Electrophysiological and Behavioral Evaluation of Intracerebral Hemorrhage Rat

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Introduction

Intracerebral hemorrhage (ICH) is one typical kind of stroke that threaten human patients. It is mainly caused by breaking down of blood-brain barrier in a particular area of the brain. Basal ganglia hemorrhage is one of the major sub type of ICH. It causes paretic effect on the contralateral side of the limbs by corrupting the motor control function of the individual. This study will focus on evaluation of basal ganglia hemorrhage and the effectiveness of physical rehabilitation treatment by electrophysiological and behavioral analysis. Based on the analysis data, physiological state of the lesion rats can be traced through signal processing. ICH modeling will be carried out in the right striatum of Sprague Dawley rat by bacterial collagenase infusion.

Method

1. Intracerebral Hemorrhage Modeling

Bacterial collagenase infusion model into right basal banglia using type IV collagenase (1.2 L, Sigma, C5138 0.25 Uin 1 L NaCl 0.9%) is performed on animals. Bacterial collagenase disrupts the basal lamina to cause blood leaking into the surrounding brain tissue. It mimics the pathophysiology and functional consequence of ICH in humans in real cases and results in long-term locomotor deficits.

2. Electrophysiological Evaluation

An evaluation platform is established using motor evoked potentials (MEP) and somatosensory evoked potentials (SSEP). MEP and SSEP is measured from time to time to observe the physiological integrity of

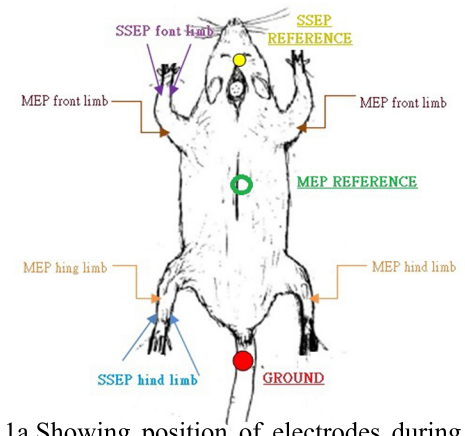


Fig.1a.Showing position of electrodes during data acquisition. For SSEP, stimulus is given to median (upper extremity) and tibial nerve (lower extremity) and signals are detected immediately above the sensormotor cortices. For MEP, stimulus is given transcranially through the motor cortex and signals are detected in bicep(upper extremity) and tibialis anterior (lower extremity) muscle belly.

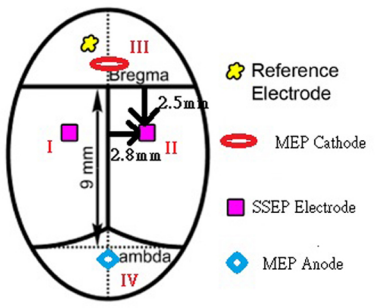


Fig.1b. Location of borehole for SSEP and MEP electrode placement.

Nicolet Endeavour CR

SSEP is a major indicator of the integrity of the nervous system. Median nerve SSEP represent dorsal horn postsynaptic activity triggered by ascending volleys from the dorsal nerve roots. Tibial nerve stimulation arises at the pontomedullary junction. Stimulation of approximately 3mA will be applied to limbs and SSEP can be measured transcranially in the sensorimotor cortex.

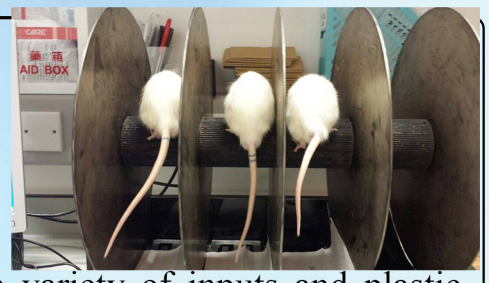
MEP is measured directly from muscles upon transcranial electrical stimulation of the rat. The large current, short duration stimulus overcomes the high impedance of the scalp and cranium to induce a current in brain tissue and stimulate motor cortex with depolarization of pyramidal neurons or their axons and activate corticospinal tract neurons. Electrical stimulation of approximately 16mA will be applied to the motor cortex through a bipolar electrode.

Recorded electrophysiological signal will be visualized with Nicolet Endeavor™ CR.

3. Behavioral Evaluation

CatWalk™ XT will be used as a platform to perform behavioral tests. Gait analysis can be performed to observe the gait of intact and lesion rats. The rats will walk through the glass plate of CatWalk™ XT .Pressure fall on the plate will be visualized through the LED-embedded glass plate. Qualitative analysis of the data will be analysed based on step sequence distribution, regularity (RI), step distribution, base of support, duration of swing and stance phases, hind paw pressures etc.

4. Physical Rehabilitation Treatment



Lesion rats of treatment group was given Rotarod training daily for 30 minutes at a speed of 4 rpm to encourage rehabilitation. It is proposed that complex motor skill training, requiring the integration of a variety of inputs and plastic changes across multiple brain structures, had more beneficial effects on outcomes after brain injury than simple repetitive exercise. The degree of effectiveness is studied on this project.

