Front. Biol. 2016, 11(6): 459–470
DOI 10.1007/s11515-016-1427-x

REVIEW

Neuronal activity controls the development of interneurons in the somatosensory cortex

Rachel Babij[1,2], Natalia De Marco Garcia (✉)[1]

[1] *Center for Neurogenetics, Brain and Mind Research Institute, Weill Cornell Medical College, New York, NY 10065, USA*
[2] *Weill Cornell/Rockefeller/Sloan Kettering Tri-Institutional MD-PhD Program, New York, USA*

BACKGROUND: Neuronal activity in cortical areas regulates neurodevelopment by interacting with defined genetic programs to shape the mature central nervous system. Electrical activity is conveyed to sensory cortical areas via intracortical and thalamocortical neurons, and includes oscillatory patterns that have been measured across cortical regions.
OBJECTIVE: In this work, we review the most recent findings about how electrical activity shapes the developmental assembly of functional circuitry in the somatosensory cortex, with an emphasis on interneuron maturation and integration. We include studies on the effect of various neurotransmitters and on the influence of thalamocortical afferent activity on circuit development. We additionally reviewed studies describing network activity patterns.
METHODS: We conducted an extensive literature search using both the PubMed and Google Scholar search engines. The following keywords were used in various iterations: "interneuron", "somatosensory", "development", "activity", "network patterns", "thalamocortical", "NMDA receptor", "plasticity". We additionally selected papers known to us from past reading, and those recommended to us by reviewers and members of our lab.
RESULTS: We reviewed a total of 132 articles that focused on the role of activity in interneuronal migration, maturation, and circuit development, as well as the source of electrical inputs and patterns of cortical activity in the somatosensory cortex. 79 of these papers included in this timely review were written between 2007 and 2016.
CONCLUSIONS: Neuronal activity shapes the developmental assembly of functional circuitry in the somatosensory cortical interneurons. This activity impacts nearly every aspect of development and acquisition of mature neuronal characteristics, and may contribute to changing phenotypes, altered transmitter expression, and plasticity in the adult. Progressively changing oscillatory network patterns contribute to this activity in the early postnatal period, although a direct requirement for specific patterns and origins of activity remains to be demonstrated.

Keywords interneuron, neurodevelopment, neuroplasticity, thalamocortical, NMDA receptors, neuronal maturation

Introduction

Development of neocortical areas follows a defined sequence in which excitatory and inhibitory neurons, generated in the dorsal and ventral telencephalon respectively, migrate to their final locations (Fishell and Rudy, 2011). As they mature, neurons participate in nascent electrical patterns, and ultimately extend dendritic and axonal branches to form functional connections. During these periods, proper development is dependent not only on genetic patterns and progression of intrinsic programs, but also on the activity of input connections (Erzurumlu and Gaspar, 2012). In this review, we will focus on the activity-dependent processes within the mouse somatosensory cortex, highlighting some recent pertinent findings in other sensory cortices. The somatosensory cortex has been extensively studied in this context because of its well-characterized anatomy and ease of experimental manipulation (for reviews on the auditory and visual sensory systems see (White and Fitzpatrick, 2007; Sanes and Kotak, 2011; Espinosa and Stryker, 2012; Kral, 2013; Arroyo and Feller, 2016; Chaudhury et al., 2016)). Although we focused our discussion on the developmental processes occurring within the somatosensory cortex of mouse, these processes are likely mirrored throughout the neocortex. In particular, similar cell types (Wichterle et al., 1999; Wichterle et al., 2001; Zeisel et al., 2015; Tasic et al., 2016), dependence on sensory input for maturation (Siegel et al., 2012; Ji et al., 2016), and network activity (Colonnese et al., 2010; Siegel et al., 2012) have been identified throughout

Received September 4, 2016; accepted October 14, 2016
Correspondence: Natalia De Marco Garcia
E-mail: nad2018@med.cornell.edu

sensory cortices. Further, the human neocortex has been shown to display early network patterns similar to that of the mouse and rat (Milh et al., 2007), and as such, findings in this area may be extended to the understanding of human developmental neurobiology.

Somatosensory information from the periphery is relayed through the trigeminal nucleus of the brain stem and sensory nuclei of the thalamus, which conveys this information to the cortex. Topographic information from the whisker pad is represented in barrel formations of axons, dendrites, and somata in the barrel cortex (Lorente de No, 1922; Woolsey and Van der Loos, 1970; Welker, 1971; Killackey, 1973; Welker 1976). Remarkably, sensory inputs shape the formation of these barrels (van der Loos and Woolsey, 1973; Petersen, 2007). The local cortical circuitry targeted by sensory afferents includes excitatory neurons and inhibitory neurons. We will limit the scope of the review to cover the activity-dependent development of interneurons (for a review on the role of activity on excitatory neurons see (Erzurumlu and Gaspar, 2012). Although they comprise only about 20% of cortical neurons, interneurons exhibit extreme diversity and can be divided into two main groups: early-born neurons arising from the medial ganglionic eminence (MGE), and later-born neurons from the caudal ganglionic eminence (CGE) (Van Eden et al., 1989; DeDiego et al., 1994; Butt et al., 2005). In addition, these groups can be further subdivided into at least 15 subtypes by biochemical markers and electrophysiological properties (Miyoshi et al., 2007; Ascoli et al., 2008; Miyoshi et al., 2010; Rudy et al., 2011). The emergence of subtype-specific features is controlled by intrinsic genetic programs as well as activity-dependent mechanisms (Kepecs and Fishell, 2014). Upon being generated ventrally, cortical interneurons undergo prolonged migration into the cortex, which is already populated with pyramidal neurons and other early-born neuronal types (Sultan et al., 2013). Furthermore, the development of these neurons continues into the first postnatal month (Okaty et al., 2009). This extended maturation renders interneurons particularly susceptible to the early influence of environmental factors such as electrical activity.

Activity-dependent neuronal migration

Activity, including calcium transients and neurotransmitter signaling, plays a role in neuronal migration (Uhlén et al., 2015). In addition to its role in modulation of the migration of glutamatergic neurons (Behar et al., 1999; Behar et al., 2000; Kihara et al., 2002; Heck et al., 2007; Liu et al., 2008; Liu et al., 2010; Bony et al., 2013; Luhmann et al., 2015; Bando et al., 2016), neuronal activity regulates gamma aminobutyric acid (GABA)-ergic interneuron migration in the cortex. In this section, we will discuss evidence for the role of activity in interneuron migration, as well as the specific roles that GABA and other neurotransmitters may play in this process.

In CGE-derived interneurons, a cell-autonomous decrease in excitability leads to aberrant interneuron allocation into deep cortical layers (De Marco Garcia et al., 2011). Similarly, the migration of MGE-derived interneurons (Close et al., 2012; Denaxa et al., 2012) relies on the expression of the activity-dependent gene special AT-rich binding protein 1 (*Satb1*). This gene was initially identified in a microarray-based screen as a target of the homeobox transcription factor Lhx6 (Liodis et al., 2007), which is fundamental for the normal migration and specification of cortical interneuron subtypes. *Satb1* expression has been further characterized in developing interneurons (Batista-Brito et al., 2008). Consistent with the role of these transcriptional cassettes in migration, interneuron-specific deletion of *Satb1* causes abnormal laminar distribution of SST-expressing interneurons. Altogether these results indicate that neuronal excitability is required for the induction of activity-dependent programs, which enable the migration of cortical interneurons.

In vitro experimental evidence indicates that GABA modulates interneuron migration (Soria and Valdeolmillos, 2002; Bortone and Polleux, 2009; de Lima et al., 2009). Pharmacological treatment of cortical slices with GABA-A receptor antagonists decreases the percent of interneurons tangentially migrating into the cortex whereas GABA-A receptor agonists have the opposite effect (Cuzon et al., 2006; Cuzon Carlson and Yeh, 2011; Kilb et al., 2013). Further, *in vivo* experiments reveal that blockade of GABA-A receptor, blockade of sodium-potassium-chloride co-transporter (NKCC1), and chelation of intracellular calcium all significantly reduce the tangential motility rate, while diazepam increases motility (Inada et al., 2011). In addition to its role in tangential migration, GABA both stimulates motion, and acts as a stop signal for radial migration. Although *in vitro* experiments suggest that this change in responsiveness, from increasing motility to halting, results from the upregulation of potassium chloride co-transporter 2 (KCC2) (Bortone and Polleux, 2009), further *in vivo* experiments using spatiotemporally controlled elimination of this protein are necessary to demonstrate the requirement for KCC2.

