Effect of Task-Specific Training on Eph/Ephrin Expression After Stroke

Neural Repair Mechanisms

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Stroke is the leading cause of adult disability because of the brain's limited capacity for repair. Several processes like angiogenesis, neurogenesis, axonal reorganization and synaptic plasticity act in concert to restore neurologial functions after stroke. Although some degree of spontaneous axonal sprouting occurs after stroke, regeneration of lesioned axons and formation of new connection is limited. The Eph/ephrin signaling has recently been identified to play important roles in activity dependent plasticity, angiogenesis and stem cell differentiation in adulthood as well as axon guidance in development.

To investigate the effect of task-specific training on Eph/ephrin expression in peri-infarct area and corticospinal tract after stroke, we compared the expression of Eph receptors and ephrin ligands in cortex and corticospinal tract between control and task-specific training group.

Rats were subjected to photothrombotic infarct. Task-specific training (single pellet reaching, 300 pellets/day or 20min/day) was initiated at 5 days post-stroke and continued for 4 weeks. Behavioral tests such as single pellet reaching test, parallel bar test and cylinder test were performed at 1 day pre-stroke, 5 days post-stroke, 1 week, 2, 3, and 4 weeks post-task-specific training. The expressions of Eph receptors (EphA2 and EphA4) and ephrin ligands (ephrinA1, ephrinA2, and ephrinA5) in the peri-infarct cortex, pyramid and spinal cord at 2 and 5 weeks after stroke were determined by Western blot analysis. Eph/ephrin expression levels after stroke were compared them after task-specific training for 1 week or 4 weeks.

Task-specific training group showed significantly better recovery in the behavioral tests. The expression level of ephrinA1, ephrinA2, and ephrinA5 in the pyramid containing corticospinal tract was increased at 2 W post-stroke. Increased ephrin A1 and ephrinA5 levels at 2 W post-stroke were decreased in ipsilateral pyramid by task-specific training for 1 W. However, increased expression levels of ephrinA1, ephrinA2, and ephrinA5 in the pyramid at 5 W post-stroke have not changed by task-specific training for 4 W.

These data suggest that task-specific training alter the expression of ephrin ligands in corticospinal tract at 2 W post-stroke. Controlling expression of ephrin ligands and task-specific training may be a promising therapeutic strategy to enhance stroke recovery.