Variability of manual dexterity performance in non-human primates at different time points during the learning phase and stabilization phase, before and after a primary motor (M1) cortical lesion.

E. Rouiller, **M. Fregosi**, P. Chatagny, J. Savidan, A.D. Gindrat, S. Badoud, S. Borgognon, J. Cottet, E. Schmidlin, M. Kaeser

Unit of Physiology, Department of Medecine, University of Fribourg

UNIVERSITÉ DE FRIBOURG
UNIVERSITÄT FREIBURG

SWISS NATIONAL SCIENCE FOUNDATION

Neural Plasticity and Repair
National Center of Competence in Research

INTRODUCTION

Manual dexterity has evolved greatly in primates and corresponds to the ability of controlling independently and precisely each finger. In particular, the precision grip (opposition between the index and the thumb) is an aspect of manual dexterity crucial for the manipulation of small objects.

Our aim was to analyse in adult non-human primates both the inter-individual variability of manual skills as well as the intra-individual variability of manual performance, at three different stages of training: the learning phase, the plateau phase before a lesion and the plateau phase after a lesion of the hand area in the primary motor cortex (M1). To perform the present study two different behavioral tasks were used: the «Modified Brinkman board» task and the «Reach and grasp drawer» task.

The main hypothesis is that manual dexterity performance and variability in the «Modified Brinkman board» task, when acquired, can be predicted from the duration of the learning phase, and/or from the learning slope and/or from the initial score before any training took place. Moreover, after a lesion we expect the variability to increase in relation to the lesion›s size.

METHODS

The experiment was conducted on 20 adult *Macaca fascicularis*. Only data about the dominant hand are presented.

The «Modified Brinkman board» task (Figure 1):

- it consists of a perspex board containing 50 slots whereof 25 are oriented vertically and 25 horizontally. Each slot contains a banana flavoured pellet.

- 4 parameters were analyzed: the score, the contact time (CT), the temporal sequence and the types of movements and strategies.

The «Reach and grasp drawer» task (Figure 2):

- it consists in a drawer at which five different resistances can be applied to. The monkey has to pull the drawer against the resistance and pick up the pellet inside. The grip force is the force needed to hold the knob whereas the load force is the force necessary to pull the drawer against the resistance.

- 4 parameters were analyzed: the maximal grip force, the maximal load force, the grip force duration and the load force duration.

Figure 1: The «Modified Brinkman board» task from which a monkey is retrieving food pellets using his right hand.

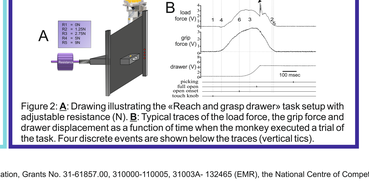

Figure 2: **A**: Drawing illustrating the «Reach and grasp drawer» task setup with adjustable resistance (N). **B**: Typical traces of the load force, the grip force and drawer displacement as a function of time when the monkey executed a trial of the task. Four discrete events are shown below the traces (vertical tics).

Score

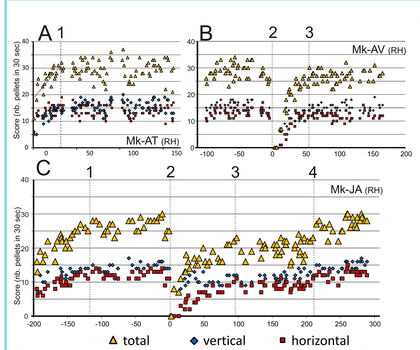

Figure 3: Graphs showing the score obtained by three monkeys in the «Modified Brinkman board» task using their dominant hand (RH= right hand, LH= left hand). The score (number of pellets retrieved in 30s) are represented as a function of time on the x-axis. The yellow triangles represent the total score, whereas the the blue diamonds represent the score for the vertical slots and the red squares the score for the horizontal slots. The vertical dashed lines represents different time points: 1) end of learning phase-beginning plateau pre-lesion, 2) lesion, 3) beginning of the plateau post-lesion, 4) rebound effect due to the treatment. **A**: Graph showing the comparison between learning phase and the plateau phase before the lesion. **B**: Graph showing the comparison between the plateau pre-lesion and the recovery after the lesion. **C**: Graph representing all the time events togheter.

