SEMINAR FOR NEUROTRAUMA AND DISEASES

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ABSTRACT

Approximately 18,000 patients each year are affected by spinal cord injury causing motor, sensory and autonomic dysfunction. Children 16 years of age or younger account for 5% of cases with the majority being cervical level that effect forelimb function. To improve their current lifestyle, patients affected by SCI desire return of hand and digit function. However, most spinal cord injury studies examined recovery of locomotion after thoracic lesions in adults and not goal-directed or skilled forelimb movements after cervical injuries, especially in younger animals. In general, the corticospinal tract drives skilled forelimb movements with support from indirect brainstem regions. After lesions to the corticospinal tract there is a significant loss of forelimb function. Our data shows good recovery in juvenile rats when modulated by altering the excitation of the forelimb motor cortex using chemogenetic channels during play which provided a form of physical and social enrichment. Here expression of Designer Receptors Exclusively Activated by Designer Drugs (Dreadds) showed a hierarchy of recovery of forelimb function. Excitatory Dreadds showed the best recovery with significant increases in recovery above control levels, whereas reduced recovery below control levels was observed when inhibitory Dreadds were expressed within the motor cortex of lesioned CST axons. Likewise, we saw a similar recovery in forelimb kinematics and muscle activity, in which expression of excitatory Dreadds in cortical motor neurons showed the best recovery, followed by mCherry controls with expression of inhibitory Dreadds showing the poorest outcome. We hypothesize that cortical activity modulates axonal sprouting of the lesioned CST, while physical play shapes the controls to promote circuit adaptation rerouting motor commands through brainstem and propriospinal motor systems. We further show that these brainstem and propriospinal networks are involved in relaying the motor command around the spinal cord lesions. Following these circuits, we have developed a novel approach to motor control theory and circuits involved in motor learning supporting rehabilitation.