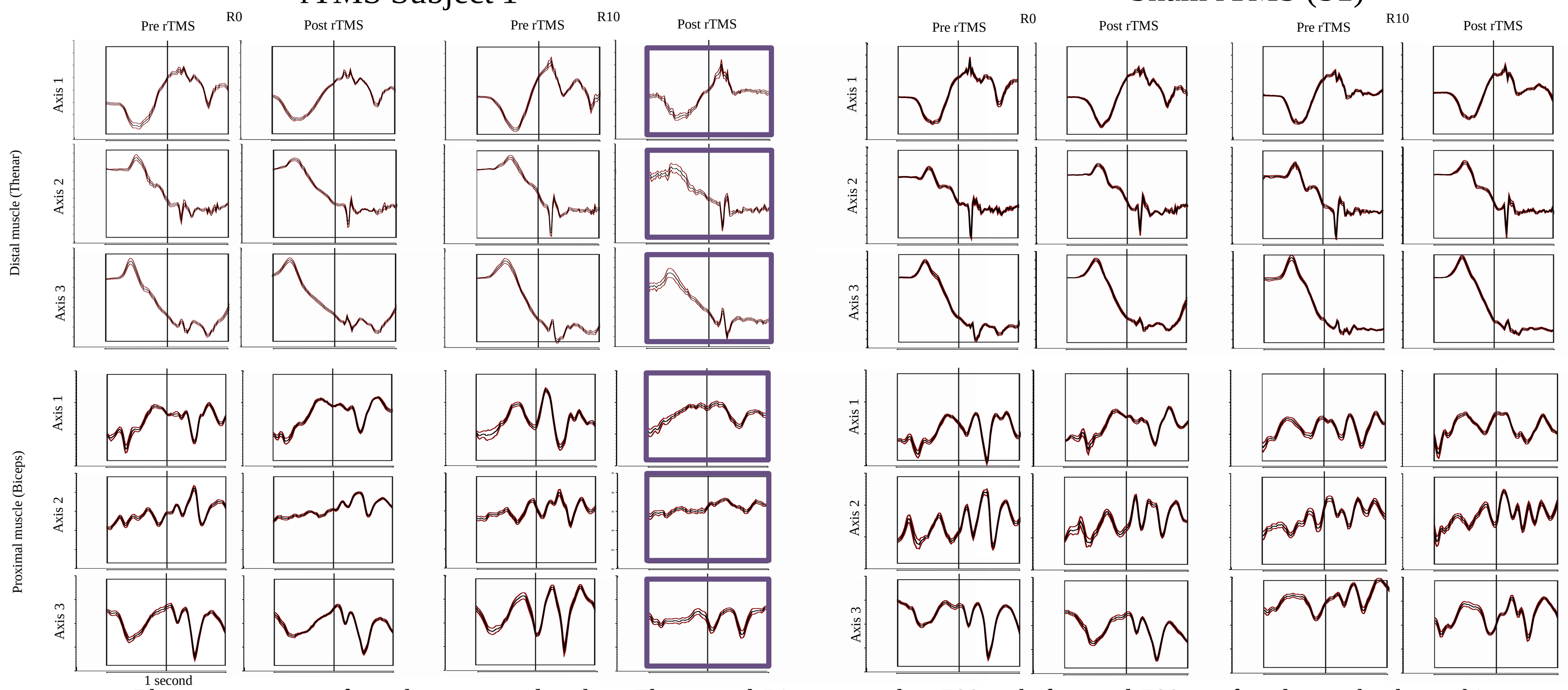
Boxplots showing averages (40 purified trials) of time intervals between various key timepoints (reaching time, onset time and opening time) in the course of the drawer task's execution at two levels of resistance to the opening (R0=0N and R10=9N), before (green) and after (red) rTMS application in 2 subjects and sham rTMS in 1 subject.

C EMG activity



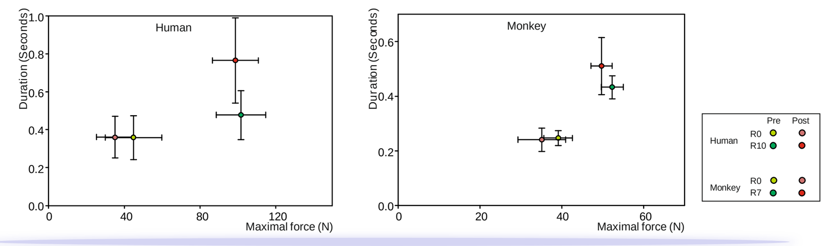
Boxplots showing averages (40 purified and rectified trials, aligned on knob touch (Thenar, 1DI and Palmaris longus) or on start openig (Biceps)) of EMG activity of hand and arm muscles before (green) and after (red) rTMS application in 2 subjects and sham rTMS in 1 subject performing the drawer task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

D Accelerations



Three axes traces of accelerometers placed on Thenar and Biceps muscles, 500ms before and 500ms after drawer knob touching (Thenar) and open start (Biceps) by rTMS subject 1 and by sham rTMS subject 1 (2 months later). Traces patterns pre-rTMS are similar between the 2 sessions, showing the stability of the acquired data. Differences are observed in waves' forms as well as in standard deviations in subject 1 after rTMS application at higher resistance.

E Comparison Human-Monkey (Cf. poster C082)



Scatters showing a correlation between maximal and duration of grip force.

Similar pattern is observed between 1 human (left panel) and 1 monkey (right 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.

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Neural Plasticity and Repair National Center of Competence in Research
FNSNF Fonds national suisse de la recherche scientifique
Basel Declaration

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 or when receiving a sham stimulation, as shown first by a direct effect of rTMS on EMG activity, on MEP's amplitude and on silent period, and second by EMG and behavioral modifications when performing the reach and grasp drawer task.

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. More subjects are needed in both rTMS and sham groups.

In a similar procedure experiment with a monkey, the same type of behavioral pattern changes were observed. Further experiments should complete these comparisons between human and monkey.

Furthermore, 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.