Current experimental evidence indicates that glutamatergic signaling is not required for the migration of cortical CGE-derived interneurons. Genetic elimination of thalamic input as well as whisker plucking do not affect the migration of CGE-derived interneuron cell types (De Marco García et al., 2015). Furthermore, application of kynurenic acid, a blocker of both NMDA- and AMPA-mediated signaling, resulted in no migratory defects of CGE-derived interneuron subtypes (De Marco Garcia et al., 2011). In contrast, *in vitro* experiments suggest that pharmacological blockade of ionotropic receptors in cortical slices causes aberrant MGE interneuron migration (Manent et al., 2006, Yozu et al., 2008; Bortone and Polleux, 2009). However, the lack of *in vivo* experiments in which glutamatergic inputs onto MGE-derived interneurons are genetically ablated precludes the analysis of the impact of glutamatergic signaling on the migration of MGE-derived interneurons.

In addition to GABA and glutamate, serotonin and glycine modulate interneuron migration (Luhmann et al., 2015). Interference of serotonin signaling early in development leads to alterations in migration and the laminar position of interneurons (Vitalis et al., 2007; Riccio et al., 2009; Murthy et al., 2014; Frazer et al., 2015). This manipulation selectively affects CGE-derived interneurons. In particular, serotonin acts via the 5HT3a receptor, which is selectively upregulated in these interneurons as they invade the developing cortex (Murthy et al., 2014), suggesting a role for serotonin signaling in interneuron circuit assembly (Vitalis et al., 2013). The role of serotonin in neuronal migration is further supported by the fact that increases in extracellular serotonin, in both serotonin transporter (SERT) knockout mice and in mice treated with SERT inhibitor fluoxetine, lead to increased migratory speed and altered laminar distribution (Frazer et al., 2015). Furthermore, these manipulations also alter the expression-level of a host of genes, including some involved in neuronal migration (Frazer et al., 2015). Altogether, these findings have potential clinical relevance, as selective-serotonin reuptake inhibitors (SSRIs) are currently used for the treatment of neuropsychiatric disorders in pregnant women, and may affect the migration, or more generally the genetic programs, of fetal developing cortical interneurons. In addition to the impact of GABA and serotonin on interneuron migration, genetic disruption of the alpha-2 subunit of the glycine receptor causes migratory defects (Avila et al., 2013). In brief, interneuron migration is modulated by signaling from a diversity of neurotransmitter receptors whose relative contribution changes dynamically throughout development.

Activity-dependent maturation of cortical interneurons

Once interneurons reach their target laminae in the cortex, they begin to acquire mature properties including characteristic morphologies, intrinsic electrophysiological properties, and molecular features, such as the expression of neuropeptides and calcium binding proteins (De Marco García et al., 2011; Miyoshi and Fishell, 2011; Karayannis et al., 2012). Subsequently, interneurons influenced by environmental cues form contacts with defined synaptic partners (Batista-Brito and Fishell, 2009; Chu and Anderson, 2015). In this section, we will discuss the role of neuronal activity in interneuron maturation.

Both MGE- (Close et al., 2012; Denaxa et al., 2012) and CGE-derived (De Marco García et al., 2011) interneuron cell types undergo activity-dependent differentiation. In a subtype of MGE-derived interneurons, the somatostatin-positive (SST) neurons, *Satb1* is necessary for synaptic integration and survival, as well as its previously discussed role in migration (Close et al., 2012, Denaxa et al., 2012). In addition, neuronal excitability is required after postnatal day 3 (P3) for the morphological development of both reelin (Re) and calretinin (Cr)-expressing interneurons (De Marco García et al., 2011). In these experiments, hyperpolarization induced after expression of an inward rectifying potassium channel, which leads to attenuation of neuronal excitability, caused defects in the maturation of neuronal processes (De Marco García et al., 2011). Mechanistically, a reduction in neuronal excitability may impair the activation of NR2B-containing N-methyl-D-aspartate receptors (NMDARs) (see next section).

In addition to its contribution to the maturation of neuronal processes, neuronal activity influences emerging synaptic formation. A complete blockade of GABA signaling results in over proliferation of small synapses and overgrowth of axons, demonstrating a role for GABA in the pruning of synapses during a critical period of synaptic remodeling (Wu et al., 2012). Similarly, a suppression of neurotransmitter release in single basket cells induces the formation of denser arbors and increases the number of smaller-sized boutons, without a change in the number of innervated somata (Baho and Di Cristo, 2012). In contrast, GABA signaling via the GABA-A receptor and voltage gated calcium channels induces the formation of inhibitory synapses in layer II/III pyramidal cells during early development (Oh et al., 2016). Thus, the role of GABA in circuit maturation is context dependent.

In sum, rather than being exclusively controlled by intrinsic genetic programs, interneuron differentiation and survival are under the strong influence of activity-dependent programs. However, it remains unclear whether a certain threshold of excitability or certain sources of inputs trigger activity-dependent development.

Thalamic inputs and the maturation of cortical microcircuits

After region-specific genetic programs pattern the cortex into basic functional subdivisions (Miyashita-Lin et al., 1999), sensory inputs shape its connectivity and structure (Sur and Leamey, 2001). Here we will discuss the specialization of sensory inputs, as well as the interaction between these inputs and circuit formation in the mouse neocortex (for a review of thalamocortical connectivity in the adult somatosensory cortex, see (Feldmeyer, 2012) and (Feldmeyer et al., 2013)). In addition, we summarize the evidence implicating the importance of N-methyl-D-aspartate (NMDA)-receptors as important in shaping this circuit.

Thalamocortical (TC) axons have distinct arborization patterns within the lamina of the somatosensory cortex depending on their anatomical origin. The main input from the ventroposteriormedial nucleus (VPM) to the somatosensory cortex is to layer IV with some axonal ramifications targeting layer VI. In contrast, projections from the rostral posterior nucleus (PO) target layers I and Va (Feldmeyer, 2012). Therefore, somatic or dendritic location within cortical layers may be the sole determinant for TC innervation. Alternatively, input may be further restricted according to cell type identity within layers. In support of this notion, fast-spiking interneurons and excitatory cells receive TC input

(Agmon and Connors, 1992; Agmon and O'Dowd, 1992; Sun et al., 2006; Cruikshank et al., 2010), which evokes robust responses in both of these cell types in layer IV. In contrast, only weak responses are detected in SST interneurons within the same layer (Cruikshank et al., 2010). Further, evoked action potentials can be recorded from 60% of inhibitory neurons, but less than 5% of excitatory neurons in layer IV and V (Porter et al., 2001). The wiring of other sensory cortices also seems to support the concept that TC connectivity within cortical layers is cell type-restricted. Electrophysiological recordings in the auditory and visual cortices show that PV interneurons and excitatory cells throughout cortical layers are innervated by thalamic axons. However, only a fraction of SST and vasoactive intestinal peptide-expressing (VIP) interneurons in layer IV, and none of the SST and VIP cells elsewhere, receive thalamic innervation (Ji et al., 2016). Taken together, this data supports the idea that TC connectivity may be specified by a combination of cell-type identity and laminar allocation. Importantly, these experiments were performed in adult animals, and as a result, it remains unclear whether similar patterns are present during development and whether dedicated molecular mechanisms restrict TC innervation to select cell types.

Increasing experimental evidence indicates that maturing sensory cortices possesses certain circuits in place at birth that exist only transiently to give way to adult circuitry (Luhmann et al., 2003; Luhmann et al., 2014). Subplate neurons, a cohort of early born neurons that become dramatically reduced in number after the first postnatal week, are the initial recipients of TC axons and are fundamental in promoting synaptic scaling as well as the maturation of TC connections onto cortical excitatory cells (Molnár et al., 1998; Hanganu et al., 2002; Kanold, 2004; Higashi et al., 2005). The importance of this transient population is highlighted in ablation experiments that result in absence of anatomical segregation of thalamic inputs and weakened TC synaptic transmission in adult (Kanold et al., 2003). Another example of transient circuitry involves SST interneurons. In the first postnatal week, these neurons receive transient TC innervation and project from infra-granular layers to layer IV, a pattern of connectivity that is necessary for proper circuit assembly within the recipient layer (Anastasiades et al., 2016; Marques-Smith et al., 2016; Tuncdemir et al., 2016). The progressive elimination of TC innervation to infra-granular SST interneurons (Anastasiades et al., 2016; Tuncdemir et al., 2016) is in agreement with the observation that infra-granular SST interneurons are unresponsive to TC stimulation in adult (Ji et al., 2016).

