Behavioral and electrophysiological follow-up in monkeys subjected to cervical hemisection, in presence or absence of anti-Nogo-A antibody and BDNF treatments.

J. Savidan[1], T. Wannier[1], J. Bloch[2], M-L. Beaud[1], E.M. Rouiller[1] and A. Belhaj-Saif[1]

(1) Dept Medicine, University of Fribourg - (2) Dept Neurosurgery, University Hospital Lausanne

Contact: julie.savidan@unifr.ch

INTRODUCTION

The anti-Nogo-A antibody treatment has shown improvement of the recovery of hand dexterity in non-human primate following spinal hemisection. Such improvement of recovery parallels enhanced sprouting of CS axons caudal and rostral to the lesion in anti-Nogo-A antibody treated animals. In clinical practice, motor evoqued potential (MEP) induced by transcranial electric stimulation (TES) is commonly used to document changes in conduction time of motor tracts in neurological diseases. Using TES, the present study aimed to assess the functional properties of this CS sprouting. Moreover, in this study, we used anti-Nogo-A treatment combined with brain-derived neurotrophic factor (BDNF).

METHODS

Experiments were conducted on four adult monkeys (*macaca fascicularis*)

1. Behavioural assessment: Functional recovery of the manual dexterity was investigated using a modified version of the Brinkman Board task.

2. Hemisection of the spinal cord in the four monkeys at the cervical segment C7, on the right side.

3. Four weeks intrathecal treatment with anti-Nogo-A antibody and BDNF in two monkeys (MK-ABMa and MK-ABB) and control antibody in the other two monkeys (MK-CGa and MK-CBo). Treatment started immediately after the spinal hemisection.

4. TES was conducted few weeks before and after the lesion, one session a week.

6. TES was done under anesthesia (a mixture of Ketamine and Domitor) and subjects were placed in ventral decubitus inside a Faraday cage.

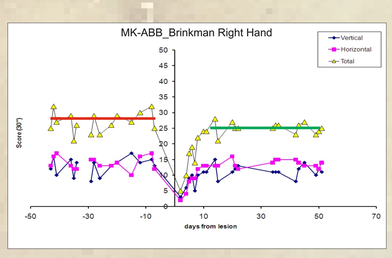
First, TES consisted of a single pulse (0.2 ms duration) starting at 50 volts up to 500 volts to determined thresholds.

Subsequently, TES consisted of single repetitive pulse (30x0.2 ms duration) at fixed voltage (100 volts and 250 volts) and double repetitive pulses (30x0.2 ms duration) at fixed voltage (50dbl volts and 100dbl volts).

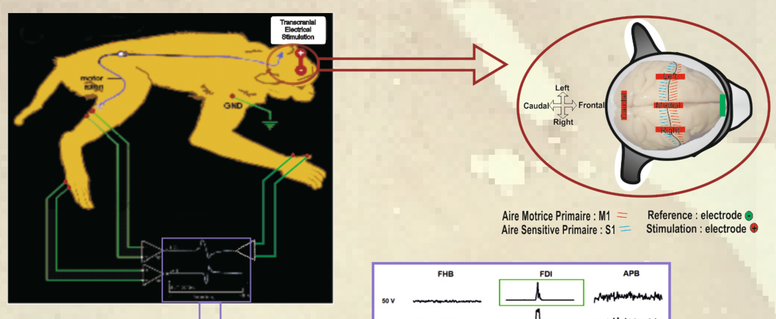
A custom software program (Neural Average, University of Washington, Seattle, WA) was used for data acquisition and averaging.

7. EMG was recorded from intrinsic hand muscles (IHM) (FDI: *first dorsal interosseus*, and APB: *abductor polliciss brevis*) and intrinsic foot muscle (FHB: *flexor halluciss brevis*), using pairs of multi-stranded stainless steel wires.

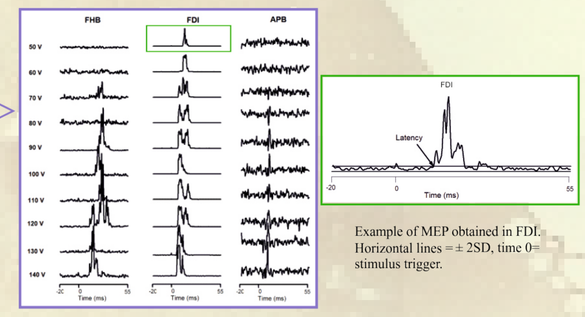
Manual dexterity assessed using the modified Brinkman board task.



Example of recovery of manual dexterity as reflected by the Brinkman board test, in an anti-Nogo-A antibody and BDNF treated animal before and after lesion.
The behavioral score was assessed by counting the number of pellets retrieved from vertical and horizontal slots during the first 30sec of the task, before and after the lesion.



