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Cortical control of manual dexterity is differentially affected by permanent or transitory inactivation in non-human primates

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INTRODUCTION

The contribution of the motor system in the execution of **voluntary movements of the hand** can be investigated using different forms of cortical inactivation in non-human primates.

As the main contributor to the origin of the corticospinal tract controlling the motoneurones of hand muscles, the **primary motor cortex (M1)** is the obvious target for such an inactivation. In addition, the mechanisms of cortical plasticity inducing functional recovery depend on the type of the lesion.

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

➡ In this study, we directly compared the behavioral consequences of **three different types of cortical inactivation** : two invasive methods of targeted inactivation using direct injection of neurotoxic drug in the hand representation area in M1, and a non-invasive method based on a particular paradigm of transcranial magnetic stimulation, resulting in a decreased cortical excitability.

METHODS

Behavior:

The modified Brinkman board task (Fig. 1A):
- Total number of pellets retrieved within 30".
- Motor strategy.

The "reach and grasp drawer" task (Fig. 1B):
- Maximal grip force and duration of the force application (Fig. 1C).
- Motor strategy (Fig. 1D).

Motor strategy: scoring of the involvement of thumb and index finger (active movement =2, passive =1 and no movement =0).

Cortical inactivation:

Invasive permanent inactivation (Fig. 1F): Microinfusion of ibotenic acid (neuronal death induced by excitotoxicity; N=2).

Invasive transient* inactivation (Fig. 1E): Microinfusion of GABA-A agonist Muscimol (N=1).
*Transient inactivation refers to the behavior

Non-invasive repetitive transcranial magnetic stimulation (rTMS) (Fig. 1G): rTMS at 80% of active motor threshold over M1 using a pediatric coil (Magventure©)(N=1).

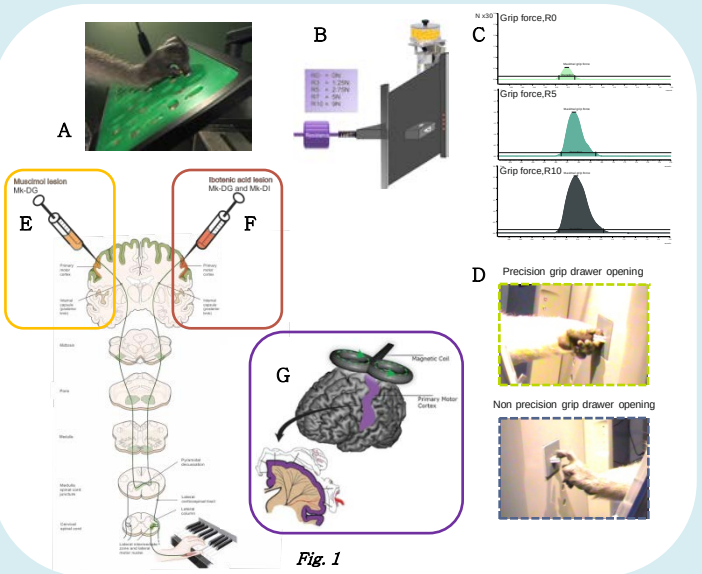


Fig. 1

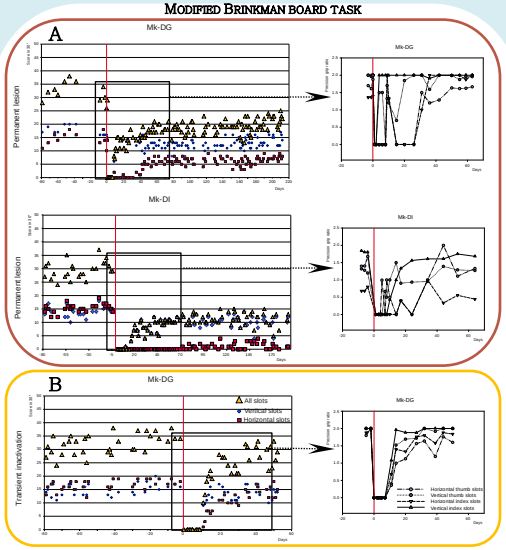


Fig. 2: *Effect of the lesion type (A. ibotenic acid, B. muscimol) and time course of functional recovery of fine manual dexterity illustrated by the score in 30" in the modified Brinkman board task (left panel) and by the precision grip score of index and thumb finger (right panel). Red vertical line: lesion.*