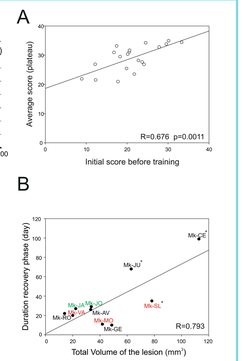

Figure 4: **A**: Graph showing the correlation between the initial score before the monkey was trained and the averaged score once the monkey as reached the plateau pre-lesion.
B: Graph showing the correlation between the total volume of the lesion and the duration of the recovery phase for ten monkeys. * indicates monkeys having a subcortical lesion too.

Motor habit

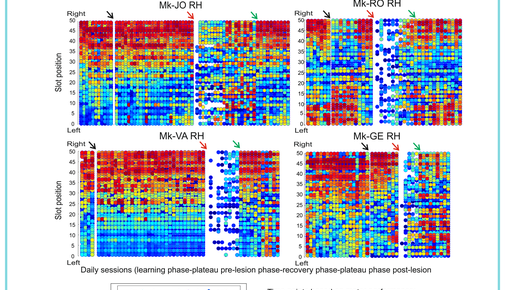

Figure 6: Temporal sequence used by the monkey to visit the 50 slots in the «Modified Brinkman board» task in four monkeys that are representative for the four different behavioral profiles found. The picking sequence is shown by a color scale in the bottom inset in which the slots visited first are in blue whereas those visited last are in red. For instance in the illustrated session, the monkey grasped the pellets from the right side to the left side of the board. The x-axis displays the time in daily sessions, whereas every vertical column corresponds to a daily session of the behavioral task. For each column dots at the bottom are for slots located at the left extremity whereas those at the top are for slots at the right extremity.

CT

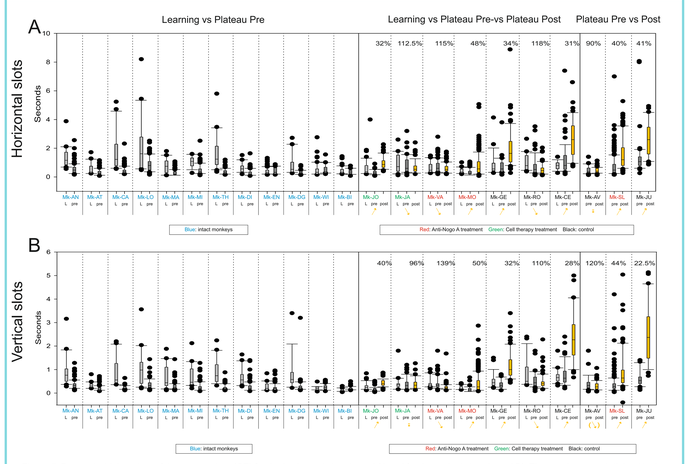

Figure 5: Box and whisker plots of the contact time (CT) for the horizontal slots (panel A) and for the verical slots (panel B). The graphs are subdivised in three parts: the first one is about the comparison between the learning phase and the plateau phase, the second one considers the post-lesion phase as well, whereas the last part is about the comparison between the pre-lesion phase with the post-lesion phase without taking into account the learning phase. In yellow are represented the box plots concerning the post-lesion data, whereas the boxes in heavy gray corresponds to the pre-lesion data. The yellow arrows represents the direction of the variability in the post-lesion period compared to the variability in the pre-lesion period. The values given in percentage correspond to the recovery index.

Drawer task

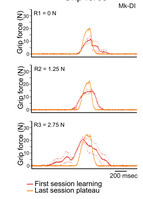

Figure 7: Average traces (over 5 trials) in Newtons (N) for the grip force (orange) in one typical monkey. The two color shades distinguish traces obtained at the beginning of the learning phase and the end of the plateau phase. The traces are shown for three levels of resistances (R1, R2 and R3). The variability is represented by the envelope in dahed lines.