Although the mechanism that regulates the disappearance of transient circuitry is currently unknown, neurotransmitter receptors are attractive candidates. NMDARs are present in TC synapses at early stages of development (LoTurco et al., 1991; Iwasato et al., 2000; Laaris et al., 2000). These receptors contain one obligatory NR1 subunit and two NR2 subunits, of which there are at least 4 isoforms (Paoletti et al., 2013). NMDAR signaling to excitatory cells greatly affects the formation of barrel columns. After perturbation of this signaling pathway, TC axonal projections are more diffuse and the somata and dendritic orientation of excitatory cells within barrels does not develop (Iwasato et al., 2000; Lee et al., 2005; Reiprich et al., 2005; Espinosa et al., 2009; Mizuno et al., 2014). Furthermore, elimination of TC glutamatergic inputs results in changes in cortical lamination (Reiprich et al., 2005; Narboux-Nême et al., 2012; Li et al., 2013).

Given that NMDARs are one of the most highly regulated postsynaptic receptors during development, their dynamic expression, activation, or change in subunit composition could influence the developmental changes in TC signaling. A developmental decrease in the relative amount of NR2B-containing receptors compared with NR2A-containing receptors has been long appreciated. Specifically, there is a progressive increase in the contribution of NR2A-containing receptors, which parallels the increase in synaptic activity between P2 and P15 (Crair and Malenka, 1995; Flint et al., 1997; Liu et al., 2004; Zhang and Sun 2011; Paoletti et al., 2013). Both MGE- and CGE-derived hippocampal interneurons possess high ratios of NR2B-containing NMDARs at birth. Whereas MGE-derived interneurons undergo the NR2B-to-NR2A developmental switch in subunit composition, CGE-derived interneurons retain high levels of the NR2B-containing receptors into adulthood, when compared with NR2A (Matta et al., 2013). Taken together, these experiments suggest that cell type specific differences in NMDAR composition may be an important regulatory mechanism for circuit maturation.

Direct TC innervation to cortical interneurons is important for the development of somatosensory circuitry. Whisker trimming during the second postnatal week leads to a reduction in PV expression and a decrease in inhibitory currents onto spiny stellate cells (Jiao et al., 2006). Furthermore, sensory inputs influence interneuron development at even earlier stages of maturation. Direct TC inputs are required for the axonal and dendritic development of CGE-derived Re-expressing interneurons during the first postnatal week (De Marco García et al., 2015). Mechanistically, NR2B-containing NMDARs, which are enriched in TC synapses onto Re-expressing interneurons, regulate the maturation of cell morphology (De Marco García et al., 2015). In addition, SST interneurons, which receive transient thalamic innervation, are necessary for the establishment of mature TC inputs to pyramidal and PV interneurons in deep cortical layers (Tuncdemir et al., 2016). However, whether the role of SST interneurons in circuit development can be attributed to the presence of transient TC connectivity remains to be determined. Given existing data on the complexity and specialization of long- and short-range connections, and the presence of a clear critical period of plasticity (Daw et al., 2007), it is tempting to hypothesize that transient connectivity and integration of inputs onto specific neuronal subtypes regulates the maturation of cortical circuitry.

The emergence of early network patterns

Neurons exhibit changing patterns of electrical activity throughout development. This activity is asynchronous at early embryonic stages (Allène et al., 2008), but becomes synchronized around birth (McCabe et al., 2006; Allène et al., 2008; Golshani et al., 2009; Allene and Cossart, 2010). The synchronous patterns of activity, which parallel neurodevelopmental maturation of physiological and morphological properties (Allene and Cossart 2010), are conserved in humans (Milh et al., 2007; Tolonen et al., 2007; Koolen et al., 2016). Though much work has been performed to describe these patterns, it is currently unknown whether they play an instructive role in the development of the somatosensory cortex. Complicating the analysis of activity patterns, the spatiotemporal characteristics of these oscillations vary depending on the methodology used to record them (Allene and Cossart, 2010). In this section, we focus on reconciling the oscillatory patterns as seen in different experimental conditions, first discussing *in vitro* studies, and then examining data from two types of *in vivo* experiments – field recordings and calcium imaging. We then review possible pacemakers of oscillatory activity.

Three main types of activity have been recorded *in vitro* in cortical slices: synchronous plateau assemblies (SPAs), cortical early network oscillations (cENOs), and cortical giant depolarizing potentials (cGDPs). The earliest postnatal forms of correlated activity recorded in rat cortical slices are SPAs, which rely on gap junction coupling to activate small groups of neurons (Allène et al., 2008; Allene and Cossart, 2010). Studies have revealed that SPAs occur primarily between P0 and P3 and co-exist with cENOs (Corlew et al., 2004; Allène et al., 2008). Unlike SPAs, cENOs are tetrodotoxin (TTX)-sensitive (Rheims et al., 2008) and require NMDAR activity (Garaschuk et al., 2000; Allène et al., 2008). These oscillations occur at low frequency (~0.01 Hz), involve large cortical areas (Allène et al., 2008), and are observed between embryonic day 17 (E17) and P3 in the developing mouse (Corlew et al., 2004; McCabe et al., 2006). In contrast, cGDPs predominate in the cortex in the latter half of the first postnatal week through most of the second week. cGDPs are synaptically-driven recurrent oscillations (~0.1 Hz) that synchronize localized neuronal assemblies (Allène et al., 2008) and are dependent upon GABA (Rheims et al., 2008). In short, in *in vitro* experiments show that developing neurons follow a temporal sequence of network activity patterns, starting with gap junction-mediated SPAs and NMDA-mediated cENOs followed by GABA-A receptor mediated cGDPs.

In addition to network patterns recorded in cortical slices, oscillatory activity can be observed *in vivo* using field recordings. Synchronous activity has been described in the form of spindle bursts, gamma oscillations, and long oscillations in rat pups age P0 through P7 (Yang et al., 2009, 2016). Spindle bursts appear every 10 s for 1-2 s, exhibit a frequency of 8-25 Hz rhythmic activity (Yang et al., 2009) and are often associated with overt movement, including muscle twitches, limb/body jerks, crawling and suckling, but can occur either preceding or following movement (Khazipov et al., 2004; Milh et al., 2007; An et al., 2014). Superimposed on this activity is a 30-40 Hz gamma wave pattern, lasting 150 to 300 ms and occurring every 10 to 30 s (Khazipov and Luhmann 2006; Yang et al., 2009). In addition, 10-20 Hz long oscillations occur concurrently with the spindle bursting and gamma oscillations (Yang et al., 2009), but differ from other activity types in their long-range propagation and their sparse occurrence (Sun and Luhmann, 2007). Thus, oscillations are observed in field recordings *in vivo*, and synchronized activity can be broken down into three main waveforms—spindle, gamma, and long oscillations. However, as these activities show overlapping time courses *in vivo*, a parallel progression of the activity types like that seen *in vitro,* is not apparent in the living animal.

Two-photon imaging coupled with voltage-sensitive dyes or genetic calcium indicators (Stosiek et al., 2003) is often used as an alternative method for visualizing neuronal activity. However, limited studies with this methodology have been performed in the developing somatosensory cortex. Calcium oscillations are evident in the somatosensory cortex of resting pups at a cortical depth of 300-400 μm in the early postnatal time period (P0 to P3) (Adelsberger et al., 2005). Given their developmental time course, the number of events, and the rate at which they occur and decay, it is possible that these waves are the *in vivo* correlate to cENOs (Adelsberger et al., 2005). In the first postnatal week, oscillations also occur in layer I, a layer populated predominantly by Re-CGE interneurons and Cajal-Retzius neurons. Calcium transients in Re-interneurons, but not Cajal-Retzius cells, are synchronized, and this synchrony depends on a range of neurotransmitters and neuromodulators, but not on gap junctions or glycine (Schwartz et al., 1998). From P5 to P12, layer II/III is synchronized across large areas—with oscillations extending beyond the boundaries of the barrel—and this activity becomes asynchronous after the second postnatal week (Golshani et al., 2009). While *in vivo* imaging demonstrates a de-synchronization of the somatosensory cortical neurons in general, imaging of specific subtypes of neurons using genetically encoded calcium indicators shows that even in mature networks, there is cooperative firing of specific interneuronal subtypes (Sippy and Yuste, 2013; Karnani et al., 2016), though it is unknown whether this cooperation emerges early in development.

Both GABAergic and glutamatergic transmission modulate early patterns of cortical activity (Kilb et al., 2011). Excitatory post-synaptic potentials and inhibitory post-synaptic potentials are associated with spindle bursts in the first postnatal week (Khazipov et al., 2004). Spindle-bursts and delta waves are NMDAR-dependent (Minlebaev et al., 2009) whereas alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) blockade suppresses spindle bursts (Minlebaev et

al., 2007). In the second half of the first postnatal week, NMDAR antagonists suppress cortical rhythms (Dupont et al., 2006). In addition, GABA antagonists decrease the compartmentalization of spontaneously generated rhythms (Voigt et al., 2001; Kirmse et al., 2015), suggesting a role for this neurotransmitter in confining the spread of oscillations (Minlebaev et al., 2007). All together these experiments suggest that glutamate is necessary to drive cortical oscillations, while GABA regulates their propagation.

