Direct comparison of two techniques of transient inactivation of the primary motor cortex in macaque monkeys affecting motor control and precision grip.

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INTRODUCTION

In human patients, to assess possible roles played by motor areas in the spontaneous recovery of **voluntary movements of the hand** observed after unilateral motor stroke, non-invasive transient inactivation such as repetitive transcranial magnetic stimulation (rTMS) is a frequently used technique to functionally block cortical control.

The non-human primate model is adequate to compare directly the efficiency on motor behavior of a transient inactivation of the motor cortex by a non-invasive technique such as rTMS, and by an invasive method such as micro-infusion of a GABA-ergic agonist, muscimol, allowing the distinction between a **network inactivation (rTMS)** and a **focal cellular inactivation (muscimol)**.

Thus, a direct comparison of the motor consequences resulting from different cortical inactivation methods observed in the same subjects and for the same behavioral tasks could give valuable information on the **role played by the primary motor cortex (M1) and/or the motor network involved in functional recovery**.

METHODS

Subjects:

2 adult long-tailed macaques, 1 male (Mk-DG) and 1 female (Mk-CA).

Behavior:

The modified Brinkman board task (Fig. 1B):
- Precision grip ratio (PGR ; N=2): Quantification of separate involvement of index and thumb finger ; 0 (no movement), 1 (passive movement) and 2 (active movement).

The "reach and grasp drawer" task (Fig. 1C):
- Maximal grip force and duration of the force application (N=2).
- EMG quantification (N=1).

Cortical inactivation (Fig. 1A):

Invasive transient* inactivation: Microinfusion of GABA-A agonist Muscimol (Sigma, 5µg/µl) in several tracks in M1 eliciting single joint finger movements when stimulated using intracortical microstimulation (ICMS: train of 6-9 pulses 0.2 ms width at 333 Hz) (N=2).
*Transient inactivation refers to the behavior

Non-invasive repetitive transcranial magnetic stimulation (rTMS): rTMS at 80% of active motor threshold over hand area M1, identified by functional mapping, using a pediatric coil (Magventure©, theta burst stimulation: 600 pulses within 30 seconds at trains of 3 pulses) (N=2).

RESULTS

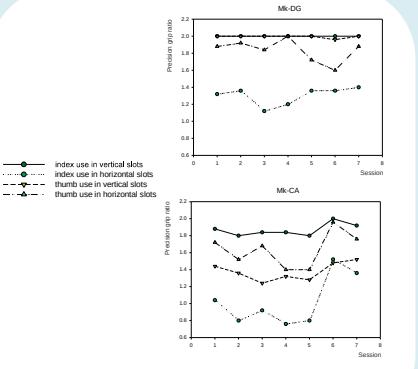


Fig. 2: *Precision grip ratio of index and thumb finger in the modified Brinkman board task for vertical and horizontal slots (N=2).*

Precision Grip Ratio (PGR) (Fig. 2) :

In both monkeys, PGR in the plateau of motor performance showed a strong involvement of the index finger in the vertically oriented slots, and a strong involvement of the thumb in the retrieving of pellets in the horizontally oriented slots.

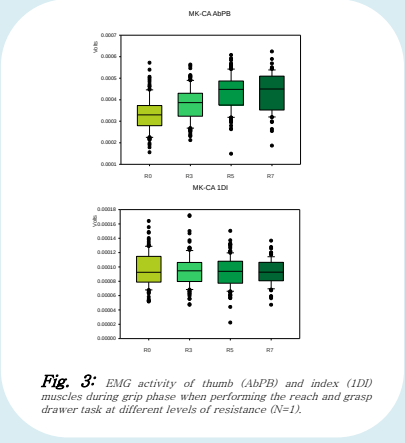


Fig. 3: *EMG activity of thumb (AbPB) and index (1DI) muscles during grip phase when performing the reach and grasp drawer task at different levels of resistance (N=1).*

EMG activity when performing the reach and grasp drawer task (Fig. 3):

Averaged EMG activity of Thumb (AbPB) and Index finger (1DI) muscles showed an increased involvement of the thumb to perform the precision grip in correlation with an increased resistance to the opening, whereas the EMG activity of 1DI was not affected by an increase of resistance to the opening.