Results and Discussion

1. Effect of ICH Modeling on Electrophysiological pattern

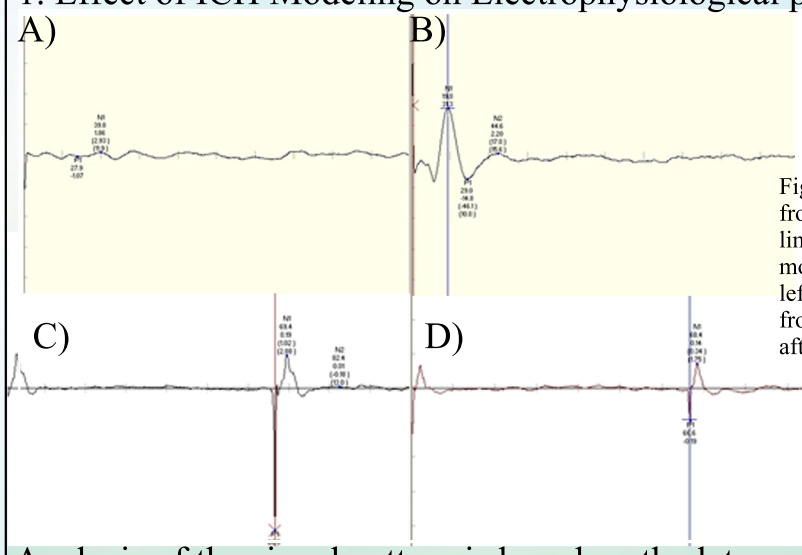
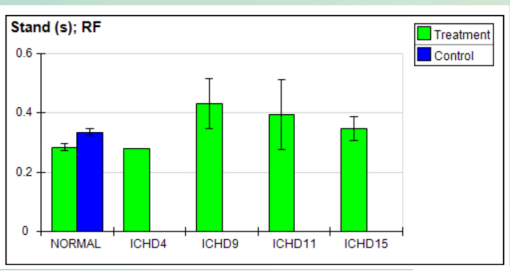
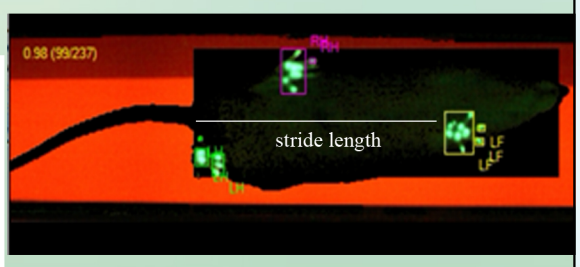


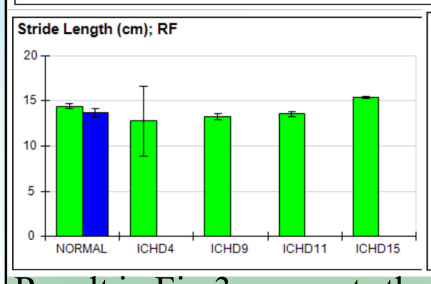
Fig.2. SSEP pattern of A) left front limb and B) right front limb of ICH rats, 7 days after modeling. MEP pattern of C) left front limb and D) right front limb of ICH rats, 7 days after modeling.

Analysis of the signal pattern is based on the latency and amplitude of the positive and negative waves recorded. Results of ICH day7 rats show only baseline signal recorded from the left limb of the animal. Such result suggests that there is no proximal connection in the nervous path of the animal. For the right limb only slight deflection comparing to the control is present which suggests that the ipsilateral side of the body to the brain lesion is normal.

2. CatWalk™ XT Analysis







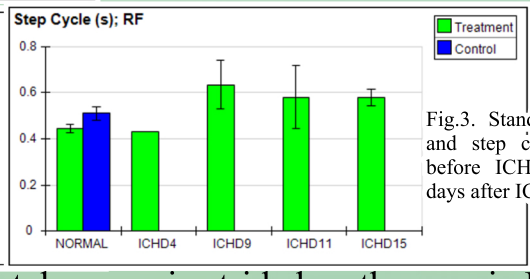


Fig.3. Stand, Stride length and step cycle of animal before ICH and 4,9,11,15 days after ICH.

Result in Fig.3. suggests that decrease in stride length occur in ICH rats due to impairment in motor functions. The animal tend to walk in a slower body speed and narrower stride length due to balancing deficits on contralateral sides of the body. There is an increase in stand time(duration of contact of a paw with the glass plate in a step cycle) and step cycle (the sum of stance and swing duration) after ICH and the effect is the most significant 9days after ICH modeling. This may also be due to the impairment in motor functions causing the animal to be more hesitant when walking through the glassway. Normal stride length, stand duration and step cycle is gradually restored throughout the study. The restoration may be due to natural absorption of hematoma inside the lesion individual and regeneration of damaged tissue in the right cortex.

Conclusion

Intracerebral hemorrhage cause motor and sensory deficits in an individual. We found that gradual restoral in normal motor functions is shown. Whether the restoral is speed up by the rehabilitation treatment is not confirmed yet and need further study.

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