This Week in The Journal

How Neogenin 1 Aids Neurulation

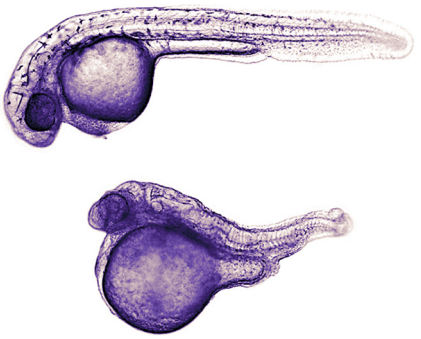
Sharlene Brown, Pradeepa Jayachandran, Maraki Negesse, Valerie Olmo, Eudorah Vital, et al.

(see pages 7465–7484)

The first step in CNS development is columnarization (elongation) of ectoderm cells to form the neural plate. This plate develops into the neural tube via different mechanisms, depending on the species. In mammals, the edges of the neural plate thicken and the center bends, forming neural folds on either side of a neural groove. Ultimately, the folds join on the dorsal side of the groove, forming a neural tube. The edges of the neural plate also thicken in teleost fishes, but, rather than forming neural folds and grooves, the plate forms a solid rod of cells, the neural keel, which sinks into the underlying mesoderm. A lumen forms subsequently in the neural keel to form the neural tube. Despite these differences, many of the same molecules guide neural tube formation across species. These include the transmembrane receptor Neogenin 1 (Neo1) and one of its ligands, the repulsive guidance molecule RGM1.

Brown, Jayachandran, et al. investigated the roles of Neo1 and RGM1 in zebrafish neurulation. As expected, depletion of either molecule disrupted nervous system development. The defects were attributed to impaired elongation of neuroepithelial cells during the early stages of neurulation, which resulted in impaired infolding of the neural plate to form the neural keel. The impaired elongation, in turn, likely resulted from improper alignment of microtubules. As in other mutants in which infolding is disrupted, neuroepithelial cell division occurred ectopically in Neo1- and RGM1-deficient embryos, resulting in duplication of the midline. Unlike in a previous report (Kee et al., 2008, J Neurosci 28:12643), however, there was no evidence that Neo1 or RGM1 depletion affected the establishment of apico-basal polarity in neuroepithelial cells.

Additional experiments revealed that binding of RGM1 to Neo1 in embryos increased Neo1 cleavage by α- and γ-secretases. This led to release of the Neo1 intracellular domain, which was targeted to the nucleus. Introducing this intracellular domain in embryos depleted of full-length Neo1 partially rescued neural tube defects. Altogether, the results suggest that RGM1 contributes to neurulation by promoting Neo1 cleavage, generating an intracellular fragment that likely regulates gene transcription. Future work should identify the genes regulated by Neo1, which might include regulators of microtubule stability and organization.



Neo1 deficiency (bottom) impairs neurulation in zebrafish embryos (compare with control; top). See Brown, Jayachandran, et al. for details.

Testing Theories of Consciousness with Single-Unit Recordings

Jean-Paul Noel, Yumiko Ishizawa, Shaun R. Patel, Emad N. Eskandar, and Mark T. Wallace

(see pages 7485–7500)

Neuroscientists generally agree that consciousness stems from activity in the cerebral cortex, but beyond that, there is much debate—not only about specific mechanisms and areas involved, but also about what neural signatures one should look for when investigating these mechanisms. Several theories regarding the neural bases of consciousness have been put forth, with varying levels of experimental support. Few studies have compared theories using the same experimental data, however. Noel, Ishizawa, et al. performed such a comparison using data from single-unit recordings obtained simultaneously in macaque primary somatosensory cortex (S1) and ventral premotor cortex (vPM) as animals responded to auditory, tactile, or combined auditory–tactile stimuli, as well as after the animals were rendered unconscious by propofol anesthesia.

The authors first tested predictions derived from the Integrated Information Theory (ITT) of consciousness. This theory defines various quantifiable attributes required for a physical system to generate the essential features of consciousness. These attributes include integrated information, Φ. According to Noel, Ishizawa, et al., the mathematics of ITT indicates that Φ of integrative neurons (defined as those whose responses to auditory–tactile stimuli differed from responses to unimodal stimuli) is greater than that of convergent neurons (which responded similarly to multimodal and unimodal stimuli). Therefore, integrative neurons should have a larger role in consciousness and be more affected by loss of consciousness than convergent neurons. The opposite was true: loss of consciousness eliminated responses of more convergent neurons than integrative neurons. Moreover, increases in noise correlations between neurons, which typically occur as animals lose consciousness, were greater for convergent than for integrative neurons. The authors also tested a prediction of the Global Neuronal Workspace (GNW) theory of consciousness, which holds that conscious experiences stem from widespread activation across the cortex. They asked whether there was more concurrent activity in S1 and vPM when monkeys were conscious than when unconscious. There was.

These data are inconsistent with at least one prediction of the ITT, but are consistent with the GNW theory. Nonetheless, similar tests should be completed using data from larger networks and from brain areas that might have a greater role in generating consciousness before one rejects or embraces any particular theory.

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