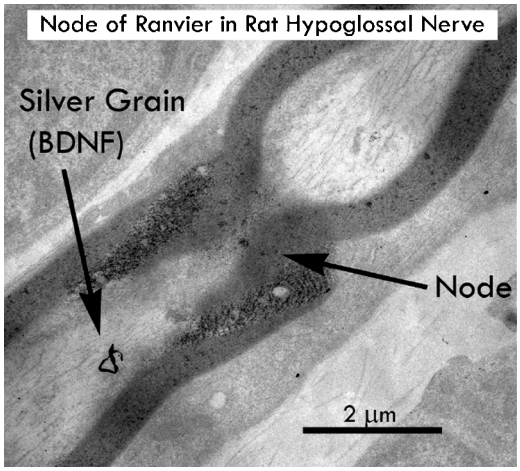

Fig. 1. Node of Ranvier in rat hypoglossal nerve.

conditions such as cooling and/or delayed fixation can increase MVBs in axons. Indeed, the number and area of MVBs in the axon shaft was significantly increased by such conditions. We conclude that abnormal cargoes and/or manipulations of axons stimulate de-novo formation of MVBs as an artifact or secondary response to dystrophic conditions, abnormal slowing of transport, and aggregation of vesicles that does not occur during normal conditions in vivo.

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[P2.12]

Early valproic acid exposure impairs orientation selectivity in ferret visual cortex columns

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Keywords: Valproic acid; Visual cortex columns; Ferret

Epilepsy is one of the most common neurologic disorders affecting 0.5–1% of pregnant women. The use of antiepileptic drugs, which usually must be continued throughout the pregnancy, can cause in offspring mild to severe sensory deficits. While the mechanisms by which prenatal anticonvulsants exposure disrupts sensory processing are poorly understood, there is growing evidence that this disruption result from abnormalities of neuronal plasticity. In general, the formation of sensory cortical maps in composed by an initial phase when the basic structure of the map is formed followed by a subsequent phase when the map is refined by process that requires activity-dependent neuronal plasticity. An alteration on this process might result in poorly defined sensory maps. Here we investigate the effects of valproic acid (VPA), a commonly used antiepileptic, on the maturation of orientation selectivity columns. Ferrets pups were exposed to VPA (200 mg/kg), every other day, starting at postnatal day (P) 10, when the functional properties and connectivity of neocortical neurons start to develop. VPA exposure ended at P30, just before eye opening at P32. Control animals received i.p. injection of saline during the same period. Following a prolonged VPA-free period (15–35 days), long-term effects of early VPA exposure on cortical orientation selectivity were examined at P48–P65, when orientation selectivity in normal ferret cortex has reached a mature state. Optical imaging of intrinsic signals revealed decreased contrast of orientation maps in VPA—but not saline-treated animals. Moreover, early VPA treatment weakened neuronal orientation selectivity preserved robust visual responses. These findings indicate that VPA exposure during a brief period of development disrupts cortical processing of sensory information at a later age and suggest a neurobiological substrate for some types of sensory deficits in fetal anticonvulsant syndrome.

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[P2.13]

Early monocular deprivation causes later deficit in visual signal-in-noise discrimination

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Keywords: Visual development; Experience-dependent development

Binocular visual experience is necessary for the normal fine-tuning of neural circuits in the visual cortex and the emergence of optimal signal-to-noise processing. Previous studies have suggested that the loss of visual acuity and contrast sensitivity after early monocular deprivation are a result of increased neural noise in the visual cortex. Here, our purpose is to determine the long-term effect of early monocular deprivation on neural signal-to-noise. We reared cats with either normal vision or a short period (2 weeks) of monocular deprivation early in the critical period. We then compared the developmental trajectory and mature visual thresholds for discriminating a high contrast orientation-in-noise grating. The ability to discriminate the orientation-in-noise stimulus improved gradually and reached adult levels at about 4 months of age. The short period of monocular deprivation did not alter the developmental trajectory, however, it did lead to slightly poorer adult performance. Compared to normal cats, the deprived eye required 10-15% more orientation signal to discriminate the target from noise. Surprisingly, even the non-deprived eye was affected, requiring 5-10% more orientation signal at threshold. When tested binocularly, performance was limited by the better eye. These findings reveal a prolonged developmental time course for the maturation of visual signal-in-noise processing. Furthermore, the deficit in the deprived eye is not apparent until many weeks after the end of monocular deprivation. It remains unclear what changes in the central visual pathway are caused by the short period of deprivation that do not result in a visual deficit until much later.