One possible origin for synchronous cortical activity is the thalamus. Spindle-bursts are evoked by thalamic inputs (Khazipov et al., 2004; Minlebaev et al., 2009), and early gamma oscillations are driven by these inputs (Minlebaev et al., 2011). Moreover, the subplate has been hypothesized to play a role in the generation and maintenance of these oscillations (Kanold and Luhmann, 2010). Removal of the subplate abolishes spontaneous and sensory evoked spindles in the somatosensory cortex (Tolner et al., 2012) suggesting that both of these activity patterns are modulated by inputs relayed via the thalamus and amplified by the subplate (Dupont et al., 2006; Kilb et al., 2011). Since correlated activity in developing (Golshani et al., 2009) and mature pyramidal cells (Cohen-Kashi Malina et al., 2016) is independent of thalamic inputs, cortical interneurons are attractive candidates as mediators of thalamic-induced cortical oscillations. GABAergic neurons outside of the cortex may also play a role in the generation, maintenance, or dampening of network oscillations (Cossart et al., 2005). The piriform cortex and septal nucleus are pacemaker locations, and the wave initiation sites are highly correlated to the position of GABAergic neurons (Conhaim et al., 2011). There are both GABAergic and glutamatergic fractions of waves that propagate from ventral structures; although, the glutamatergic fraction seems to preferentially propagate to the neocortex, particularly as postnatal development proceeds (Easton et al., 2014). It is possible that both thalamic and other subcortical patterns interact to produce the oscillatory patterns observed in the developing somatosensory cortex.

In sum, the neonatal somatosensory cortex undergoes different patterns of oscillatory activity, though the descriptions of this activity can vary with method of recording. These oscillations provide the electric drive necessary for the processes discussed in this review. However, it remains to be determined whether specific patterns are required for the proper assembly of cortical circuits. Due to limitations in existing knowledge and experimental tools, it has not yet been possible to replay rhythms of distinct origin and sequence to directly implicate cortical oscillations as instructive for neuronal connectivity. Furthermore, the distinct contribution of different cell types to these oscillations is not yet known, but the increasing availability of tools to dissect cell populations should enable specific analyses in the future. Regardless of their cellular origin and spatiotemporal features, these rhythms are conserved in the human neonatal cortex (Milh et al., 2007) strongly suggesting that they subserve an important role during cortical development.

Plasticity of adult neuronal identity and connectivity

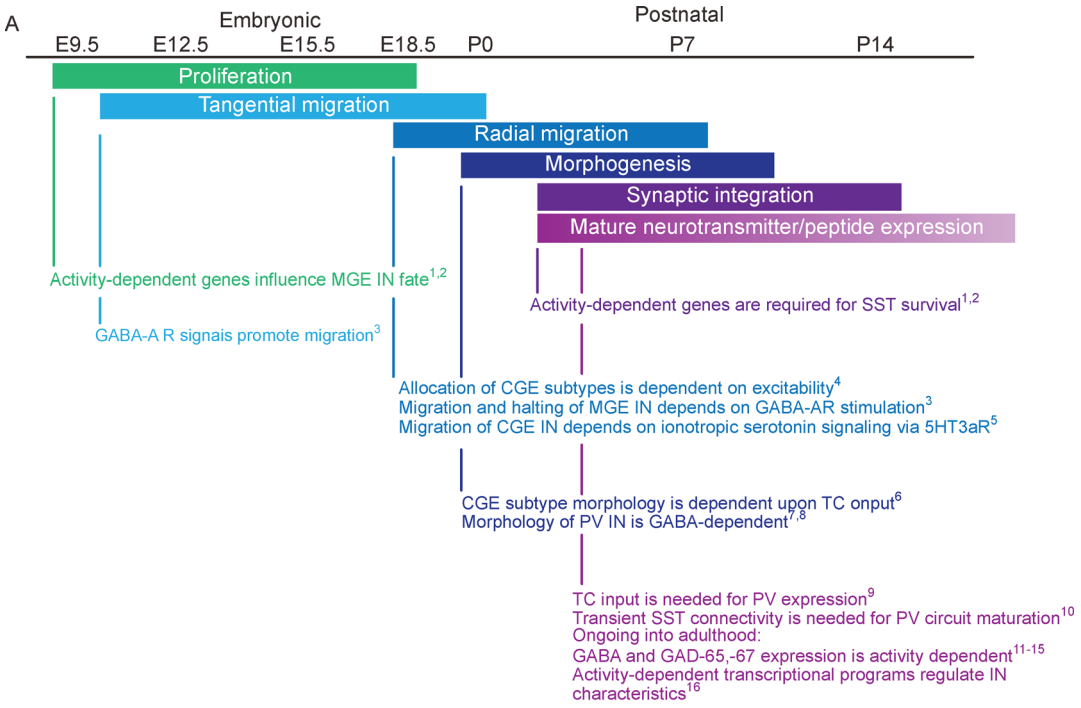
Neuronal intrinsic properties have been considered to be set early during differentiation and maintained through adulthood (Kepecs and Fishell, 2014). In fact, these properties are currently used for the classification of interneuron subtypes (Butt et al., 2005; Miyoshi et al., 2007; Miyoshi et al., 2010). However, recent experimental evidence revealed that cortical activity can trigger changes in intrinsic properties in the adult animal.

It has been shown that *Er81*, a member of the ETS family of transcription factors that delineates PV interneurons in layers II/III, is required for the modulation of their intrinsic properties in mature animals. Specifically, cell-autonomous elimination of *Er81* results in reduced spiking latency, a hallmark of inhibitory gating mediated by Kv1.1 potassium channels. Kv1.1 expression is also reduced in *Er81*-ablated cells. Furthermore, motor learning regulates Er81 expression in PV interneurons (Dehorter et al., 2015). Adult plasticity has also been demonstrated in the hippocampus, where repeated high-frequency stimulation of PV basket cells in CA1 results in potentiation of intrinsic neuronal excitability through the downregulation of potassium channels (Campanac et al., 2013). These examples provide mechanistic evidence for activity-dependent plasticity of interneuron properties in adult through transcriptional regulation. With the new advent of single-cell RNA-sequencing technology, it has been possible to classify interneuronal subtypes into increasingly defined categories (Zeisel et al., 2015; Tasic et al., 2016). It would be interesting to assess whether the expression of genes that confer interneurons with subtype identity are also subject changes in neuronal excitability.

In addition to regulating mature neuronal excitability, neuronal activity is required for the proper regulation of GABA expression in mature interneurons. Sensory deprivation leads to a decrease of GABA expression (Rutherford et al., 1997; Huang et al., 2007). Furthermore, the expression of GABA-synthesizing enzymes, glutamic acid decarboxylase (GAD) −65 and 67, is also activity dependent (Liang et al., 1996; Gierdalski et al., 2001; Mix et al., 2015), and can be specifically induced after sensory learning (Gierdalski et al., 2001), suggesting that activity can influence interneuron output even after these neurons become integrated into the mature circuit.

Concluding remarks

It is clear that neuronal activity impacts the development and integration of cortical interneurons, by influencing their migration and maturation (Fig. 1). In addition, activity-



