Functional recovery of manual dexterity in non-human primates following a motor cortex lesion assessed with the Brinkman box task

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Introduction

Motor and somatosensory cortical areas are densely interconnected and participate together to the motor control, forming the functional sensorimotor system. The primary somatosensory cortex (S1) sends corticospinal projections and somatosensory inputs to the primary motor cortex (M1), contributing to the control of voluntary movements, such as the precision grip. Moreover, the somatosensory system plays a key role in active motor exploration by palpation in the absence of visual feedback.

A behavioural task was initially developed by Brinkman and Kuypers (1973) to test the precision grip ability in non-human primates, and an improved version - the modified Brinkman board task - is currently used in our laboratory. The animal has to retrieve banana pellets contained in 25 vertically and 25 horizontally oriented wells distributed on a rectangular board.

Hypothesis

After a lesion in M1, the sensorimotor system will be affected in parallel with the motor control itself. The resulting impairments can be highlighted with another test derived from the Brinkman board task: the **Brinkman box (BB) task,** which was specifically designed to assess the role of sensory inputs in a precision grip task performed with or without visual feedback before and after a lesion of the hand representation of M1.

- Different behaviours and strategies were observed among the monkeys to retrieve the pellets before and after the cortical lesion. Moreover, the post-lesion time course of recovery in a given monkey varied according to the analysed parameters. Therefore, these parameters are differentially relevant according to the animals.
- All monkeys except Mk-RO exhibited post-lesion somatosensory-related deficits similar to a sensory agnosia: in several trials, they did a precision grip but failed to grasp the pellet, removed the hand from the well and then from the box, brought the hand to or near the mouth, then visually inspected the empty palm and only at that time realised that they retrieved no pellet (see graph in Mk-VA).
- In Mk-AV, there was an obvious adverse effect of the prefrontal cortical biopsy, inducing among others an increase in the time needed to shape the precision grip. Conversely, the functional recovery from the lesion was excellent.
- In Mk-JO, the negative effect of the lesion was clearly visible on the contralesional hand performing the task with and without vision. It went with a significant improvement in the performance of the ipsilesional hand in the Brinkman box task without vision.
- As expected, the level of recovery for the Brinkman box task without vision was usually lower than the one for the modified Brinkman board task, given that the former is more difficult to perform than the latter.
- The Brinkman box task is very sensitive and relevant to test the exploratory ability and tactile sense in a lesional context. It allows detecting subtle impairments and highlights the importance of the somatosensory feedback, especially in tasks performed without visual control.

Prospects

- Computation of a composite performance score (Pizzimenti et al., 2007) taking into account the different parameters studied as a global indicator of the ability of the monkeys to perform the task
- Study of the reorganisation of the sensorimotor system following an M1 lesion with somatosensory evoked potential recordings at the scalp

References

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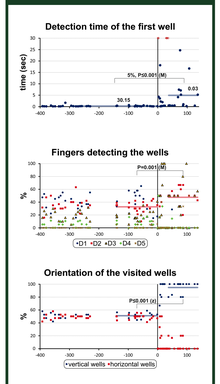
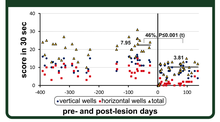
Results

Mk-GE

BB without vision contralesional hand

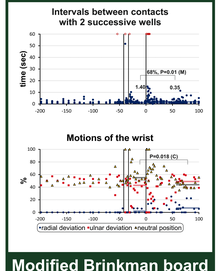


Modified Brinkman board



Mk-RO

BB without vision contralesional hand



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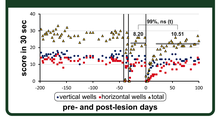
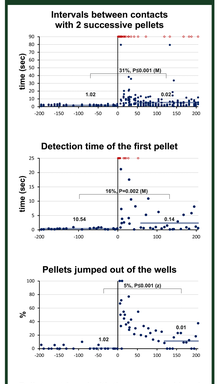
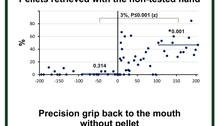