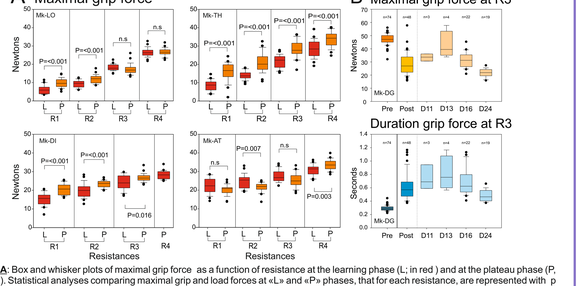

Figure 8: **A**: Box and whisker plots of maximal grip force as a function of resistance at the learning phase (L; in red) and at the plateau phase (P, in orange). Statistical analyses comparing maximal grip and load forces at «L» and «P» phases, that for each resistance, are represented with p values when statistically different (t-test/Mann-Whitney test) and with "n.s" when the difference is not statistically significant (P>0.05).**B**: Box and whisker plots of maximal grip force and of duration time of the grip force after a lesion of the hand area in M1. The first box plot represents the pre-lesion data pulled togheter, whereas the second one represents the data post-lesion pulled together. D11-24 represent individual daily sessions after the lesion. *n* corresponds to the number of data acquired during the session.

RESULTS

«Modified Brinkman board» task:

At the learning phase, monkeys showed a substantial inter-individual variability, while their score progressively increase with time. At the plateau phase, the inter-individual variability remained large, though smaller than during learning, together with a sizable intra-individual variability across sessions.

At the plateau phase, the contact time (CT) was shorter in vertical slots than in horizontal slots where the variability was greater between sessions. The contact time shortened from the onset of the learning phase to the plateau phase, demonstrating a reinforcement of the precision grip performance. After a lesion of M1 the CT tended to increase overall in monkeys showing a low recovery index.

The motor habits aquired during the learning phase remained, for some monkeys, the same at the plateau before the lesion. Four different profiles of motor habit have been found between monkeys. Once the lesion occurred all the animals showed a total loss of their usual motor strategy, however there was a tendency to regain the same habit after a period of training. To note also that motor habit can be affected by unilateral lesion of dorsolateral prefrontal cortex (Keaser et al., 2013).

The variability of the contact time was higher during the learning phase compared to the plateau phase before the lesion. The data post-lesion showed a general increase in the variability as compared to the plateau before the lesion.

Generally, monkeys showing a decrease in the variability are those whose recovery index was high and whose lesion was small. In contrast monkeys with a larger lesion size were those showing a lower recovery index, associated with a larger variability.

«Reach and grasp drawer» task results:

Results show an increase of the maximal grip force at plateau phase compared to the beginning of the learning phase. Moreover, the variability was larger at the onset of the learning phase than at the plateau. Grip force duration decreased at plateau phase. Post-lesion analyses showed a decrease of the maximal grip force, due to the lesion associated with increases in grip force duration, as well as to a change in strategy.

CONCLUSIONS

The hypothesis that the performance of manual dexterity, which progressively increases up to the plateau phase, can be predicted from the initial score before training has been verified. Furthermore the relation between the increasing of the variability during the post-lesion period and the size of the lesion, has been largely verified.

Motor learning during the learning phase led to an optimization of manual dexterity parameters at the plateau phase, including their variability.

There is a substantial inter-individual variability in manual dexterity in non-human primates, to be taken into account in lesional studies. In fact after a lesion the variability tends to increase in the majority of the monkeys analysed depending on the lesion size.

FUTURE PERSPECTIVES

The relation between the variability before the lesion and the variability after the lesion should be verified by statistical analysis.

Furthermore, analyses of the variability during the acute phase, as well as during the first 2-3 learning sessions, with regard to the recovery index, should be carried out

Grant sponsors: Swiss National Science Foundation, Grants No. 31-61857.00, 310000-110005, 31003A- 132465 (EMR), 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: http://www.unifr.ch/neuro/rouiller/SPCCR/welcome.html).