BDNF-induced scaling of climbing fiber inputs during development of the cerebellum

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We investigated the role of brain-derived neurotrophic factor (BDNF) for the synaptic rearrangement of the climbing fiber (CF)-Purkinje cell inputs in the mouse cerebellum during early neonatal life. At birth, every Purkinje cell is innervated by several different CFs. Of these multiple afferent connections, only one survives into adulthood. We found that BDNF evoked large inward currents (see Kafitz *et al*., Nature, 1999) in Purkinje cells of cerebellar slices obtained from P6 (postnatal-day-6) to P9 old mice. Pairing BDNF-puffs with low frequency stimulation of small CFs (synaptic currents of < 800 pA) induced a persistent reduction (approx. 40%) of the CF response. By contrast, large CFs (> 800 pA) were resistant to this long-term depression (LTD) and exhibited sometimes even a synaptic potentiation. Our results indicate that these opposing effects are critically determined by distinct levels of intracellular Ca^{2+} accumulation in the postsynaptic Purkinje cells. Indeed, repeated application of BDNF, producing a large Ca^{2+} influx, caused a synaptic potentiation even at small CFs. Interestingly, at very early stages (≤ P4), the CF-Purkinje cell synapses were insensitive to this form of LTD, indicating that BDNF-mediated CF-LTD is firmly restricted to a narrow window of postnatal development. Taken together, our results suggest an unexpected scaling action that consists in the elimination of the weak, redundant CF synapses and the strengthening of the surviving 'winner' CF axon. Currently, we are investigating the influence of spike-timing on CF long-term plasticity.

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