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Development of the whisker-to-barrel cortex system

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This review provides an overview on the development of the rodent whisker-to-barrel cortex system from late embryonic stage to the end of the first postnatal month. During this period the system shows a remarkable transition from a mostly genetic-molecular driven generation of crude connectivity, providing the template for activity-dependent structural and functional maturation and plasticity, to the manifestation of a complex behavioral repertoire including social interactions. Spontaneous and sensory-evoked activity is present in neonatal barrel cortex and control the generation of the cortical architecture. Half a century after its first description by Woolsey and van der Loos the whisker-to-barrel cortex system with its unique and clear topographic organization still offers the exceptional opportunity to study sensory processing and complex behavior.

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Introduction

In the auditory, visual and somatosensory system neuronal processing of sensory information from the periphery to the cerebral cortex reveals a topographic organization. The somatosensory system of rodents is organized in a patterned representation of the whiskers on the animal's snout: so-called 'barrels' in layer (L) 4 of the primary somatosensory cortex (S1), 'barreloids' in the ventroposteromedial nucleus of the thalamus (VPM) and 'barrelettes' in the brainstem principal trigeminal nucleus (PrV), which receives via trigeminal ganglion (TG) neurons the topographic inputs from the whiskers [1]. Over the last 50 years this whisker-to-barrel cortex system was intensively studied in rodents and we gained a lot of knowledge on the function, plasticity and development of this system. This review aims to provide a comprehensive overview on the early development of the rodent barrel cortex from the cellular to the behavioral level (Figure 1).

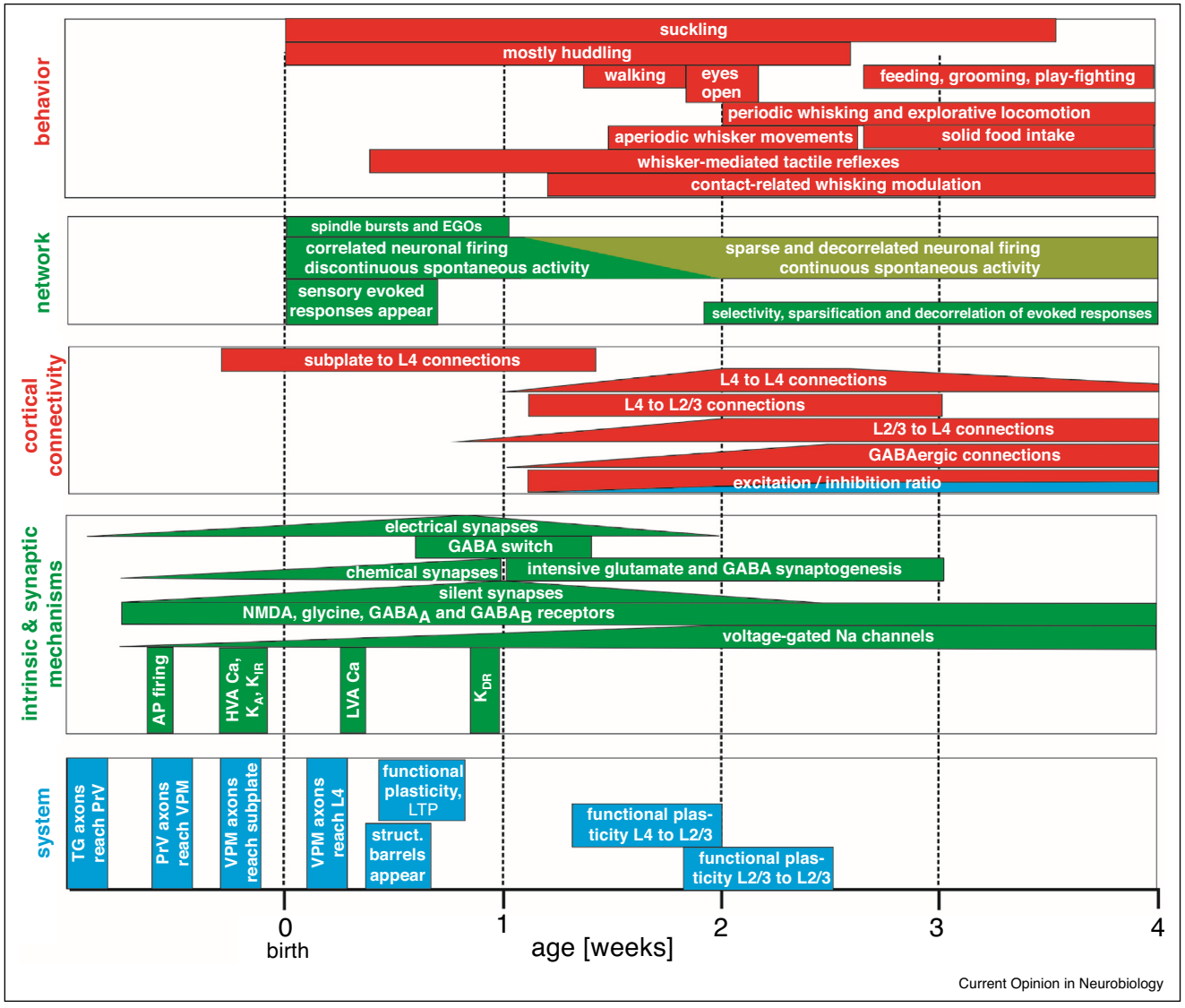
Somatosensory system: from sensory periphery to cortex

