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MEETING ABSTRACT

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Presynaptic mechanisms underlying post-tetanic potentiation at hippocampal mossy fiber synapses

Yuji OKAMOTO, David VANDAEL and Peter JONAS*

Institute of Science and Technology Austria (IST Austria), Klosterneuburg, Austria

Background: The hippocampal mossy fiber synapse onto CA3 pyramidal neurons (MF–CA3 synapse) is a key element in information processing in the hippocampal trisynaptic circuit. This synapse acts as a 'conditional detonator', implying that temporal and/or spatial summation of presynaptic inputs is required to trigger CA3 pyramidal neuron firing. Post-tetanic potentiation (PTP) is a transient enhancement of synaptic transmission that lasts tens of seconds following sustained high-frequency presynaptic activity. This form of short-term plasticity converts the MF–CA3 synapse into a 'full detonator' so that single presynaptic inputs can trigger postsynaptic action potentials [1]. PTP at this synapse primarily increases the size of the readily releasable pool of synaptic vesicles (RRP), leaving release probability (Pr) largely unaffected. Although the cAMP–PKA pathway is thought to be involved in the synaptic potentiation at the MF–CA3 synapse [2], the exact molecular mechanism and the effect on quantal parameters (RRP and Pr) remain to be elucidated.
Methods: To investigate the involvement of the cAMP–PKA pathway in PTP at the unitary synaptic level, we performed paired recordings from mossy fiber boutons and CA3 pyramidal neurons in brain slice preparations, with selective and minimally invasive stimulation of single mossy fiber boutons in the tight-seal cell-attached configuration. We applied adenylyl cyclase activators and PKA inhibitors to test how these pharmacological manipulations affect the quantal parameters estimated from cumulative EPSC amplitudes during 50-Hz trains of 10 stimuli [3].
Results: First, we applied forskolin (50 µM), which is thought to increase intracellular cAMP levels via stimulating adenylyl cyclase. Forskolin potentiated synaptic responses in CA3 pyramidal neurons by increasing RRP size but not Pr ($n = 10$), suggesting that the cAMP-dependent pathway is involved in PTP at the MF–CA3 synapse. Therefore, cAMP activation and PTP might lead to similar changes in single-synapse computations. Second, a blocker of the catalytic sites of PKA (H89, 10 µM) reduced basal transmission and largely abolished PTP induction ($n = 7$), suggesting that PTP accompanied by increase in RRP size requires PKA activation.
Discussion: Unlike in other synapses [4], the cAMP–PKA pathway seems to be involved in PTP in the MF–CA3 synapse. Given that neuromodulators such as dopamine and noradrenaline can induce cAMP signalling cascades via activating G protein-coupled receptors, their role in synaptic potentiation at the MF–CA3 synapses needs to be investigated.
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Keywords: hippocampus – mossy fiber synapse – post-tetanic potentiation – cAMP – PKA

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*Corresponding author e-mail: *peter.jonas@ist.ac.at*