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Long term depression of vestibular afferent EPSCs in medial vestibular nucleus neurons in vitro

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Abstract: Predictions from a computational analysis of the two-site model of cerebellum-dependent VOR gain adaptation [1] indicate that the efficacy of the vestibular afferent mediated EPSCs in medial vestibular nucleus (MVN) neurons may be modulated by Purkinje cell mediated IPSCs, according to a spike timing-dependent plasticity rule. Co-incidence of EPSCs and IPSCs in MVN neurons is predicted to lead to LTD at the vestibular afferent synapse.
In a recent study on deep cerebellar nucleus (DCN) neurons from P13-P16 mice [2] observed that LTP rather than LTD occurred at the mossy fibre excitatory synapse, when EPSPs were superimposed on a membrane hyperpolarisation. We investigated the effects of coincident hyperpolarising current injections on vestibular nerve evoked EPSCs in MVN neurons. Coronal brainstem slices (300 um) containing the rostral MVN and vestibular afferent tract were prepared from Lister Hooded rats (either sex, P17-P26). The brain stem ventrolateral to the MVN was stimulated (single 400 usec pulse; 50-300 uA) to evoke EPSCs in the presence of picrotoxin. Control EPSC recordings were followed by an induction protocol applied at a membrane potential of -65 mV: brief 20 msec hyperpolarising pulses were accompanied by a single electrical stimulus, which was applied either at the end of the membrane hyperpolarisation pulse, or at the start of the hyperpolarising pulse. Timing the electrical stimulus to coincide with the end of the hyperpolarising pulse reliably depressed EPSC amplitude by ~50%. By contrast, applying the stimulus at the start of the hyperpolarising pulse decreased the EPSC amplitude by <10%. These data indicate that membrane hyperpolarising pulses, mimicking Purkinje cell mediated IPSCs in MVN neurons, lead to LTD at the vestibular afferent synapse, supporting the predictions of the computational analysis. The occurrence of LTP rather than the expected LTD at the DCN synapse [2] may reflect a difference between the DCN and MVN neuronal mechanisms, or it may be an age-dependent change with LTD being expressed only after P17.
[1] Dean P, Porrill J (2004) Soc Neurosci Abstr
[2] Pugh JR, Raman IM (2006) Neuron 51:113-123.
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