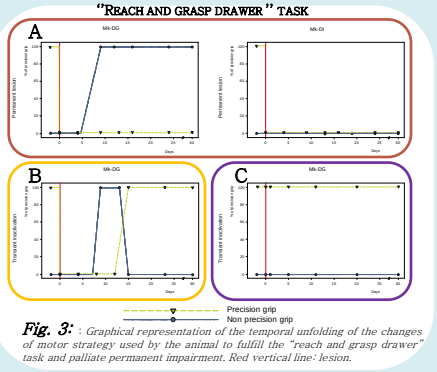


Fig. 3: *: Graphical representation of the temporal unfolding of the changes of motor strategy used by the animal to fulfill the "reach and grasp drawer" task and palliate permanent impairment. Red vertical line: lesion.*

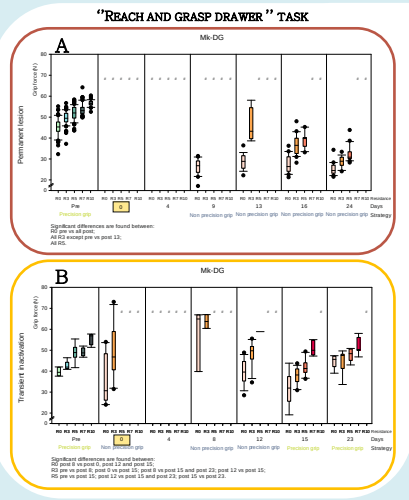
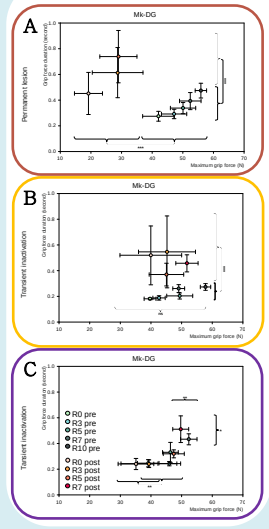


Fig. 4: *Representation of maximal grip forces developed by the animal to perform the "reach and grasp drawer" task at different levels of resistance, one session before and six sessions after ibotenic acid injection (upper panel) and muscimol injection (lower panel).*

Fig. 5: *Bi-directional error bar plots representing the measure of duration and maximal grip force applied by the animal to perform the "reach and grasp drawer" task at different levels of resistance, one session before and five sessions after ibotenic acid injection (upper panel) and muscimol injection (middle panel), and one session before and one sessions after rTMS inactivation (lower panel).*



RESULTS

Cortical invasive inactivation :

I. Decrease of the score in 30" in the modified **Brinkman board task** (Fig. 2, left panel).

II. Decrease of the precision grip score of both fingers involved in precision grip (Fig. 2, right panel); with the horizontal wells more affected than the vertical wells.
Recovery of the index finger more regular than of the thumb. Precision grip score returning to normal contrarily to the score in 30".
As expected, better improvements after transient inactivation than after permanent lesion, and less marked variability in strategy during the recovery phase.

III. Either an inability to peform the task (Mk-DI, Fig. 3A, right panel), or a **non precision grip strategy in the drawer task** (Mk-DG, Fig. 3A, left panel).
Recovery of precision grip ability only after transient inactivation.

IV. Decrease of maximal grip force (Fig. 4), and **increase of duration** in the drawer task (Fig. 5A and 5B). Again, better manual recovery after transient inactivation than after permanent lesion.

Cortical non-invasive inactivation (rTMS) :

Less pronounced loss of manual dexterity to perform the "reach and grasp drawer" task (only task assessed), **for the strategy as well as for the force and duration** applied (Fig. 3C and 5C).

CONCLUSIONS AND PERSPECTIVES

Depending on the nature of the cortical inactivation of M1 in non-human primates, the consequences on motor performance and grasp motor strategy are different.

➡ The behavioral effects of the local **invasive inactivation** of the primary motor cortex resulted in **dramatic impairment of precision grip**, as compared to non-invasive rTMS inactivation: **rTMS induces plastic changes in M1 rather than a real inactivation**. Meanwhile, the incomplete functional recovery resulting from the permanent inactivation of M1 markedly differed as compared to the complete recovery following the transient inactivation.

➡ The analysed data show a critical period of behavioral changes in motor strategy in the precision grip, **particularly affecting the thumb**, which is more represented in M1 and possesses a larger degree of freedom, as compared to the index finger. Depending on the aspect assessed (e.g. score in 30") or on the task (e.g. drawer task), other parameters than precision grip *per se* seem to play a role in the recovery of manual dexterity, such as force and wrist movement.

➡ Differences observed between the permanent lesion and the GABA-A inactivation could be explained by a possible difference of neuronal population within the motor cortex affected by the drug, being probably more general with the ibotenic acid injection.

➡ Detailed analysis of motor performance after cortical lesion allows detection of even minor improvements of hand function, as a crucial step in the frame of therapeutic perspectives enhancing cortical plasticity and functional recovery.