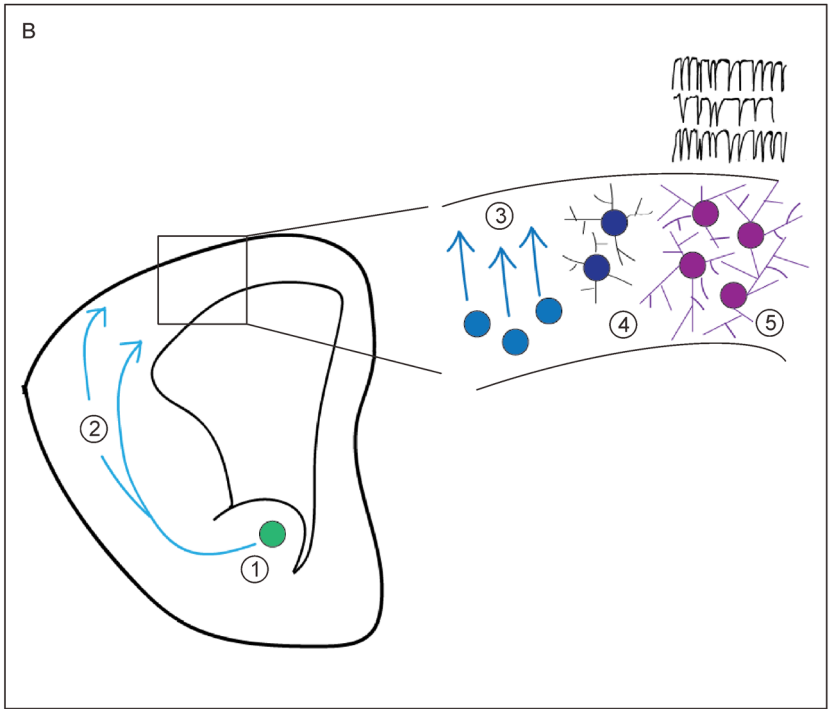


Figure 1 Activity-dependent development of somatosensory cortex interneurons. Cortical interneurons (IN) follow a defined sequence of development, shown above. (Green – proliferation, light blue – tangential migration, blue – radial migration, navy – morphogenesis, purples – synaptic integration, transmitter expression, and mature characteristics.) (A) Timeline of interneuron development with summary of major findings of activity influence. 1 – Close et al., 2012; 2 – Denaxa et al., 2012; 3 – Bortone and Polleux, 2009; 4 – De Marco Garcia et al., 2011; 5 – Murthy et al., 2014; 6 – De Marco Garcia et al., 2015; 7 – Baho and DiCristo, 2012; 8 – Wu et al., 2012; 9 – Ji et al., 2006; 10 – Tuncdemir et al., 2016; 11 – Rutherford et al., 1997; 12 – Huang et al., 2007; 13 – Liang et al., 1996; 14 – Mix et al., 2015; 15 – Giardalski et al., 2001; 16 – Dehorter et al., 2015; 17-Campanac et al., 2013 (B) Cortical IN are born in the ganglionic eminences of the ventral telencephalon (1) and migrate tangentially to their cortical destination (2). Within the cortex, they migrate radially to the laminae (3), undergo morphological maturation (4), then begin to integrate into nascent networks and express characteristic transmitters, neuropeptides and calcium binding proteins (5). Neuronal activity is required along the way as these neurons acquire their mature characteristics.

dependent transcription programs control the electrophysiological properties and output of mature interneurons. Thus, a complex, dynamic interplay between intrinsic genetic programs and environmental influences shape cortical circuits from early developmental stages into adulthood. Because defects in interneurons and GABAergic signaling have been implicated in neurodevelopmental and neuropsychiatric diseases, including autism (Marín, 2012; Takano, 2015), schizophrenia (Marín, 2012; Lewis, 2014), and epilepsy (Coulter, 2001; Trevelyan et al., 2015), it is of high importance to determine the factors regulating interneuron maturation, as further research in this area will illuminate possible treatments for these clinical problems.

Acknowledgements

We are grateful to A. Che, P. Chu, and S. Z. Duan for comments on the manuscript. N.V.D.M.G. is supported by grants from the National Institutes of Health (5 R00 MH095825 05; 1 R01 MH110553 01), the Leon Levy Foundation, and Citizens United for Research in Epilepsy (CURE). R.B. is supported by a Medical Scientist Training Program grant from the National Institute of General Medical Sciences of the NIH under award number T32GM07739 to the Weill Cornell/Rockefeller/Sloan-Kettering Tri-Institutional MD-PhD Program.

Compliance with ethics guidelines

Rachel Babij, Natalia De Marco Garcia declare that they have no conflict of interest. This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Adelsberger H, Garaschuk O, Konnerth A (2005). Cortical calcium waves in resting newborn mice. Nat Neurosci, 8(8): 988–990

Agmon A, Connors B W (1992). Correlation between intrinsic firing patterns and thalamocortical synaptic responses of neurons in mouse barrel cortex. J Neurosci, 12(1): 319–329

Agmon A, O'Dowd D K (1992). NMDA receptor-mediated currents are prominent in the thalamocortical synaptic response before maturation of inhibition. J Neurophysiol, 68(1): 345–349

Allène C, Cattani A, Ackman J B, Bonifazi P, Aniksztejn L, Ben-Ari Y, Cossart R (2008). Sequential generation of two distinct synapse-driven network patterns in developing neocortex. J Neurosci, 28(48): 12851–12863

Allene C, Cossart R (2010). Early NMDA receptor-driven waves of activity in the developing neocortex: physiological or pathological network oscillations? J Physiol, 588(Pt 1): 83–91

An S, Kilb W, Luhmann H J (2014). Sensory-evoked and spontaneous gamma and spindle bursts in neonatal rat motor cortex. J Neurosci, 34 (33): 10870–10883

Anastasiades P G, Marques-Smith A, Lyngholm D, Lickiss T, Raffiq S, Kätzel D, Miesenböck G, Butt S J (2016). GABAergic interneurons form transient layer-specific circuits in early postnatal neocortex. Nat Commun, 7: 10584

Arroyo D A, Feller M B (2016). Spatiotemporal Features of Retinal Waves Instruct the Wiring of the Visual Circuitry. Front Neural Circuits, 10: 54

Ascoli G A, Alonso-Nanclares L, Anderson S A, Barrionuevo G, Benavides-Piccione R, Burkhalter A, Buzsáki G, Cauli B, Defelipe J, Fairén A, Feldmeyer D, Fishell G, Fregnac Y, Freund T F, Gardner D, Gardner E P, Goldberg J H, Helmstaedter M, Hestrin S, Karube F, Kisvárday Z F, Lambolez B, Lewis D A, Marin O, Markram H, Muñoz A, Packer A, Petersen C C, Rockland K S, Rossier J, Rudy B, Somogyi P, Staiger J F, Tamas G, Thomson A M, Toledo-Rodriguez M, Wang Y, West D C, Yuste R, Yuste R, and the Petilla Interneuron Nomenclature Group (2008). Petilla terminology: nomenclature of features of GABAergic interneurons of the cerebral cortex. Nat Rev Neurosci, 9(7): 557–568

Avila A, Vidal P M, Dear T N, Harvey R J, Rigo J M, Nguyen L (2013). Glycine receptor α2 subunit activation promotes cortical interneuron migration. Cell Reports, 4(4): 738–750

Baho E, Di Cristo G (2012). Neural activity and neurotransmission regulate the maturation of the innervation field of cortical GABAergic interneurons in an age-dependent manner. J Neurosci, 32(3): 911–918

Bando Y, Irie K, Shimomura T, Umeshima H, Kushida Y, Kengaku M, Fujiyoshi Y, Hirano T, Tagawa Y (2016). Control of spontaneous Ca^{2+} transients is critical for neuronal maturation in the developing neocortex. Cereb Cortex, 26(1): 106–117

Batista-Brito R, Fishell G (2009). The developmental integration of cortical interneurons into a functional network. Curr Top Dev Biol, 87: 81–118

Batista-Brito R, Machold R, Klein C, Fishell G (2008). Gene expression in cortical interneuron precursors is prescient of their mature function. Cereb Cortex, 18(10): 2306–2317

Behar T N, Schaffner A E, Scott C A, Greene C L, Barker J L (2000). GABA receptor antagonists modulate postmitotic cell migration in slice cultures of embryonic rat cortex. Cereb Cortex, 10(9): 899–909

Behar T N, Scott C A, Greene C L, Wen X, Smith S V, Maric D, Liu Q Y, Colton C A, Barker J L (1999). Glutamate acting at NMDA receptors stimulates embryonic cortical neuronal migration. J Neurosci, 19(11): 4449–4461

Bony G, Szczurkowska J, Tamagno I, Shelly M, Contestabile A, Cancedda L (2013). Non-hyperpolarizing GABAB receptor activation regulates neuronal migration and neurite growth and specification by cAMP/LKB1. Nat Commun, 4: 1800

Bortone D, Polleux F (2009). KCC2 expression promotes the termination of cortical interneuron migration in a voltage-sensitive calcium-dependent manner. Neuron, 62(1): 53–71

Butt S J, Fuccillo M, Nery S, Noctor S, Kriegstein A, Corbin J G, Fishell G (2005). The temporal and spatial origins of cortical interneurons predict their physiological subtype. Neuron, 48(4): 591–604

Campanac E, Gasselin C, Baude A, Rama S, Ankri N, Debanne D (2013). Enhanced intrinsic excitability in basket cells maintains excitatory-inhibitory balance in hippocampal circuits. Neuron, 77(4): 712–722

Chaudhury S, Sharma V, Kumar V, Nag T C, Wadhwa S (2016). Activity-dependent synaptic plasticity modulates the critical phase of brain development. Brain Dev, 38(4): 355–363

Chu J, Anderson S A (2015). Development of cortical interneurons.

