“Neuronal regeneration after ischemia brain injury”

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Brain is well known for its vulnerability to ischemia. In particular, neurons in the hippocampal CA1 region and the striatum die selectively following a brief period of ischemia, leading to memory disturbance and motor disability. Various experimental researches to prevent such ischemic neuronal death, however, could not provide effective treatment modalities. On the other hand, a new approach to replace lost neurons emerged in 1990s, when endogenous neural stem cell were shown to exist in the adult mammalian brain.

Neural stem cells were first identified in the two neurogenic regions, namely anterior subventricular zone and the dentate gyrus of the hippocampus, where new neurons are continuously generated under physiological condition. Subsequent research, however, have shown that these neural stem cells exist in wider brain regions, migrate to various lesion sites, and to maturate electrophysiologically to repair lost functions after ischemia.

On such example is hippocampal CA1 region, where neural stem cells have not been identified under physiological condition. In this region, brief period of growth factor infusion has been shown to augment ischemia-induced neurogenesis from the dormant stem cells located above the CA1 region, and to replace 40% of lost neurons, leading to improvement of memory disturbance. This finding indicated the existence of dormant stem cell in broad regions of the brain, which could be recruited after ischemia. In the striatum, ischemic neuronal injury was also shown to activate the stem cells in the subventricular zone, which migrate to the lesion site and mature into region specific phenotype. Recent research further demonstrated various endogenous factors that inhibit neuronal regeneration, proposing a

new approach to potentiate endogenous regenerative mechanism.

These advances in regenerative approach to ischemic neuronal injury, as well as future direction in the reconstruction of neural network, are presented. The elucidation of endogenous mechanism of neurogenesis after ischemia in the adult mammalian brains would contribute to future clinical application of regenerative therapy.