Bmal1^{fbrainKO} Mice Exhibit Deficits in Learning and Memory Processes

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The time-of-day effect on cognitive performance has been investigated by various behavioral tools and is supported by anecdotal evidence. However, the molecular details of the interaction between the circadian and cognitive systems remain underexplored. Recent studies suggest an endogenous slave-oscillator in the hippocampus, the primary seat of all learning and memory processes. Furthermore, in mammals *Arntl* (*Bmal1*) is the only indispensable transcription factor in the core transcriptional and translational feedback loop (TTFL) of the circadian-clock. Global deletion of the Bmal1 locus (Bmal1$^{-/-}$) leads to arrhythmic locomotor activity but also many other behavioral and physiological deficits, complicating the relationship between the clock and these phenotypes. We hypothesized that conditional tissue-specific deletion of Bmal1 in the hippocampus will function as a proxy for disabling the 'hippocampal-clock' leading to learning and memory deficits. To test this, we ablated the Bmal1 loci in post-natal mouse hippocampi using the CamKII-Cre driver line (referred hereafter as Bmal1^{fbrainKO}). The circadian locomotor activity rhythms of Bmal1^{fbrainKO} are comparable to wild-type mice. However, the behavioral performance of Bmal1^{fbrainKO} in hippocampal-dependent tasks like classical-fear conditioning and spatial-object recognition was significantly impaired compared to littermate controls. We also observed differences in the hippocampal molecular-network of Bmal1^{fbrainKO} and wild-type mice that provides some insight into the molecular correlates of this performance.