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## Neural crest cells utilize primary cilia to regulate ventral forebrain morphogenesis via Hedgehog-dependent regulation of oriented cell division

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### Abstract

Development of the brain directly influences the development of the face via both physical growth and Sonic hedgehog (SHH) activity; however, little is known about how neural crest cells (NCCs), the mesenchymal population that comprises to the developing facial prominences, influence the development of the brain. We utilized the conditional ciliary mutant, *Wnt1-Cre;Kif3a<sup>fl/fl</sup>*, to demonstrate that loss of primary cilia on NCCs resulted in a widened ventral forebrain. We found that neuroectodermal *Shh* expression, dorsal/ventral patterning, and amount of proliferation in the ventral neuroectoderm was not changed in *Wnt1-Cre;Kif3a<sup>fl/fl</sup>* mutants; however, tissue polarity and directional cell division were disrupted. Furthermore, NCCs of *Wnt1-Cre;Kif3a<sup>fl/fl</sup>* mutants failed to respond to a SHH signal emanating from the ventral forebrain. We were able to recapitulate the ventral forebrain phenotype by removing Smoothed from NCCs (*Wnt1-Cre;Smo<sup>fl/fl</sup>*) indicating that changes in the ventral forebrain were mediated through a Hedgehog-dependent mechanism. Together, these data suggest a novel, cilia-dependent mechanism for NCCs during forebrain development.

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