Mk-VA

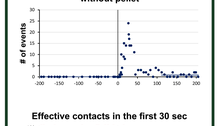
BB without vision contralesional hand



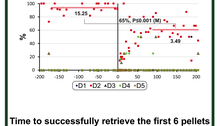
Pellets retrieved with the non-tested hand



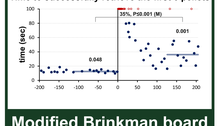
Precision grip back to the mouth without pellet



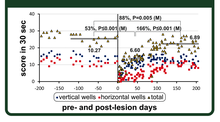
Effective contacts in the first 30 sec



Time to successfully retrieve the first 6 pellets

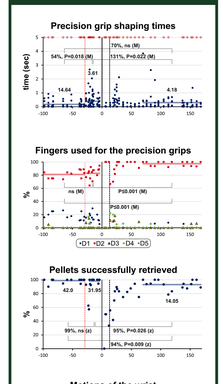


Modified Brinkman board

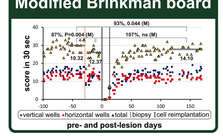


Mk-AV

BB without vision contralesional hand



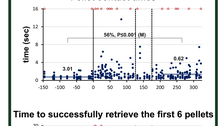
Modified Brinkman board



Mk-JA

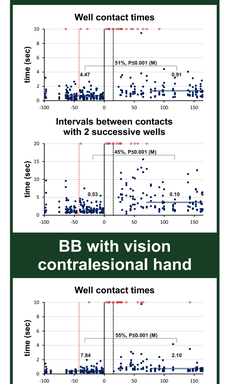
BB without vision contralesional hand

Modified Brinkman board

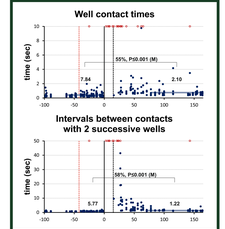


Mk-JO

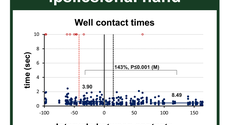
BB without vision contralesional hand



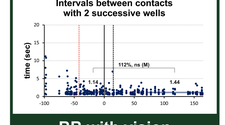
BB with vision contralesional hand



BB without vision ipsilesional hand



BB with vision ipsilesional hand

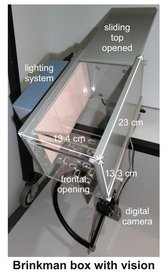


Modified Brinkman board

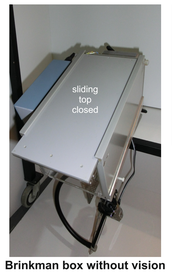
As a first approach, pre- and post-lesion **mean plateaux** were visually defined for each analysed parameter (need to use more systematic criteria in the near future) and are displayed in a lighter colour than the corresponding data.
The **percentage of recovery** is defined for appropriate parameters as (mean post-lesion plateau/mean pre-lesion plateau)*100 when a higher plateau value means a better performance and as 1/(mean post-lesion plateau/mean pre-lesion plateau)*100 when a lower plateau value represents a better performance.
Pre- and post-lesion plateaux were statistically compared with t-test (t), Mann-Whitney test (M), z-test (z) or Chi-square test (C), as the case may be. The corresponding p-value or ns (non-significant, P>0.05) is indicated.
The **performance ratio** (Pizzimenti et al., 2007) is defined for appropriate parameters as mean plateau/SD when a higher plateau value implies a better performance and as (1/mean plateau)/SD when a lower plateau value suggests a better performance. This measure takes into account the variability of the data and, thus, a more stable performance is indicated by a higher performance ratio. Partially or completely missing values at a given date are represented by o.