Neuropsychopharmacology, 40(1): 16–23

Close J, Xu H, De Marco García N, Batista-Brito R, Rossignol E, Rudy B, Fishell G (2012). Satb1 is an activity-modulated transcription factor required for the terminal differentiation and connectivity of medial ganglionic eminence-derived cortical interneurons. J Neurosci, 32(49): 17690–17705

Cohen-Kashi Malina K, Mohar B, Rappaport A N, Lampl I (2016). Local and thalamic origins of correlated ongoing and sensory-evoked cortical activities. Nat Commun, 7: 12740

Colonnese M T, Kaminska A, Minlebaev M, Milh M, Bloem B, Lescure S, Moriette G, Chiron C, Ben-Ari Y, Khazipov R (2010). A conserved switch in sensory processing prepares developing neocortex for vision. Neuron, 67(3): 480–498

Conhaim J, Easton C R, Becker M I, Barahimi M, Cedarbaum E R, Moore J G, Mather L F, Dabagh S, Minter D J, Moen S P, Moody W J (2011). Developmental changes in propagation patterns and transmitter dependence of waves of spontaneous activity in the mouse cerebral cortex. J Physiol, 589(Pt 10): 2529–2541

Corlew R, Bosma M M, Moody W J (2004). Spontaneous, synchronous electrical activity in neonatal mouse cortical neurones. J Physiol, 560 (Pt 2): 377–390

Cossart R, Ikegaya Y, Yuste R (2005). Calcium imaging of cortical networks dynamics. Cell Calcium, 37(5): 451–457

Coulter D A (2001). Epilepsy-associated plasticity in gamma-aminobutyric acid receptor expression, function, and inhibitory synaptic properties. Int Rev Neurobiol, 45: 237–252

Crair M C, Malenka R C (1995). A critical period for long-term potentiation at thalamocortical synapses. Nature, 375(6529): 325–328

Cruikshank S J, Urabe H, Nurmikko A V, Connors B W (2010). Pathway-specific feedforward circuits between thalamus and neocortex revealed by selective optical stimulation of axons. Neuron, 65 (2): 230–245

Cuzon V C, Yeh P W, Cheng Q, Yeh H H (2006). Ambient GABA promotes cortical entry of tangentially migrating cells derived from the medial ganglionic eminence. Cereb Cortex, 16(10): 1377–1388

Cuzon Carlson V C, Yeh H H (2011). GABAA receptor subunit profiles of tangentially migrating neurons derived from the medial ganglionic eminence. Cereb Cortex, 21(8): 1792–1802

Daw M I, Scott H L, Isaac J T (2007). Developmental synaptic plasticity at the thalamocortical input to barrel cortex: mechanisms and roles. Mol Cell Neurosci, 34(4): 493–502

de Lima A D, Gieseler A, Voigt T (2009). Relationship between GABAergic interneurons migration and early neocortical network activity. Dev Neurobiol, 69(2-3): 105–123

De Marco García N V, Karayannis T, Fishell G (2011). Neuronal activity is required for the development of specific cortical interneuron subtypes. Nature, 472(7343): 351–355

De Marco García N V, Priya R, Tuncdemir S N, Fishell G, Karayannis T (2015). Sensory inputs control the integration of neurogliaform interneurons into cortical circuits. Nat Neurosci, 18(3): 393–401

DeDiego I, Smith-Fernández A, Fairén A (1994). Cortical cells that migrate beyond area boundaries: characterization of an early neuronal population in the lower intermediate zone of prenatal rats. Eur J Neurosci, 6(6): 983–997

Dehorter N, Ciceri G, Bartolini G, Lim L, del Pino I, Marín O (2015). Tuning of fast-spiking interneuron properties by an activity-dependent transcriptional switch. Science, 349(6253): 1216–1220

Denaxa M, Kalaitzidou M, Garefalaki A, Achimastou A, Lasrado R, Maes T, Pachnis V (2012). Maturation-promoting activity of SATB1 in MGE-derived cortical interneurons. Cell Reports, 2(5): 1351–1362

Dupont E, Hanganu I L, Kilb W, Hirsch S, Luhmann H J (2006). Rapid developmental switch in the mechanisms driving early cortical columnar networks. Nature, 439(7072): 79–83

Easton C R, Weir K, Scott A, Moen S P, Barger Z, Folch A, Hevner R F, Moody W J (2014). Genetic elimination of GABAergic neurotransmission reveals two distinct pacemakers for spontaneous waves of activity in the developing mouse cortex. J Neurosci, 34(11): 3854–3863

Erzurumlu R S, Gaspar P (2012). Development and critical period plasticity of the barrel cortex. Eur J Neurosci, 35(10): 1540–1553

Espinosa J S, Stryker M P (2012). Development and plasticity of the primary visual cortex. Neuron, 75(2): 230–249

Espinosa J S, Wheeler D G, Tsien R W, Luo L (2009). Uncoupling dendrite growth and patterning: single-cell knockout analysis of NMDA receptor 2B. Neuron, 62(2): 205–217

Feldmeyer D (2012). Excitatory neuronal connectivity in the barrel cortex. Front Neuroanat, 6: 24

Feldmeyer D, Brecht M, Helmchen F, Petersen C C, Poulet J F, Staiger J F, Luhmann H J, Schwarz C (2013). Barrel cortex function. Prog Neurobiol, 103: 3–27

Fishell G, Rudy B (2011). Mechanisms of inhibition within the telencephalon: “where the wild things are”. Annu Rev Neurosci, 34 (1): 535–567

Flint A C, Maisch U S, Weishaupt J H, Kriegstein A R, Monyer H (1997). NR2A subunit expression shortens NMDA receptor synaptic currents in developing neocortex. J Neurosci, 17(7): 2469–2476

Frazer S, Otomo K, Dayer A (2015). Early-life serotonin dysregulation affects the migration and positioning of cortical interneuron subtypes. Transl Psychiatry, 5(9): e644

Garaschuk O, Linn J, Eilers J, Konnerth A (2000). Large-scale oscillatory calcium waves in the immature cortex. Nat Neurosci, 3 (5): 452–459

Gierdalski M, Jablonska B, Siucinska E, Lech M, Skibinska A, Kossut M (2001). Rapid regulation of GAD67 mRNA and protein level in cortical neurons after sensory learning. Cereb Cortex, 11(9): 806–815

Golshani P, Gonçalves J T, Khoshkhoo S, Mostany R, Smirnakis S, Portera-Cailliau C (2009). Internally mediated developmental desynchronization of neocortical network activity. J Neurosci, 29 (35): 10890–10899

Hanganu I L, Kilb W, Luhmann H J (2002). Functional synaptic projections onto subplate neurons in neonatal rat somatosensory cortex. J Neurosci, 22(16): 7165–7176

Heck N, Kilb W, Reiprich P, Kubota H, Furukawa T, Fukuda A, Luhmann H J (2007). GABA-A receptors regulate neocortical neuronal migration *in vitro* and *in vivo*. Cereb Cortex, 17(1): 138–148

Higashi S, Hioki K, Kurotani T, Kasim N, Molnár Z (2005). Functional thalamocortical synapse reorganization from subplate to layer IV during postnatal development in the reeler-like mutant rat (shaking rat Kawasaki). J Neurosci, 25(6): 1395–1406

Huang Z J, Di Cristo G, Ango F (2007). Development of GABA innervation in the cerebral and cerebellar cortices. Nat Rev Neurosci, 8(9): 673–686

Inada H, Watanabe M, Uchida T, Ishibashi H, Wake H, Nemoto T,

Yanagawa Y, Fukuda A, Nabekura J (2011). GABA regulates the multidirectional tangential migration of GABAergic interneurons in living neonatal mice. PLoS ONE, 6(12): e27048

Iwasato T, Datwani A, Wolf A M, Nishiyama H, Taguchi Y, Tonegawa S, Knöpfel T, Erzurumlu R S, Itohara S (2000). Cortex-restricted disruption of NMDAR1 impairs neuronal patterns in the barrel cortex. Nature, 406(6797): 726–731

Ji X Y, Zingg B, Mesik L, Xiao Z, Zhang L I, Tao H W (2016). Thalamocortical Innervation Pattern in Mouse Auditory and Visual Cortex: Laminar and Cell-Type Specificity. Cereb Cortex, 26(6): 2612–2625

Jiao Y, Zhang C, Yanagawa Y, Sun Q Q (2006). Major effects of sensory experiences on the neocortical inhibitory circuits. J Neurosci, 26(34): 8691–8701

Kanold P O (2004). Transient microcircuits formed by subplate neurons and their role in functional development of thalamocortical connections. Neuroreport, 15(14): 2149–2153

Kanold P O, Kara P, Reid R C, Shatz C J (2003). Role of subplate neurons in functional maturation of visual cortical columns. Science, 301(5632): 521–525

