Pathophysiology of Neurotrauma

Establishing the Ferret as a Gyrencephalic Animal Model of Neurotrauma

Blast injury is a hallmark of recent military battlefield conflicts. The gyrencephalic ferret is an excellent small animal model to study human-pertinent consequences of neurotrauma because it possesses an extensive distribution of white matter and a strong presence of sulci and gyri.

Researchers at the Center for Neuroscience and Regenerative Medicine conducted studies to develop a ferret model of traumatic brain injury (TBI) to identify the changes in pathophysiological, behavior, and magnetic resonance imaging after injury (*Schwerin et al. 2017*; Figure 1).

In one study, using controlled cortical impact to create a TBI in the ferret model, revealed a progression of inflammation that originates in the neocortex near the site of the injury and progresses deep into the white matter with time after injury. Memory impairments coincide with the greatest degree of inflammation in the cortex, while motor impairments coincide with progression of microglial clustering in the white matter. This ferret model represents an important opportunity to explore clinical therapies addressing progressive damage in brain white matter after TBI.

In a second study, adult male and female ferrets were exposed to one to four explosive blasts and survived for 1-12 weeks. In contrast to the limited distribution of astroglia observed after a restricted impact injury, the astroglia distribution after explosive blast is wide-spread and immunoreactivity against glial fibrillary acidic protein (GFAP; astrocytic marker) occurs throughout the telencephalon. Particularly strong GFAP label distributes through much of the extensive white matter present in the ferret. GFAP infrared thermography is found at the interface between grey and white matter, in the fundus of sulci, just below the pia, and surrounding blood vessels. Immunoreactive staining against markers for phosphorylated tau is also strong in animals receiving a blast injury and varies regionally within the brain. The intensity of immunoreactivity for both markers varies in proportion with the number of blasts each animal receives. Many of the experimental features in the ferret are similar to the pattern of astroglial scarring seen in humans, making this animal model crucial for continued study and to compare with human pathology and potential treatments. Thus, this ferret animal model represents an important opportunity to explore potential treatments addressing the astroglial scarring seen in human brain after blast injury.

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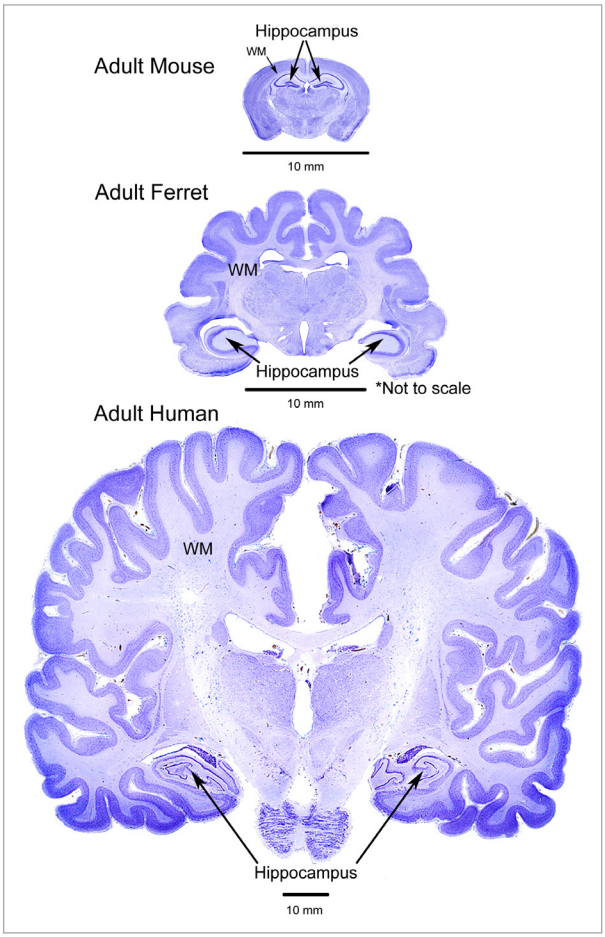

FIGURE 1: Comparative anatomy. Comparison of the brains of the adult mouse, ferret and human (not to scale – see scale bars) showing coronal slices stained with cresyl violet. Note the location of the hippocampus in the ferret is similar to the location in the human. In addition, the amount of white matter is much greater in the ferret han the mouse. The gyral folds in the ferret are also obvious, displaying greater similarity to the human than the mouse. Human brain slice adapted with permission from http://www.brains.rad.msu.edu, supported by the US National Science Foundation and the National Institutes of Health. Brain images were modified in color, brightness and contrast for optimal comparison purposes. (For interpretation of the references to color in this figure legend, the reader is referred to the web version http://www.sciencedirect.com/science/article/pii/S0165027017301292?via%3Dihub; (Figure 9 from Schwerin et al. (2017) used with permission from the authors)

REFERENCES:

Schwerin, S. C., Hutchinson, E. B., Radomski, K. L., Ngalula, K. P., Pierpaoli, C. M., and Juliano, S. L. 2017. "Establishing the Ferret as a Gyrencephalic Animal Model of Traumatic Brain Injury: Optimization of Controlled Cortical Impact Procedures." J Neurosci Methods 285:82-96. doi: 10.1016/j.jneumeth.2017.05.010.