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Chinese Medicine

In vivo direct reprogramming restores local circuit connectivity after focal stroke

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Abstract

Stroke is a leading cause of severe morbidity and mortality. Neuronal loss is accompanied by proliferation of reactive astrocytes and the formation of a glial scar, which is a major hurdle to re-innervation and functional recovery following stroke. In vivo direct reprogramming is a novel technology that transforms reactive astrocytes into mature neurons by overexpressing the gene, NeuroD1. This is a promising candidate therapy to replenish the neuronal population, reduce the level of gliosis, and restore local circuit functionality. We used Channelrhodopsin Assisted Circuit Mapping (CRACM) to measure local circuit connectivity in mouse visual cortex after endothelin-1 induced local ischemia. We found that after focal stroke and without reprogramming, the local connectivity of surviving neurons in the visual cortex was minimal. In vivo direct reprogramming transformed reactive astrocytes into functional neurons. These astrocyte-derived neurons demonstrated physiological properties of mature cortical neurons, and had increased circuit connectivity compared to neurons in control animals without reprogramming. Same functional recovery was seen from visually evoked potentials (VEPs) recorded from the primary visual cortex of awake animals. Our work demonstrates that in vivo direct reprogramming achieved circuit repair following stroke.

~ All are welcome ~