LONG-TERM REARRANGEMENTS OF HIPPOCAMPAL MOSSY FIBER TERMINAL CONNECTIVITY IN THE ADULT REGULATED BY EXPERIENCE

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SUMMARY

The hippocampus has been shown to encode the sequences of places and events that compose episodic memories, and plays a critical role between the initial formation and their final repository elsewhere in the brain (Gabrieli et al. 1997 and Henke et al. 1997). However, we have only begun to conceptualize how information is encoded and preserved for long periods within the hippocampus. In fact, the exact contribution of each hippocampal cell type, which molecules are predominant and which kind of plasticity is crucial, is still poorly understood. We found new insights of the hippocampal granule cell organization that might be crucial to encode information that compose episodic learning and memory. In this study we provide evidence that functionally important presynaptic complexes in the hippocampus rearrange their local connectivities throughout life, and that these rearrangements are influenced by experience and age. We first show how LMT-Cs are local presynaptic terminal arborizations of mossy fibers, exhibiting large differences in the magnitude and divergence of their local connectivities with pyramidal neurons in CA3. We then provide two independent lines of evidence that LMT-Cs rearrange their connectivities in the adult: we show that subsets of LMT-Cs expand along CA3 dendrites throughout life, and that the complexities of LMT-Cs are dramatically enhanced by housing mice in an enriched environment. We then analyze identified LMT-Cs longitudinally in organotypic slice cultures, and show that: 1) the arrangements and heterogeneities of

LMT-Cs in slice cultures resemble closely those in vivo; 2) subsets of LMT-Cs rearrange their connectivities, and grow over weeks and months in slice cultures in patterns resembling those detected in vivo; 3) the anatomical rearrangements reflect corresponding rearrangements in functional connectivity; 4) the marked differences with respect to plasticity and growth reflect local properties of individual LMT-Cs, not their mossy fibers; 5) LMT-C growth and maintenance require spiking activity in the slices, and mGluR2-sensitive transmitter release from LMTs; 6) the stable maintenance of LMT-C size heterogeneities involves PKC activity. Taken together, these results demonstrate the existence of sustained local rearrangements of connectivity by defined terminal arborization structures regulated by activity in the adult.