

Assessing Cognitive Function Following Medial Prefrontal Stroke in the Rat

Cognitive/Language Rehabilitation

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Cognitive impairments are prevalent following clinical stroke. However, to date, preclinical research has focused almost exclusively on motor deficits. In order to conduct systematic evaluations into the nature of post-stroke cognitive dysfunction and recovery, it is crucial to develop focal stroke models that affect cognition while leaving motor function intact. Furthermore, in order to investigate potential cognitive post-stroke treatments, it is important that deficits are persistent in the chronic phase. This experiment was performed to evaluate a focal medial prefrontal cortex (mPFC) stroke model using a battery of tests that examined a range of cognitive functions 1-4 months following stroke. Male Sprague-Dawley rats weighing 250-300 g underwent focal ischemia induced in the mPFC using bilateral intracerebral injections of endothelin-1, or sham surgery. Beginning at 1 month post-stroke, cognitive function was assessed using open field, temporal object recognition, object-context recognition, object-placement recognition, attentional set-shifting, light-dark box, spontaneous alternation, Barnes maze, and win-shift/win-stay tests. Prefrontal cortex injury resulted in bilateral damage to the prelimbic and cingulate cortices, extending typically between 4.22 to 1.34 mm anterior to bregma. Animals that underwent stroke surgery exhibited significant changes in all object recognition functions compared to Sham animals ($p < 0.05$). Stroke animals also exhibited impaired performance on the Barnes maze ($p = 0.012$), and took significantly more trials to learn the second rule in the win-shift/win-stay test ($p = 0.013$). Further, they exhibited reduced anxiety-like behaviour in the open field ($p = 0.049$). Spontaneous alternation behaviour and locomotion in the open field were not affected. The deficits observed are consistent with some of the key characteristics of prefrontal stroke in humans. Our results show that this model produces persistent deficits in multiple prefrontal cognitive functions, and therefore may be useful for identifying and developing potential therapies for improving cognitive dysfunction in the chronic phase following stroke.