Kanold P O, Luhmann H J (2010). The subplate and early cortical circuits. Annu Rev Neurosci, 33(1): 23–48

Karayannis T, De Marco García N V, Fishell G J (2012). Functional adaptation of cortical interneurons to attenuated activity is subtype-specific. Front Neural Circuits, 6: 66

Karnani M M, Jackson J, Ayzenshtat I, Tucciarone J, Manoocheri K, Snider W G, Yuste R (2016). Cooperative Subnetworks of Molecularly Similar Interneurons in Mouse Neocortex. Neuron, 90 (1): 86–100

Kepecs A, Fishell G (2014). Interneuron cell types are fit to function. Nature, 505(7483): 318–326

Khazipov R, Luhmann H J (2006). Early patterns of electrical activity in the developing cerebral cortex of humans and rodents. Trends Neurosci, 29(7): 414–418

Khazipov R, Sirota A, Leinekugel X, Holmes G L, Ben-Ari Y, Buzsáki G (2004). Early motor activity drives spindle bursts in the developing somatosensory cortex. Nature, 432(7018): 758–761

Kihara M, Yoshioka H, Hirai K, Hasegawa K, Kizaki Z, Sawada T (2002). Stimulation of N-methyl-D-aspartate (NMDA) receptors inhibits neuronal migration in embryonic cerebral cortex: a tissue culture study. Brain Res Dev Brain Res, 138(2): 195–198

Kilb W, Kirischuk S, Luhmann H J (2011). Electrical activity patterns and the functional maturation of the neocortex. Eur J Neurosci, 34 (10): 1677–1686

Kilb W, Kirischuk S, Luhmann H J (2013). Role of tonic GABAergic currents during pre- and early postnatal rodent development. Front Neural Circuits, 7: 139

Killackey H P (1973). Anatomical evidence for cortical subdivisions based on vertically discrete thalamic projections from the ventral posterior nucleus to cortical barrels in the rat. Brain Res, 51: 326–331

Kirmse K, Kummer M, Kovalchuk Y, Witte O W, Garaschuk O, Holthoff K (2015). GABA depolarizes immature neurons and inhibits network activity in the neonatal neocortex in vivo. Nat Commun, 6: 7750

Koolen N, Dereymaeker A, Räsänen O, Jansen K, Vervisch J, Matic V, Naulaers G, De Vos M, Van Huffel S, Vanhatalo S (2016). Early development of synchrony in cortical activations in the human. Neuroscience, 322: 298–307

Kral A (2013). Auditory critical periods: a review from system's perspective. Neuroscience, 247: 117–133

Laaris N, Carlson G C, Keller A (2000). Thalamic-evoked synaptic interactions in barrel cortex revealed by optical imaging. J Neurosci, 20(4): 1529–1537

Lee L J, Iwasato T, Itohara S, Erzurumlu R S (2005). Exuberant thalamocortical axon arborization in cortex-specific NMDAR1 knockout mice. J Comp Neurol, 485(4): 280–292

Lewis D A (2014). Inhibitory neurons in human cortical circuits: substrate for cognitive dysfunction in schizophrenia. Curr Opin Neurobiol, 26: 22–26

Li H, Fertuzinhos S, Mohns E, Hnasko T S, Verhage M, Edwards R, Sestan N, Crair M C (2013). Laminar and columnar development of barrel cortex relies on thalamocortical neurotransmission. Neuron, 79 (5): 970–986

Liang F, Isackson P J, Jones E G (1996). Stimulus-dependent, reciprocal up- and downregulation of glutamic acid decarboxylase and Ca^{2+}/calmodulin-dependent protein kinase II gene expression in rat cerebral cortex. Exp Brain Res, 110(2): 163–174

Liodis P, Denaxa M, Grigoriou M, Akufo-Addo C, Yanagawa Y, Pachnis V (2007). Lhx6 activity is required for the normal migration and specification of cortical interneuron subtypes. J Neurosci, 27(12): 3078–3089

Liu X, Hashimoto-Torii K, Torii M, Ding C, Rakic P (2010). Gap junctions/hemichannels modulate interkinetic nuclear migration in the forebrain precursors. J Neurosci, 30(12): 4197–4209

Liu X, Hashimoto-Torii K, Torii M, Haydar T F, Rakic P (2008). The role of ATP signaling in the migration of intermediate neuronal progenitors to the neocortical subventricular zone. Proc Natl Acad Sci USA, 105(33): 11802–11807

Liu X B, Murray K D, Jones E G (2004). Switching of NMDA receptor 2A and 2B subunits at thalamic and cortical synapses during early postnatal development. J Neurosci, 24(40): 8885–8895

Lorente de No R (1922). La Corteza Cerebral del Raton (Primera Contribucion- La Corteza Acustica). Trabajos del Laboratorio de Investigaciones Biologicas, 20: 41–78

LoTurco J J, Blanton M G, Kriegstein A R (1991). Initial expression and endogenous activation of NMDA channels in early neocortical development. J Neurosci, 11(3): 792–799

Luhmann H J, Fukuda A, Kilb W (2015). Control of cortical neuronal migration by glutamate and GABA. Front Cell Neurosci, 9: 4

Luhmann H J, Hanganu I, Kilb W (2003). Cellular physiology of the neonatal rat cerebral cortex. Brain Res Bull, 60(4): 345–353

Luhmann H J, Kirischuk S, Sinning A, Kilb W (2014). Early GABAergic circuitry in the cerebral cortex. Curr Opin Neurobiol, 26: 72–78

Manent J B, Jorquera I, Ben-Ari Y, Aniksztejn L, Represa A (2006). Glutamate acting on AMPA but not NMDA receptors modulates the migration of hippocampal interneurons. J Neurosci, 26(22): 5901–5909

Marín O (2012). Interneuron dysfunction in psychiatric disorders. Nat Rev Neurosci, 13(2): 107–120

Marques-Smith A, Lyngholm D, Kaufmann A K, Stacey J A, Hoerder-Suabedissen A, Becker E B, Wilson M C, Molnár Z, Butt S J (2016). A Transient Translaminar GABAergic Interneuron Circuit Connects Thalamocortical Recipient Layers in Neonatal Somatosensory

Cortex. Neuron, 89(3): 536–549

Matta J A, Pelkey K A, Craig M T, Chittajallu R, Jeffries B W, McBain C J (2013). Developmental origin dictates interneuron AMPA and NMDA receptor subunit composition and plasticity. Nat Neurosci, 16 (8): 1032–1041

McCabe A K, Chisholm S L, Picken-Bahrey H L, Moody W J (2006). The self-regulating nature of spontaneous synchronized activity in developing mouse cortical neurones. J Physiol, 577(Pt 1): 155–167

Milh M, Kaminska A, Huon C, Lapillonne A, Ben-Ari Y, Khazipov R (2007). Rapid cortical oscillations and early motor activity in premature human neonate. Cereb Cortex, 17(7): 1582–1594

Minlebaev M, Ben-Ari Y, Khazipov R (2007). Network mechanisms of spindle-burst oscillations in the neonatal rat barrel cortex *in vivo*. J Neurophysiol, 97(1): 692–700

Minlebaev M, Ben-Ari Y, Khazipov R (2009). NMDA receptors pattern early activity in the developing barrel cortex *in vivo*. Cereb Cortex, 19 (3): 688–696

Minlebaev M, Colonnese M, Tsintsadze T, Sirota A, Khazipov R (2011). Early γ oscillations synchronize developing thalamus and cortex. Science, 334(6053): 226–229

Mix A, Hoppenrath K, Funke K (2015). Reduction in cortical parvalbumin expression due to intermittent theta-burst stimulation correlates with maturation of the perineuronal nets in young rats. Dev Neurobiol, 75(1): 1–11

Miyashita-Lin E M, Hevner R, Wassarman K M, Martinez S, Rubenstein J L (1999). Early neocortical regionalization in the absence of thalamic innervation. Science, 285(5429): 906–909

Miyoshi G, Butt S J, Takebayashi H, Fishell G (2007). Physiologically distinct temporal cohorts of cortical interneurons arise from telencephalic Olig2-expressing precursors. J Neurosci, 27(29): 7786–7798

Miyoshi G, Fishell G (2011). GABAergic interneuron lineages selectively sort into specific cortical layers during early postnatal development. Cereb Cortex, 21(4): 845–852

Miyoshi G, Hjerling-Leffler J, Karayannis T, Sousa V H, Butt S J, Battiste J, Johnson J E, Machold R P, Fishell G (2010). Genetic fate mapping reveals that the caudal ganglionic eminence produces a large and diverse population of superficial cortical interneurons. J Neurosci, 30(5): 1582–1594

