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INTRINSIC ACTIVITY

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MEETING ABSTRACT

A1.7

Post-tetanic potentiation at the hippocampal mossy fiber – CA3 pyramidal neuron synapse shows a low induction threshold and is mediated by an increase in the readily releasable vesicle pool

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Background: The hippocampal mossy fiber synapse, the synapse formed between the axons of dentate gyrus granule cells (GCs) and the dendrites of CA3 pyramidal neurons, is a key synapse in the trisynaptic circuit of the hippocampus. Mossy fiber boutons (MFBs) are characterized by a large size, a low release probability (P_r), and the presence of an extraordinarily large number of vesicles dispersed over multiple active zones. All these peculiar features suggest that the MFB might be highly plastic. A hallmark property of the MFB – CA3 synapse is the unique magnitude of post-tetanic potentiation (PTP) [1]. Interestingly, PTP has been shown to turn the MFB from a conditional detonator into full detonation mode [2]. However, presynaptic GCs *in vivo* fire action potentials (APs) only very sparsely [3], therefore an open question is whether physiological firing patterns suffice to trigger PTP. Furthermore, whether PTP is achieved by transiently increasing the P_r or whether it depends on recruiting more vesicles to the readily releasable pool (RRP) is unknown.

Methods: Functional data were obtained by paired patch-clamp recordings between presynaptic MFBs and post-synaptic CA3 pyramidal cells. Functional results were subsequently corroborated by structural analysis using flash-and-freeze experiments in which optogenetic high-frequency stimulation of mossy fiber synapses was followed by high-pressure freezing and electron microscopy.

Results: We showed by direct recordings from single MFB – CA3 pyramidal neuron pairs that PTP can be reliably triggered at the level of a single presynaptic terminal. Furthermore, PTP does not require postsynaptic depolarization and is thus non-associative in nature. PTP could be induced by a remarkably low number of presynaptic APs, indicating that *in vivo* occurring firing patterns suffice for its induction. From a mechanistic point of view we demonstrate that PTP is achieved by mainly increasing the RRP size. This phenomenon was accompanied by a slight increase in quantal size. Tetanic optogenetic stimulation of channelrhodopsin expressing MFBs led to depletion of the docked vesicle pool, followed by pool overfilling and, in parallel, a significant increase in the average vesicle diameter.

Discussion: Our study shows for the first time at both the functional and structural level that PTP at the MFB – CA3 pyramidal neuron synapse is supported by an increase in the RRP and quantal size. This is in stark contrast to long-term potentiation (LTP) at this synapse, which depends on an increase in P_r. By affecting the RRP, PTP preserves the low-pass filter function of the MFB – CA3 synapse, which allows burst-to-burst transmission.

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Keywords: post-tetanic potentiation – mossy fiber bouton – hippocampus – plasticity

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