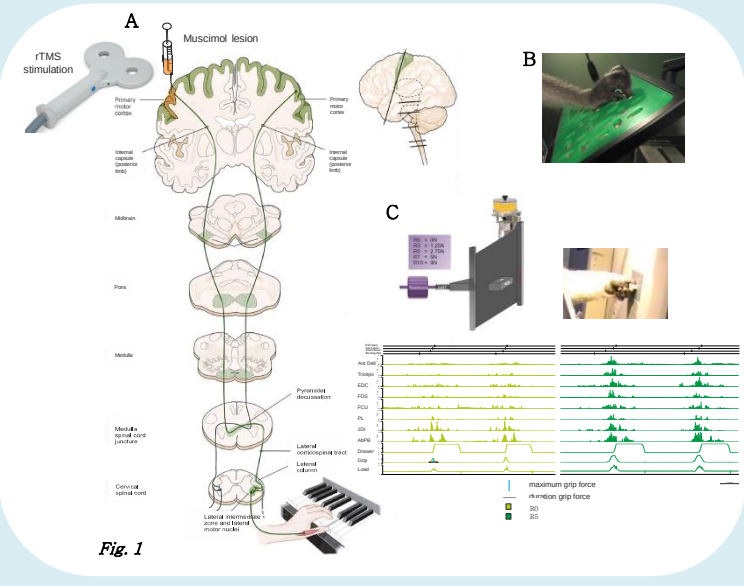
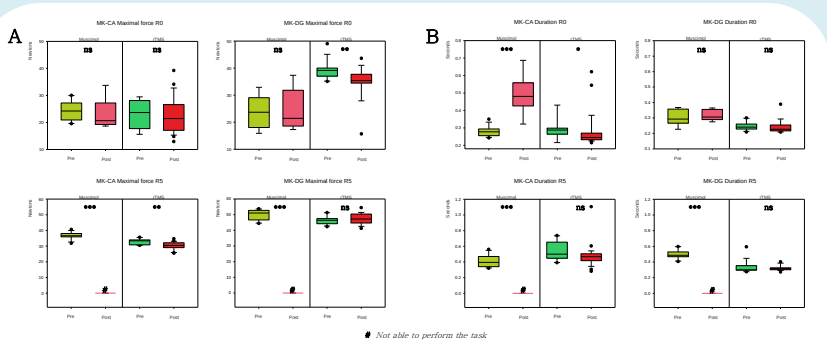


Fig. 1



\# Not able to perform the task

Fig. 4: *Effect of the reversible inactivations, muscimol versus rTMS, on maximal grip force (A) and force duration (B) to perform the reach and grasp drawer task, at resistances 0 (0N) and 5 (2.75N) (N=2).*

Cortical invasive (muscimol) versus non-invasive (rTMS) inactivation (Fig. 4):

A more challenging task obtained by increased resistance to the opening of the drawer did not affect motor performance in the cortical non-invasive inactivation (rTMS), whereas after cortical invasive inactivation (muscimol), at similar time points after the inactivation, the manual dexterity was affected in grip force and duration, as the animals were not able to perform the task at all (#).

CONCLUSIONS AND PERSPECTIVES

- Fine assessment of precision grip indicates a greater functional involvement of the thumb in more challenging tasks, such as retrieving food pellets from horizontally oriented slots in the modified Brinkman board task or to adapt muscular activity to an increased resistance to the opening in the reach and grasp drawer task.
- According to our results, when both techniques of inactivation were similarly applied in two macaque monkeys, the same patterns of effects were observed in the two animals, such as some changes in the expression of the motor behavior. Nevertheless, these were very small in network inactivation (rTMS), although sometimes significant, as compared to focal inactivation (muscimol).
- We did not measure the motor evoked potentials (MEPs) of finger muscles before and after rTMS, which is a sign of the effectiveness of the rTMS, but we confirmed the position of the coil after the rTMS by stimulating the cortex and observed the same movement as before the rTMS. Therefore, a decrease of 40 to 60% of MEPs after rTMS as observed in Goldsworthy et al. (2012) could be insufficient to obtain a behavioral effect even in a complex motor task.