Module 9 Case Study – Dominic Giannangeli

Amyloid-β (Aβ42) coagulation is a prominent observable in Alzheimer's patients [1]. Researchers developed a model that allowed them to stimulate brain regions of interest in mice to observe the effect of that stimulation on amyloid-β formation. An opsin (SSFO) with a fluorescence protein (EYFP) was injected into Perforant Pathway Neurons in mice. Combine with a CaMKIIα promoter, within an AAV vector, expression of SSFO and EYFP was achieved. A control group was injected with EYFP only. Figure 1 describes how the effectiveness of the expression was monitored. SSFO expressed in the Laterial Entrohinal Cortex (LEC) was provided light (one pulse per minute for four hours) . This caused the generation of action potentials in LEC neurons expressing SSFO. The quantity of Aβ42 in the Interstitial fluid (ISF) of the Hippocampus was measured with a microdialysis technique. Figure 2 shows a plot comparing the amount of AB42 in the ISF across time. In mice with the SSFO expressed, with LEC neurons being stimulated, AB42 in the ISF was significantly greater when comparing against the control mice. This result may indicate that environmental interactions that excessively stimulate the LEC neurons could increase the probability of Aβ42 existing in hippocampus. In turn, this could speed up the progression of Alzheimer's disease.

Figure 1

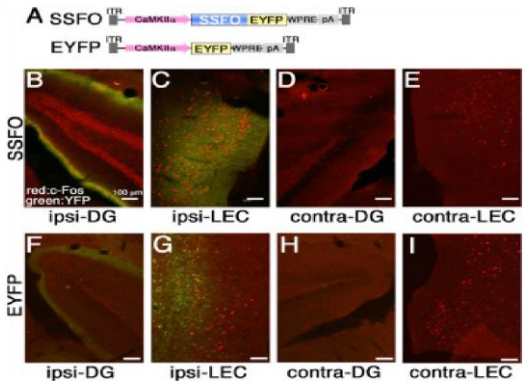
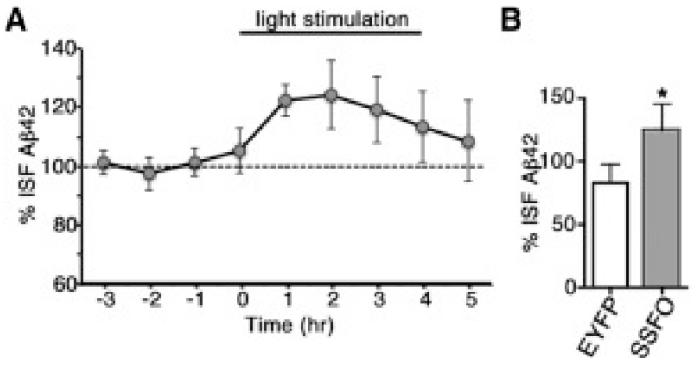


Figure 1. Optogenetic Stimulation Activated Perforant Pathway Neurons
(A) Schematic structures of SSFO-EYFP (SSFO) and EYFP (EYFP) driven under the control of CaMKIIα promoter in an AAV vector are shown. ITR, the inverted terminal repeat sequences; CaMKIIα, Ca^{2+}/calmodulin-dependent protein kinase II alpha (promoter); WPRE, woodchuck hepatitis virus posttranscriptional regulatory element; pA, polyadenylation signal.
(B–I) Immunofluorescence labeling for c-Fos (neuronal activation marker, red) and YFP (virus expression marker, green) of the coronal sections of mice infected with AAV-SSFO (B–E) or AAV-EYFP (F–I). Expression of SSFO or EYFP (green) was observed in perforant pathway neurons of the ipsilateral side of infection, i.e., LEC (ipsi-LEC, C and G) and OML of the DG (ipsi-DG, B and F), but not in those of the contralateral side (contra-DG, D and H, and contra-LEC, E and I). Unilateral optogenetic stimulation increased the levels of c-Fos at ipsilateral DG (B) and LEC (C) (red), specifically in the SSFO-infected mice. Note that non-stimulated LEC neurons show modest levels of basal c-Fos activities (E, G, and I).

Figure 2



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References

[1] “Beta Amyloid.” Beta Amyloid - an Overview | ScienceDirect Topics.