Subjects were anesthetized with Ketamine and Domitor



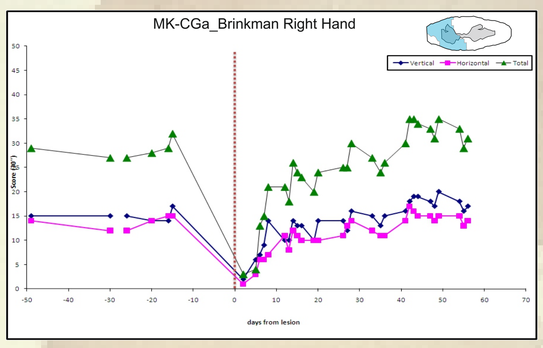
Example of MEP obtained in FDI. Horizontal lines = ± 2SD, time 0= stimulus trigger.

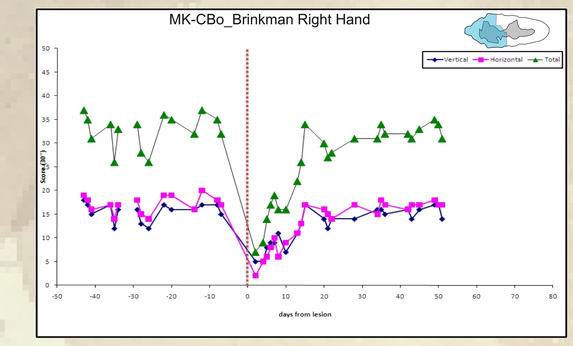
RESULTS

Control monkeys

Anti-Nogo-A antibody and BDNF treated monkeys

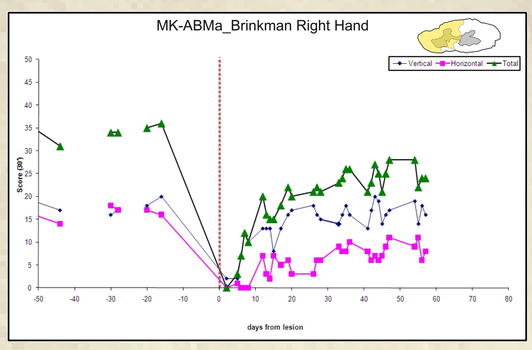
Behaviour

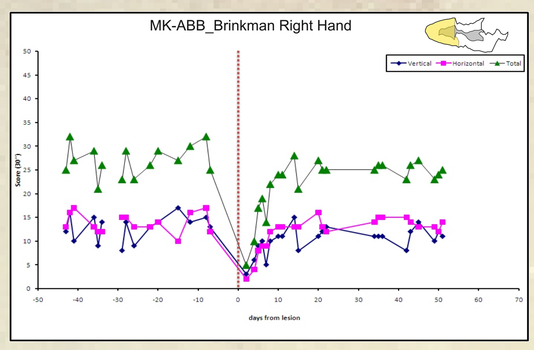




Right Left
Ventral

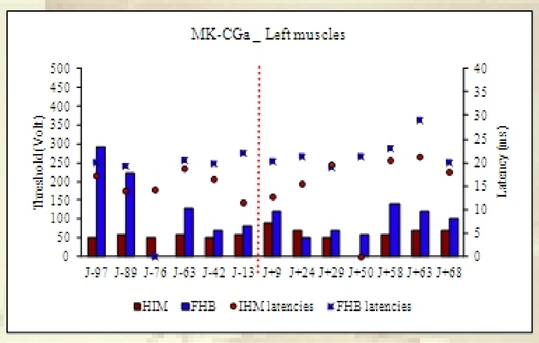
J0: Lesion day

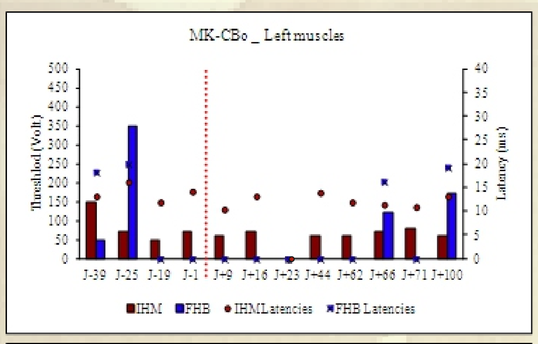


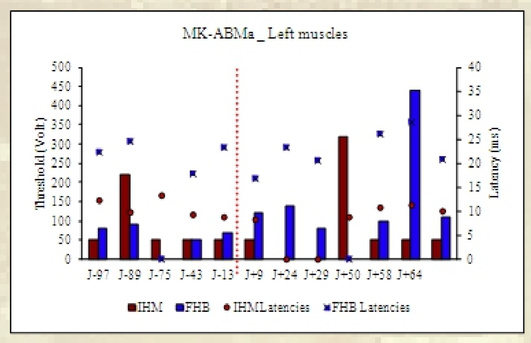


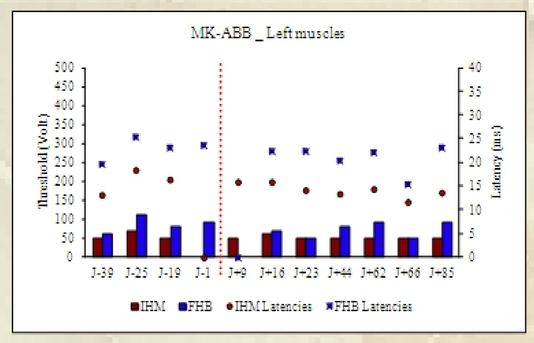
Electrophysiology

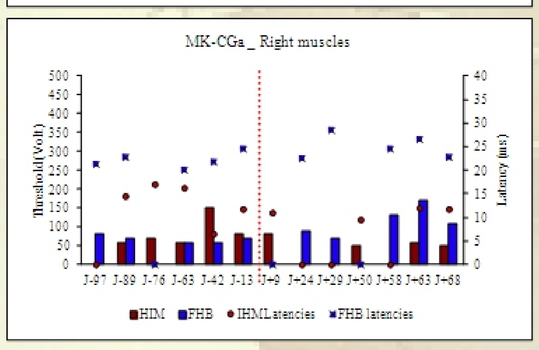
Thresholds

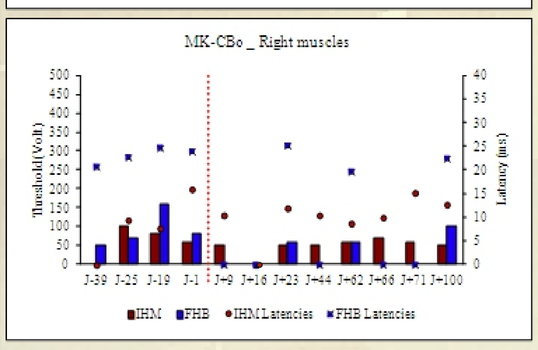




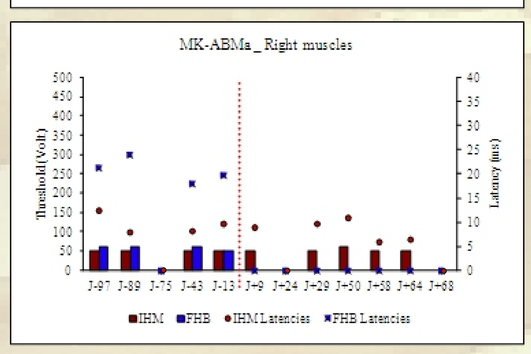


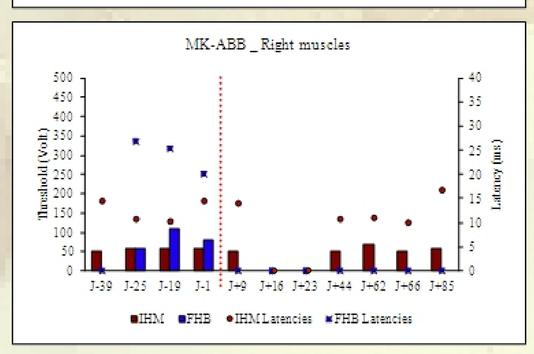