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[P2.14]

ADP-ribosylation-like factor-6 interacting protein is required for neural crest development in zebrafish embryos

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Keywords: Arl6ip; Neural crest; Danio rerio; Development

ADP-ribosylation-like factor-6 interacting protein (Arl6ip) is an interacting protein of Arl6 which is one of the small ADP ribosylation factor GTP-binding proteins that are major regulators

in intracellular traffic. Although the *in vitro* function of *arl6ip* gene is suggested as protein transport, membrane trafficking, or cell signaling during hematopoietic maturation, the *in vivo* roles that *alr6ip* plays during embryonic development are totally unknown. Here, we demonstrated that when Arl6ip was lost by injecting the zebrafish embryos an antisense morpholino oligonucleotides (MO) which inhibited *arl6ip* mRNA translation specifically, the neural crest derivatives, such as cartilage, cranial ganglia, peripheral neurons, and heart, were defective. The expressions of neural plate border specifiers, *msxb*, *dlx3b*, and *tfap2a*, were normal, but the expression of neural crest specification genes, *foxd3*, *snail1b* and *sox10* were reduced, implicating *arl6ip* is essential for neural crest specification. In addition, apoptosis was apparent occurrence in the premigratory neural crest cells, indicating a critical role for *arl6ip* in the survival of neural crest cells. Furthermore, *crestin* and *sox10*, which were expressed in the cranial and trunk migrating neural crest cells, were also decreased, suggesting that *arl6ip* is not only required for neural crest migration. Interestingly, we noticed that the hearts of the *arl6ip*-MO-injected embryos were failure to undergo normal looping and the function of heart was depressed. This defective heart may result from the loss of cardiac premigratory neural crest cells. Taken together, we conclude that *arl6ip* is required for neural crest specification, survival, and migration. This is the first report that demonstrates the *in vivo* function of *arl6ip* during neural crest development.

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[P2.15]

Oscillations in notch signaling regulate maintenance of neural progenitors

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Keywords: Neural progenitor; Notch signaling; Oscillatory expression; Hes1

Expression of the Notch effector gene *Hes1* is required for maintenance of neural progenitors in the embryonic brain, but persistent and high levels of *Hes1* expression inhibit proliferation and differentiation of these cells. Here, by using a real-time imaging method, we found that *Hes1* expression dynamically oscillates in neural progenitors. Furthermore, sustained over-expression of *Hes1* down-regulates expression of proneural genes, Notch ligands and cell cycle regulators, suggesting that their proper expression depends on *Hes1* oscillation. Surprisingly, the proneural gene *Neurogenin2* (*Ngn2*) and the Notch ligand *Delta-like1* (*Dll1*) are also expressed in an oscillatory manner by neural progenitors, and inhibition of Notch signaling, a condition known to induce neuronal differentiation, leads to down-regulation of *Hes1* and sustained up-regulation of *Ngn2* and *Dll1*. These results suggest that *Hes1* oscillation regulates *Ngn2* and *Dll1* oscillations, which in turn lead to maintenance of neural progenitors by mutual activation of Notch signaling. Our data also suggest that oscillatory expression of *Ngn2* is not sufficient for but sustained up-regulation is required for neuronal differentiation and that *Ngn2* oscillation is advantageous for activation of Notch signaling by inducing *Dll1* expression without promoting neuronal differentiation.

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[P2.16]

Requirement of continuous neurogenesis for the structural and functional integrity of the adult brain

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Keywords: Adult neurogenesis; Olfactory bulb; Dentate gyrus; Nes-CreERT2 mice

Neurogenesis occurs continuously in the forebrain of the adult mammals, but the structural and functional significance of adult neurogenesis is still unclear. We generated transgenic mice that express $CreER^{T2}$ in the germinal zone of the adult brain under the control of the nestin promoter and enhancer. In the presence of Tamoxifen, Cre-mediated recombination occurred efficiently in adult neural progenitor cells at the subventricular zone of the lateral ventricle and the subgranular zone of the dentate gyrus. Crossing with Rosa26-reporter lines, we estimated the rate of neuronal addition in the granule cell layers of the olfactory bulb and the dentate gyrus. We show that in adult mice, continuous neurogenesis results, within 12 months, in replacement of the majority of granule neurons in the olfactory bulb and significant addition of granule neurons to the dentate gyrus. To investigate the functional impact of adult neurogenesis, newly generated neurons and neuroblasts were genetically ablated by crossing with NSE-DTA mice. Strikingly, ablation of newly formed neurons in adult mice lead to the gradual decrease of the granule cell number in the olfactory bulb, inhibits increases in the number of neurons in the dentate gyrus, and impairs behaviors in contextual and spatial memory tests. These results suggest that continuous neurogenesis is required for maintenance and reorganization of the whole system in the olfactory bulb, modulation and refinement of the existing neuronal circuits in the dentate gyrus, and normal behaviors involved in some kinds of hippocampal-dependent memory.

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[P2.17]

Olig2 function in adult neural stem and progenitor cells

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Keywords: Olig; Neural stem cell; Neural progenitor

The bHLH transcription factor Olig2 is known to play critical roles during central nervous system development. Olig2 is thought to maintain neural progenitors in a replication-competent state, and is required for the specification of oligodendrocytes and subtypes of neurons. Compared to the embryo, little is known about Olig2 function in adult neural progenitors. In the subventricular zone (SVZ), which constitutes the main site of production of new neurons and oligodendrocytes in the adult brain, Olig2 is expressed in a subset of stem and progenitors cells. However, it is not clear what the role of Olig2 in these two progenitor compartments is, and whether Olig2 functions to specify oligodendrocyte vs. neuronal fate in the SVZ. To address these questions, we are using a knock-in mouse line in which TVA, the receptor for the avian retrovirus RCAS, is inserted into Olig2 locus. This RCAS-TVA system allows us to specifically target Olig2+ progenitors to follow the progeny of Olig2+ cells and to perform functional experiments.

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