Neural mechanisms of synapse remodeling in the developing brain

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Functional neural circuits of mature animals are shaped during postnatal development by eliminating early-formed redundant synapses and strengthening of necessary connections. Postnatal development of excitatory synapses from climbing fiber (CF) to Purkinje cell (PC) in the cerebellum has been a representative model of synapse remodeling in the developing brain. PCs are initially innervated by more than five CFs with similar synaptic strengths. During the first three postnatal weeks, single CFs are selectively strengthened while redundant CFs are eliminated, and most PCs become innervated by single strong CFs. These processes consist of four distinct phases: (1) selective strengthening of a single CF among multiple CFs innervating the soma of each PC from postnatal day 3 (P3) to around P7, (2) translocation and expansion of innervation territory of the strongest CF (‘winner’ CF) to PC dendrites from P9, (3) elimination of somatic synapses of the ‘winner’ CF and those of weaker CFs (‘loser’ CFs) from P7 to around P11, (4) elimination of the remaining somatic CF synapses from around P12 to P17. In this lecture, I will make an overview of molecular, cellular and neural circuit mechanisms underlying CF synapse remodeling. Then I will refer to neural circuit development in other brain regions and discuss how neural activity regulates synapse remodeling.