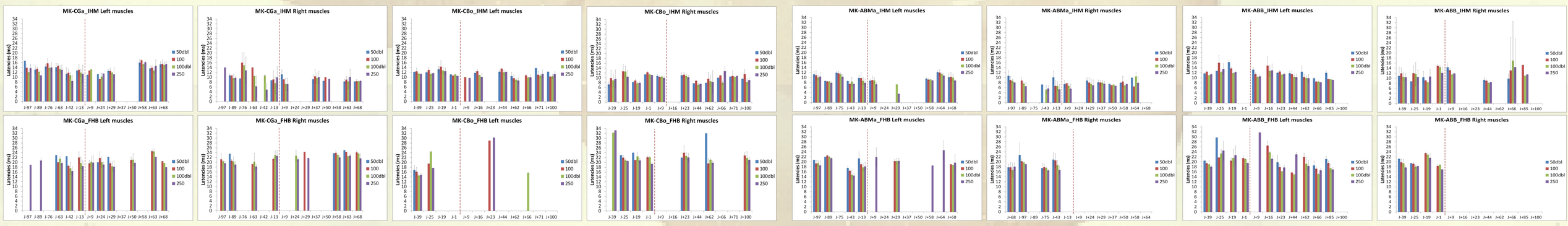
J0: Lesion day





Repetitive stimulation

J0: Lesion day



CONCLUSION

These preliminary data show that:

1- The inter-sessions variability is considerable when using data derived from a limited number of muscles. Moreover, the TES effect may be influenced by other parameters such as depth of anaesthesia, for example.

2- At the present state of the analysis, no significant electrophysiological differences were found between treated and untreated monkeys.

3- A comparison with monkeys treated with anti-Nogo-A antibody only will be of interest.

ACKNOWLEDGMENT

Supported by: SFN grants (T. Wannier: No 3100A0-104061/1, No 310000-118357 and A. Belhaj-Saif: 310030-120411); The National Center of competence in Research (NCCR): "Neuronal plasticity and repair"; Novartis Pharma.