The Effect of Optogenetics Stimulation on Kappa Opioid Receptor Signaling Following Stroke

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Introduction

Functional recovery following cerebral ischemia is mediated partly by vascular reorganization. During development, the kappa opioid system inhibits vascular development through endothelial cell differentiation and vascular pathfinding. Recently, we have shown that optogenetics stimulation can promote functional recovery. In this study, we investigate whether optogenetics stimulation can improve functional recovery by exerting an effect on kappa opioid receptor (KOR) signaling.

Methods

Focal cerebral ischemia was induced in adult male C57BL/6J mice at 8-12 weeks and mice were sacrificed at various time points. Immunohistochemistry was used to examine the expression profile of kappa opioid receptor and its ligand, dynorphin. In addition, using transgenic mice that express channelrhodopsin 2, we also performed stimulation of the primary motor cortex to assess for changes in the level of expression of KOR after stroke.

Results

Immunohistochemical analysis indicated that KOR expression was upregulated as early as day 1 post-stroke and continued to be elevated at 1 week post-stroke. The KOR up-regulation was restricted to the ischemic core with a neuronal morphology. Interestingly, there was no significant change of dynorphin expression in the ischemic core. Optogenetics stimulation leads to a reduction in the mRNA level of KOR in the peri-infarct area at 2 weeks post stroke.

Conclusions

Our preliminary results indicate that the kappa opioid receptor is significantly upregulated after stroke, and its level of expression is altered by optogenetics stimulation. Current studies will examine the effect of blocking kappa opioid receptor activation through pharmacological and optogenetics methods to determine its role in in angiogenesis and recovery post-stroke.

Learning Objectives

Understand the potential role of optogenetics stimulation in mediating post stroke plasticity; understand the role of kappa opioid receptor signaling following stroke

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