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Title:
Synapses lost and found: Developmental critical periods and Alzheimer's disease

Abstract:
How are connections wired up during brain development? Wiring occurs sequentially, first by forming a basic scaffold of connectivity according to strict molecular guidance cues and then the exact details of each circuit emerge by pruning and sculpting synapses. The process determining which synaptic connections remain and which are pruned is also genetically specified but in this case requires brain function. Prenatally, the brain generates its own internal neural activity patterns to jump-start the sculpting process. After birth as sensory systems such as vision mature, experience of the external world takes over to influence brain wiring during developmental critical periods. Neural activity and sensory experience regulate expression of sets of genes including several previously thought to act only in the immune system. These activity-regulated genes- including Major Histocompatibility Class I family members and Paired immunoglobulin-like receptor B- are required in neurons for synapse pruning and plasticity. Unexpectedly, they may also contribute to excessive synapse pruning in Alzheimer's disease. Thus, the baby's brain is not a miniature of the adult, but rather is a dynamically changing structure in which neural activity and experience ultimately select and stabilize essential details of neural circuitry that make each of us different from one another.