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Protracted morphological changes in the corticospinal tract within the spinal cord after intracerebral haemorrhage in mice

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Introduction

Throughout the years, the research field has been looking for efficacious treatment options that improve the prognosis of intracerebral haemorrhage (ICH), an acute brain insult which is associated with high morbidity and mortality rates. The sole focus of the translational research field on gray matter injury partly contributed to the failure of discovery of better treatments as white matter tracts are equally important in maintaining normal neurological functions. Damage to white matter in the brain has been demonstrated repeatedly after subcortical ICH in rodents and in patients, but this kind of abnormalities could theoretically be seen in regions distant from the primary injury site within and outside the brain since white matter tracts structurally connect different regions in order to relay signals. This longitudinal study examined the morphological changes of the dorsal corticospinal tract (CST), a major descending pathway controlling motor functions, in the spinal cord during the first five weeks after ICH.

Methods

Animals and experimental groups

Twenty-one 12- to 14-week-old adult male C57BL/6N mice were used in this study. They were separated into two groups, sham and ICH. The mice in the ICH group were sacrificed at various time points, namely week1 (W1), week 2 (W2), week 3 (W3, week 4 (W4) and week 5 (W5) post-ICH (n = 3 per group). Those in the sham group were divided into two time points: W1 and W4 post-sham operation (n = 3 per group).

Experimental ICH model

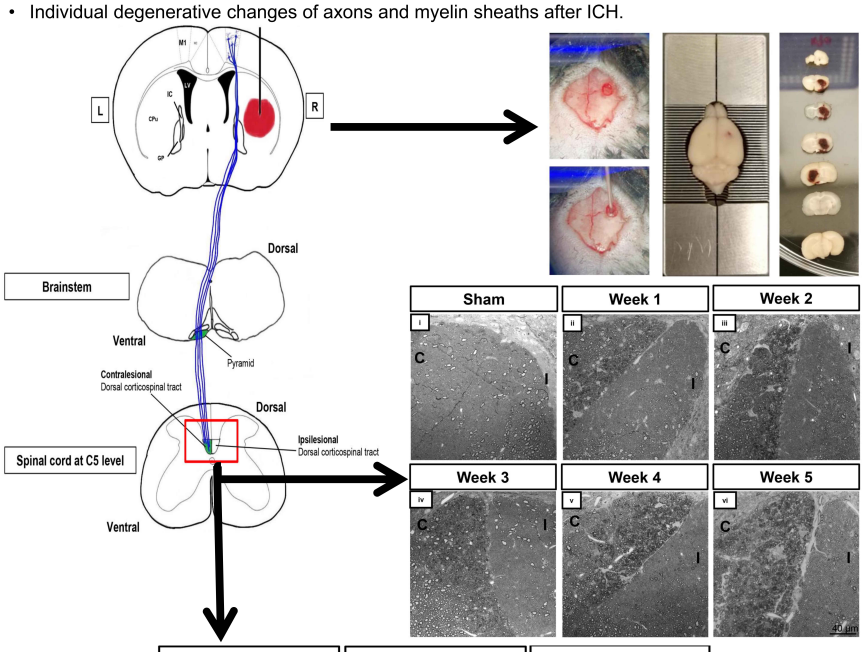
Stereotactic injection of 0.04U of type IV collagenase in 0.5 µl of 0.9% normal saline into the right corpus striatum destroyed the basal lamina of the blood vessels, resulting in spontaneous bleeding.

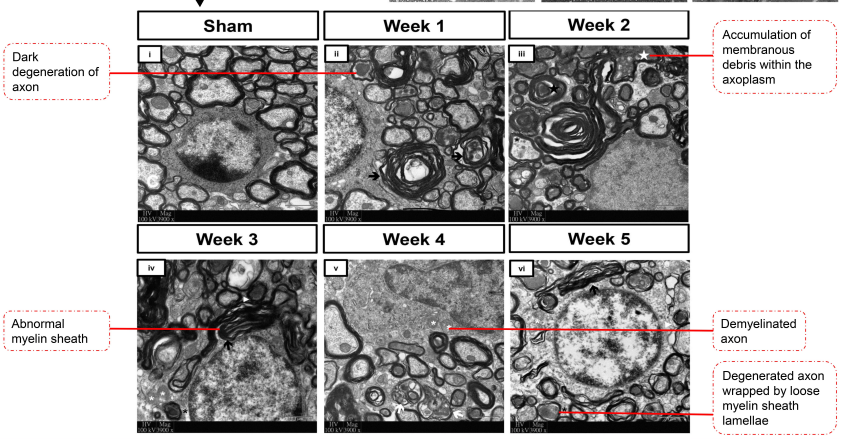
Microscopic analysis

Toluidine-blue stained horizontal sections of the spinal cord at C5 level were visualized under confocal microscope (63x, oil immersion). Transmission electron microscope was used to delineate the specific changes in white matter at a higher magnification (3900x). C = contralesional; I = ipsilesional.

Results

- Prolonged pathological changes in the contralesional dorsal CST for at least five weeks after ICH.
- Individual degenerative changes of axons and myelin sheaths after ICH.





Conclusion

The prolonged and extensive degenerative changes indicated the presence of impaired structural integrity of CST after ICH. A few clinical studies highlighted the contribution of CST integrity to motor recovery after stroke[1, 2]. Our future studies will focus on treatments that protect or improve CST integrity after ICH.

References

[1] Bigourdan, A., Munsch, F., Coupé, P., Guttmann, C. R. G., Sagnier, S., Renou, P., . . . Tourdias, T. (2016). Early Fiber Number Ratio Is a Surrogate of Corticospinal Tract Integrity and Predicts Motor Recovery After Stroke. *Stroke, 47*(4), 1053-1059. doi:10.1161/strokeaha.115.011576
[2] Byblow, W. D., Stinear, C. M., Barber, P. A., Petoe, M. A., & Ackerley, S. J. (2015). Proportional recovery after stroke depends on corticomotor integrity. *Annals of Neurology, 78*(6), 848-859. doi:10.1002/ana.24472