

C28

Samuel Sabzanov M.S.

Advisor(s): Todd Sacktor M.D.

Co-author(s): -

PKC ι / λ compensates for PKM ζ during long-term spatial memory storage in PKM ζ -null mice

Rationale: How are long-term memories (LTMs) stored in the brain? Maintenance of LTMs requires protein synthesis soon after strong synaptic stimulation or learning, and these proteins are believed to sustain synaptic potentiation or behavioral modification. One hypothesis for a mechanism of LTM maintenance involves the persistent increase of an atypical protein kinase C (aPKC) isoform, PKM ζ . Previous findings have shown that PKM ζ persistently increases in the hippocampus region CA1, including stratum radiatum (1), and that this increase positively correlates to the strength of spatial LTM (2). While PKM ζ is essential for LTM in wild-type (WT) mice, redundant compensatory mechanisms have been shown in PKM ζ -null mice, such as with another aPKC isoform, PKC ι / λ (3). Here, we eliminated both aPKCs, by conditional knockout (cKO) of PKC ι / λ in the hippocampus (PKC ι / λ -null mice are lethal) in PRKCIfl/fl-PRKCZ α /- mice, and examined the maintenance of spatial LTM and PKC ι / λ compensation for PKM ζ in the hippocampus by immunohistochemistry (IHC).

Methods: The PRKCIfl/fl-PRKCZ α /- mice received either Cre- or eGFP-adenoviral-associated virus (AAV) injections bilaterally into the hippocampus 3 weeks prior to an active place avoidance (APA) task, which requires three 30-min training trials in one day with a 2 hour inter-trial interval and rapidly forms spatial LTM. The LTM retention was examined 24 hours later, and brains were harvested, fixed, and analyzed by IHC. WT mice received Cre-AAV as a control.

Results/Discussion: Compared to WT mice, PRKCIfl/fl-PRKCZ α /- mice that received Cre-AAV (PKC ι / λ cKO and-PKM ζ KO) showed significant impairment in the memory retention test, while PRKCIfl/fl-PRKCZ α /- mice that received eGFP-AAV (PKM ζ -KO) did not. The IHC results confirm that PKM ζ -KO mice show increased expression of PKC ι / λ in the stratum radiatum of hippocampal region CA1 during spatial memory storage due to compensation for PKM ζ . These data support a key role for aPKC in LTM maintenance.