Functional maturation and topographic pattern formation shows a developmental sequence from peripheral to central somatosensory structures [2,3]. If not otherwise noted, the following embryonic and postnatal time points refer to the mouse. TG axons reach the PrV at approximately embryonic day (E) 10, ~2 days before they innervate the whisker follicles, and barrelettes appear shortly after birth. In adult rats, two distinct groups of TG neurons have been identified, which form the basis of two psychophysical channels of whisker deflection [4]. PrV axons reach the VPM at ~E17 and barreloids appear at approximately postnatal day (P) 3. At ~E13.5 thalamocortical afferents pass through a permissive corridor of guidance molecules, reach the subplate at ~E18 and innervate L4 shortly after birth [5,6]. Already at this stage, the thalamic input to the subplate shows relatively mature synaptic properties and the subplate serves as an active and important structure to regulate early cortical development [7]. A functional topographic whisker representation can be demonstrated in rat barrel cortex already at birth [8], although structural barrels become visible in L4 at ~P4 when also structural plasticity ends. The peak for functional plasticity (long-term potentiation [LTP]) in rat barrel cortex *in vivo* is at P3–P5 [9]. Functional plasticity at the L4 to L2/3 synapse is maximal at P10–P14 and for intralaminar connections in L2/3 at P13–P16. The cortico-cortical and long-range connectivity of barrel cortex has been studied with voltage-sensitive dye imaging, anatomical tracers and viral vectors mostly in adult rodents [10] and remains to be analyzed in more detail in developing animals.

Intrinsic and synaptic mechanisms

Excitability of cortical neurons is required for their migration and maturation [11•]. Pyramidal neurons are capable to generate action potentials (APs) as early as at E16 and the density of voltage-gated Na^+ channels increases 10-fold during the first two postnatal weeks. A-type (K_A) and inward rectifier (K_{IR}) voltage-gated K^+ channels (K_v) are functional at E19, while delayed rectifier K_v (K_{DR}) become functional after P7. Consequently, AP duration decreases and the resting membrane potential (RMP)

Figure 1



Summary diagram on the development of the rodent whisker-to-barrel cortex system from late embryonic stage to the end of the first postnatal month.

becomes more negative. Functional high-threshold Ca^{2+} channels (Ca_v) are present at E19 (the earliest time investigated), while low-threshold Ca_v are expressed after P3 [12]. Ligand-gated receptors are functional well before the appearance of chemical synapses. Migrating neurons express NMDA receptors, which are activated by ambient glutamate [13]. Glycine receptors are expressed already at P0 and tonically activated by non-synaptically released glycine and/or taurine [13,14•]. $GABA_A$ receptors are functional at E16. Both subunits of $GABA_B$ receptor ($GABA_BR1$ and $GABA_BR2$) are expressed at E15 [15].

Although the first chemical synaptic structures in the primordial plexiform layer are detected at ~E14, perinatally synaptic communication is predominantly mediated by gap junctions and glutamatergic synapses are generally silent [16,17]. The number of both gap junctions and silent synapses decreases during the first two postnatal weeks [18•,19]. The density of chemical synapses dramatically increases from the second postnatal week on [20]. Important hallmark of the second postnatal week is the switch from GABAergic depolarization to hyperpolarization mediated by developmental changes in expression of the chloride transporters NKCC1 and KCC2 [21]. During the second and third postnatal week synaptic activity increases about 10-fold to almost mature level. Functional maturation of synaptic connections coincides with microanatomical changes at synaptic