Material and methods

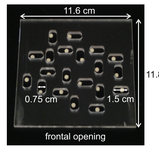
Brinkman box task



Brinkman box with vision



Brinkman box without vision

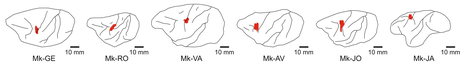


- Square board with 10 vertically and 10 horizontally oriented wells, each filled with a banana pellet
- Board located in a box whose top can be opened or closed → task performed unimanually with or without vision
- Task without vision more challenging, relying mostly on tactile inputs from the fingers and on spatial memory

Monkeys

	Mk-GE	Mk-RO§	Mk-VA	Mk-AV*	Mk-JO	Mk-JA*
Treatment	None	None	Anti-Nogo-A antibody	Sham cell therapy	Cell therapy	Cell therapy
Age at time of lesion (rounded to 0.5 year)	5	4	5.5	3.5	3.5	4
Weight at time of lesion (kg)	2.8	3.2	4.9	4.3	3.4	4.3
Volume of ibotenic acid injected (µl)	13	18	15.5	15	15	38
Number of ICMS sites injected with ibotenic acid	13	12	11	10	10	38
Total volume of lesion (mm³) in the gray matter (motor cortex + post-central gyrus)	48.7	14	20	33.2	33.6	22.2
Volume of lesion in post-central gyrus (mm³)	7.6	0	5.8	0	3.8	2.5
Volume of lesion spread to subcorticall white matter (mm³)	0	0	0	69.8	23.6	38.4
Volume of prefrontal cortical biopsy (mm³)	-	-	-	44	20.3	8.8

§Mk-RO was subjected to 3 successive cortical lesions because the first two did not produce the expected impairement on the contralesional manual dexterity assessed with the modified Brinkman board task. Day 0 was defined as the time of the 3rd lesion.
*The cortical lesion in Mk-AV was performed in the premotor cortex instead of M1.
* Mk-JA was treated post-operatively with an anti-epileptic drug, producing a neuroprotective effect against the cortical lesion performed with excitotoxic drug (ibotenic acid). This resulted in a small volume of lesion in relation to the volume of ibotenic acid injected.



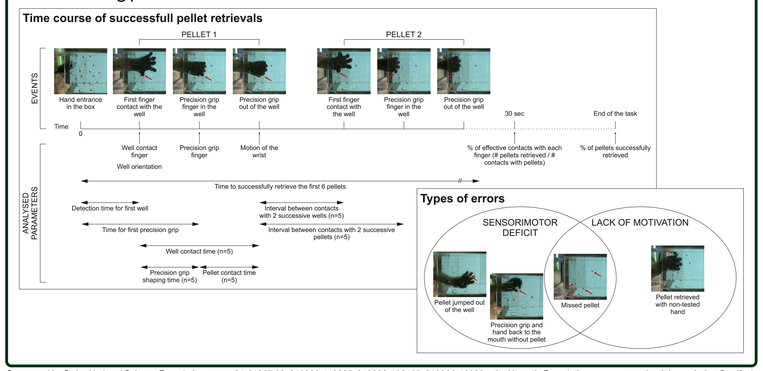
Location and extent of the permanent unilateral lesion of the M1 hand representation on lateral view of the brain. The lesion territory (in red) is derived from the lesioned zone of cerebral cortex (gray matter) visible on consecutive frontal histological sections. Spread of the lesion to the subcortical white matter below the gray matter is not represented here.

modified from Bashir et al., 2012

- 6 adult *Macaca fascicularis*
- At behavioural plateau in manual dexterity tests, unilateral permanent cortical lesion in the hand representation of M1 by infusion of ibotenic acid
- Post-lesion:
  - control group
  - anti-Nogo-A antibody treatment protocol (Hamadjida et al., 2012; Kaeser et al., 2010)
  - adult neural progenitor cell therapy protocol (prefrontal cortical biopsy) (Kaeser et al., 2011)

Data analysis

Brinkman box data **with** and **without vision** obtained from the **contralesional hand** and the **ipsilesional hand** were analysed frame by frame (25 frames/sec) with the software Kinovea. The following parameters were measured:



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