Inhibitory determinants of memory reactivation in the hippocampus

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Replay of neuronal activity patterns during sharp-wave ripples (SPWr) is a crucial event for memory consolidation. Past events reactivation can be estimated by the explained variance (EV) between the pairwise neuronal correlations of consecutive behavioral episodes.

We have investigated the physiological mechanisms of hippocampal reactivation in mice after the exploration of a linear maze. We found a strong reactivation during the subsequent SPWr events (EV=33.2±17.15%; n=19 sessions), which did not correlate with changes in the average firing rate or the ripple rate of pyramidal neurons or interneurons in the hippocampus. However, we found a small effect in the cross-correlation between spiking neurons during SPWr. These results suggest that changes in the fine neuronal population structure during SPWr supports reactivation. Next, we probed the subthreshold dynamics of the pyramidal neurons before and after the exploration episode by high-resolution optogenetics. Surprisingly, we found a significant decrease in the average neurons' excitability exclusively during SPWr ($p<10^{-9}$), supporting a reorganization of the inhibitory inputs. A generalized linear model revealed that the decrease in excitability during SPWr was the most important feature describing the changes in EV, probably mediated by inhibitory plasticity changes. To test this hypothesis, we use a quemogenetic approach to locally activate the CA1 populations of interneurons (DLX-Gq-DREADD), which led to a decrease in the total firing rate of both pyramidal cells and interneurons but no changes in the peak ripple rate. Memory reactivation was drastically decreased after the CNO injection highlighting a central contribution of interneurons dynamics plasticity in memory consolidation.