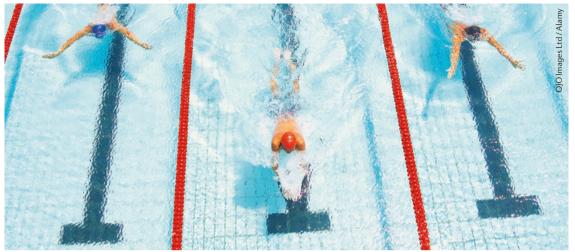
## **RESEARCH HIGHLIGHTS**

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NEURAL DEVELOPMENT

## A complex competition for spines

inducing differential levels of cadherin– catenin complex formation between neighbouring spines was sufficient to drive different spine fates *in vivo* 



During brain development, neural circuits are refined in a process that involves the elimination — or 'pruning' — of dendritic spines and the maturation of surviving spines. Yu and colleagues now cast light on the mechanisms that coordinate this process, showing that competition between neighbouring spines for cadherin–catenin complexes determines which spines are eliminated and which mature.

Spine pruning and maturation in the cortex are regulated by sensory experience. Here, the authors showed that, in mice, provision of environmental enrichment accelerated spine pruning and maturation in excitatory neurons in the sensory cortices, whereas sensory deprivation (whisker trimming) eliminated both processes. They hypothesized that the coordinated regulation of spine pruning and maturation might involve activitydependent changes in the distribution of a particular factor in neighbouring spines. The cadherin-catenin complex, consisting of N-cadherin,  $\beta$ -catenin and  $\alpha$ N-catenin, appeared to be a good candidate for such a role: N-cadherins located within the membranes of presynaptic terminals and dendritic spines can stabilize synapses through trans-synaptic homophilic interactions and also regulate synaptic function through the formation of complexes with intracellular partners, including β-catenin.

The authors found that, in mice, elimination of β-catenin from excitatory cortical neurons during the pruning period resulted in higher spine density and fewer mature spines in these neurons than were present in control mice. To further examine the role of the cadherincatenin complex in these processes, the authors cultured neurons expressing  $\beta$ -catenin in the presence of beads coated with N-cadherin. They found that dendritic spines that made contact with a bead had an increased chance of survival and maturation compared with spines in control cultures. However, their near neighbours that lacked contact with a bead had an increased chance of elimination. Thus, the relative level of cadherin-catenin complex formation regulated the fate of the spines.

Next, the authors examined whether neural activity alters the distribution of cadherin-catenin complexes. Photostimulation of cultured neurons expressing channelrhodopsin caused spines making contact with the stimulated axon to accumulate  $\beta$ -catenin and increase in size (which is indicative of spine maturation) relative to controls. At the same time, the size of neighbouring spines and their levels of  $\beta$ -catenin were decreased. The 'competitive' effect was greater the closer the two spines were to each other, supporting the concept of an activity-induced redistribution of  $\beta$ -catenin.

To confirm the importance of these mechanisms in vivo, the authors generated mice in which the expression of stabilized  $\beta$ -catenin within neuronal presynaptic terminals (enhancing the likelihood of cadherin-catenin complex formation) could be induced by infection with a Cre-expressing virus. The dendritic spines that made contact with the infected neurons accumulated more  $\beta$ -catenin and were larger than those that contacted uninfected neurons. Moreover, spine density within a 10-µm radius of spines that made contact with infected neurons was reduced in comparison with controls. Thus, inducing differential levels of cadherin-catenin complex formation between neighbouring spines was sufficient to drive different spine fates in vivo, as it was in vitro.

These findings suggest that competition for a limited quantity of cadherin-catenin complexes, which are redistributed between neighbouring spines in an activity-dependent manner, drives pruning (of the 'losing' spine) and maturation (of the 'winning' spine).

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ORIGINAL RESEARCH PAPER Bian, W.-J. et al. Coordinated spine pruning and maturation mediated by inter-spine competition for cadherin/catenin complexes. *Cell* **162**, 808–822 (2015)

FURTHER READING Koleske, A. J. Molecular mechanisms of dendrite stability. *Nat. Rev. Neurosci.* 14, 536–550 (2013)