compensate for the lack of p57. Since we did not detect any change in cyclin E mRNA level, increased cyclin/CDK activity might account for the increased cell proliferation. To characterize effects on cortex structure, we performed stereological analysis at E18.5 and found a 15% increase in total volume and 26% increase in total cells. While no change in cell density was observed, the depth of layers I and VI was increased (39% and 19%, respectively). Furthermore, using the layer VI specific marker Tbr1, we found a 40% increase in the mutants at E18.5 and a 2-fold increase in protein by western blotting. Our observations suggest that p57 is a critical regulator of cortical precursor proliferation, and may be determinant of laminar-specific cell production during cortical neurogenesis.

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[P2.40]

A requirement for the forkhead protein foxp1 and hox proteins in the columnar organization of spinal motor neurons

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Keywords: Motor neuron; Neuronal fate; Transcription factors; Axon guidance

In the spinal cord, functionally diverse motor neurons arise from a common progenitor domain. This process is mediated by the emergence of a "code" of LIM-homeodomain (LIM-HD) transcription factor expression that serves to organize motor neurons into longitudinal columns along the body axis and direct their innervation of different muscle targets. However, the mechanism by which the LIM-HD code is established in developing motor neurons has remained poorly understood. Here, we show that the Forkhead domain protein Foxp1 plays a critical role in the specification of the motor neuron classes that innervate the limbs and sympathetic ganglia. Using genetic manipulations, we demonstrate that Foxp1 function is both necessary and sufficient to alter the pattern of LIM-HD protein expression, and reorganize motor axon projections, their connectivity with peripheral targets, and the establishment of motor pools. These changes in motor neuron development occur in accordance with the underlying rostrocaudal pattern provided by Hox proteins along the length of the spinal cord. Together, these findings provide evidence that the diversity of motor neuron subtypes at each axial level is shaped by the coordinated actions of Foxp1 and Hox proteins.

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[P2.41]

Direct and indirect consequences of Fgf receptor 2 loss of function for cortical development

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Keywords: Fgf; Medial prefrontal cortex; Pyramidal neurons; Inhibitory interneurons

Introduction: Fgf ligands are critical for progenitor cell proliferation and differentiation during forebrain development. The receptors and signalling systems mediating their actions *in vivo* are not well understood. Fgf receptor 2 (Fgfr2) is expressed by embryonic neuronal progenitors, including radial-glial cells, and in astroglial cells throughout the adult brain. This is the first study to describe the adult phenotype of knock-out mice lacking Fgfr2 in radial-glial cells and their progeny and addresses innovative hypotheses about the role of Fgfr2 in cortical development.

Methods: Cerebral cortical morphometric analyses, including stereological assessment of various excitatory and inhibitory neuronal subtypes, were performed in mice with conditional null mutation of Fgfr2 restricted to telencephalic radial–glial cells ($Fgfr2KO^{GFAPCre}$).

Results: Compared to wild type mice, $Fgfr2KO^{GFAPCre}$ mice had reduced cortical volume and neuron number, as well as markedly decreased sub-cortical white matter. Excitatory pyramidal neurons and inhibitory cortical neurons, particularly those expressing parvalbumin but not calretinin, were significantly decreased in the cerebral cortex of mutant mice. Excitatory pyramidal neurons were disproportionately decreased in the medial prefrontal cortex and other frontal/midline regions. $Fgfr2KO^{GFAPCre}$ mice had fewer and smaller glutamate synapses in the dorsal bed nuclei of the stria terminalis, a projection area for neurons in medial prefrontal cortex. These sub-cortical projection areas also showed decreased density of inhibitory neurons expressing calretinin.

Discussion: Our studies demonstrate that Fgfr2 signalling in cortical precursor cells during the last week of embryonic mouse development is critical for production of cortical excitatory neurons from these cells, particularly in medial prefrontal regions. Losses of excitatory cell projections from frontal/midline regions may secondarily determine inhibitory deficits in sub-cortical components of the limbic system.

Conclusion: The normal development of the cerebral cortex and its connections within limbic circuits, arising from midline regions, are dependant on FgfR2 signalling through radial-glial cells and their progenitors.

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[P2.42]

In situ visualization of GnRH-1 neuronal migration in mouse nasal explants: Perturbation by GABA

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Keywords: GnRH-1 neuron; Migration; GABA; Time-lapse microscopy

Reproduction in vertebrates requires migration of GnRH-1 neurons from nasal regions into the brain during prenatal development. Although much is known about these neurons, our understanding of mechanisms controlling their movement is still limited. In the present work, GnRH-1 neuronal migration was analyzed *in situ* in embryonic mouse nasal explants from 3 to 6 div using time-lapse microscopy. Live views show that GnRH-1 neurons exhibited saltatory movement during migration and had a neuronal speed of ~13 μm/h. However, as a population, the fastest movement was consistently recorded at 4 div [mean rate = 18 μm/h]. Midline cues are known to influence migratory cells. Removal of the midline cartilage in nasal explants significantly reduced GnRH-1 cell movement. Chemokines such as SDF-1, known to be present in this region, will be re-introduced and changes in GnRH-1 cell movement evaluated. Among molecules involved in migration, GABA has been shown to modulate GnRH-1 neuronal development and be present in