Mizuno H, Luo W, Tarusawa E, Saito Y M, Sato T, Yoshimura Y, Itohara S, Iwasato T (2014). NMDAR-regulated dynamics of layer 4 neuronal dendrites during thalamocortical reorganization in neonates. Neuron, 82(2): 365–379

Molnár Z, Adams R, Blakemore C (1998). Mechanisms underlying the early establishment of thalamocortical connections in the rat. J Neurosci, 18(15): 5723–5745

Murthy S, Niquille M, Hurni N, Limoni G, Frazer S, Chameau P, van Hooft J A, Vitalis T, Dayer A (2014). Serotonin receptor 3A controls interneuron migration into the neocortex. Nat Commun, 5: 5524

Narboux-Nême N, Evrard A, Ferezou I, Erzurumlu R S, Kaeser P S, Lainé J, Rossier J, Ropert N, Südhof T C, Gaspar P (2012). Neurotransmitter release at the thalamocortical synapse instructs barrel formation but not axon patterning in the somatosensory cortex. J Neurosci, 32(18): 6183–6196

Oh W C, Lutzu S, Castillo P E, Kwon H B (2016). De novo synaptogenesis induced by GABA in the developing mouse cortex. Science, 353(6303): 1037–1040

Okaty B W, Miller M N, Sugino K, Hempel C M, Nelson S B (2009). Transcriptional and electrophysiological maturation of neocortical fast-spiking GABAergic interneurons. J Neurosci, 29(21): 7040–7052

Paoletti P, Bellone C, Zhou Q (2013). NMDA receptor subunit diversity: impact on receptor properties, synaptic plasticity and disease. Nat Rev Neurosci, 14(6): 383–400

Petersen C C (2007). The functional organization of the barrel cortex. Neuron, 56(2): 339–355

Porter J T, Johnson C K, Agmon A (2001). Diverse types of interneurons generate thalamus-evoked feedforward inhibition in the mouse barrel cortex. J Neurosci, 21(8): 2699–2710

Reiprich P, Kilb W, Luhmann H J (2005). Neonatal NMDA receptor blockade disturbs neuronal migration in rat somatosensory cortex *in vivo*. Cereb Cortex, 15(3): 349–358

Rheims S, Minlebaev M, Ivanov A, Represa A, Khazipov R, Holmes G L, Ben-Ari Y, Zilberter Y (2008). Excitatory GABA in rodent developing neocortex *in vitro*. J Neurophysiol, 100(2): 609–619

Riccio O, Potter G, Walzer C, Vallet P, Szabó G, Vutskits L, Kiss J Z, Dayer A G (2009). Excess of serotonin affects embryonic interneuron migration through activation of the serotonin receptor 6. Mol Psychiatry, 14(3): 280–290

Rudy B, Fishell G, Lee S, Hjerling-Leffler J (2011). Three groups of interneurons account for nearly 100% of neocortical GABAergic neurons. Dev Neurobiol, 71(1): 45–61

Rutherford L C, DeWan A, Lauer H M, Turrigiano G G (1997). Brain-derived neurotrophic factor mediates the activity-dependent regulation of inhibition in neocortical cultures. J Neurosci, 17(12): 4527–4535

Sanes D H, Kotak V C (2011). Developmental plasticity of auditory cortical inhibitory synapses. Hear Res, 279(1-2): 140–148

Schwartz T H, Rabinowitz D, Unni V, Kumar V S, Smetters D K, Tsiola A, Yuste R (1998). Networks of coactive neurons in developing layer 1. Neuron, 20(3): 541–552

Siegel F, Heimel J A, Peters J, Lohmann C (2012). Peripheral and central inputs shape network dynamics in the developing visual cortex *in vivo*. Curr Biol, 22(3): 253–258

Sippy T, Yuste R (2013). Decorrelating action of inhibition in neocortical networks. J Neurosci, 33(23): 9813–9830

Soria J M, Valdeolmillos M (2002). Receptor-activated calcium signals in tangentially migrating cortical cells. Cereb Cortex, 12(8): 831–839

Stosiek C, Garaschuk O, Holthoff K, Konnerth A (2003). *In vivo* two-photon calcium imaging of neuronal networks. Proc Natl Acad Sci USA, 100(12): 7319–7324

Sultan K T, Brown K N, Shi S H (2013). Production and organization of neocortical interneurons. Front Cell Neurosci, 7: 221

Sun J J, Luhmann H J (2007). Spatio-temporal dynamics of oscillatory network activity in the neonatal mouse cerebral cortex. Eur J Neurosci, 26(7): 1995–2004

Sun Q Q, Huguenard J R, Prince D A (2006). Barrel cortex microcircuits: thalamocortical feedforward inhibition in spiny stellate cells is mediated by a small number of fast-spiking interneurons. J Neurosci, 26(4): 1219–1230

Sur M, Leamey C A (2001). Development and plasticity of cortical areas and networks. Nat Rev Neurosci, 2(4): 251–262

Takano T (2015). Interneuron dysfunction in syndromic autism: Recent

advances. Dev Neurosci, 37(6): 467–475

Tasic B, Menon V, Nguyen T N, Kim T K, Jarsky T, Yao Z, Levi B, Gray L T, Sorensen S A, Dolbeare T, Bertagnolli D, Goldy J, Shapovalova N, Parry S, Lee C, Smith K, Bernard A, Madisen L, Sunkin S M, Hawrylycz M, Koch C, Zeng H (2016). Adult mouse cortical cell taxonomy revealed by single cell transcriptomics. Nat Neurosci, 19 (2): 335–346

Tolner E A, Sheikh A, Yukin A Y, Kaila K, Kanold P O (2012). Subplate neurons promote spindle bursts and thalamocortical patterning in the neonatal rat somatosensory cortex. J Neurosci, 32(2): 692–702

Tolonen M, Palva J M, Andersson S, Vanhatalo S (2007). Development of the spontaneous activity transients and ongoing cortical activity in human preterm babies. Neuroscience, 145(3): 997–1006

Trevelyan A J, Muldoon S F, Merricks E M, Racca C, Staley K J (2015). The role of inhibition in epileptic networks. J Clin Neurophysiol, 32 (3): 227–234

Tuncdemir S N, Wamsley B, Stam F J, Osakada F, Goulding M, Callaway E M, Rudy B, Fishell G (2016). Early Somatostatin Interneuron Connectivity Mediates the Maturation of Deep Layer Cortical Circuits. Neuron, 89(3): 521–535

Uhlén P, Fritz N, Smedler E, Malmersjö S, Kanatani S (2015). Calcium signaling in neocortical development. Dev Neurobiol, 75(4): 360–368

Van der Loos H, Woolsey T A (1973). Somatosensory cortex: structural alterations following early injury to sense organs. Science, 179 (4071): 395–398

Van Eden C G, Mrzljak L, Voorn P, Uylings H B (1989). Prenatal development of GABA-ergic neurons in the neocortex of the rat. J Comp Neurol, 289(2): 213–227

Vitalis T, Ansorge M S, Dayer A G (2013). Serotonin homeostasis and serotonin receptors as actors of cortical construction: special attention to the 5-HT3A and 5-HT6 receptor subtypes. Front Cell Neurosci, 7: 93

Vitalis T, Cases O, Passemard S, Callebert J, Parnavelas J G (2007). Embryonic depletion of serotonin affects cortical development. Eur J Neurosci, 26(2): 331–344

Voigt T, Opitz T, de Lima A D (2001). Synchronous oscillatory activity in immature cortical network is driven by GABAergic preplate neurons. J Neurosci, 21(22): 8895–8905

Welker C (1971). Microelectrode delineation of fine grain somatotopic organization of (SmI) cerebral neocortex in albino rat. Brain Res, 26 (2): 259–275

Welker C (1976). Receptive fields of barrels in the somatosensory neocortex of the rat. J Comp Neurol, 166(2): 173–189

White L E, Fitzpatrick D (2007). Vision and cortical map development. Neuron, 56(2): 327–338

Wichterle H, Garcia-Verdugo J M, Herrera D G, Alvarez-Buylla A (1999). Young neurons from medial ganglionic eminence disperse in adult and embryonic brain. Nat Neurosci, 2(5): 461–466

Wichterle H, Turnbull D H, Nery S, Fishell G, Alvarez-Buylla A (2001). In utero fate mapping reveals distinct migratory pathways and fates of neurons born in the mammalian basal forebrain. Development, 128 (19): 3759–3771

Woolsey T A, Van der Loos H (1970). The structural organization of layer IV in the somatosensory region (SI) of mouse cerebral cortex. The description of a cortical field composed of discrete cytoarchitectonic units. Brain Res, 17(2): 205–242

Wu X, Fu Y, Knott G, Lu J, Di Cristo G, