Early Events of Neocortical Histogenesis: Proliferation and Differentiation of Neural Progenitor Cells

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The process of neuron production through proliferation/differentiation of neural stem/progenitor cells (NSPCs) and its contribution to the laminar formation of the neocortex will be reviewed.

Main topic of this lecture is “the decision-making characteristics of NSPCs”, that is, either to remain in the proliferative population or to exit the cell cycle and regulatory mechanisms that govern those behaviors.

1) Neocortical neuron number is precisely controlled by cell cycle exit probability (Q) of NSPCs.
2) A subtle change in Q leads to a significant modulation in the neuron number and the brain size.

The total number of neurons to be produced during neocortical neuronogenesis will ultimately determine the size of the brain and layer architecture of the neocortex, and hence define the higher cortical function of human being. In such a context, as an example of application of stem cell biology to child neurology, a mouse model of “*In utero* exposure to valproic acid” will be presented. The model shows that the antiepileptic drug valproic acid, also known as a histone deacetylase inhibitor, induces neocortical dysgenesis by Q alteration due to a nonspecific increase of G1-phase regulatory proteins; this illustrates the mechanisms of higher cortical function deficits reported in children prenatally exposed to this drug.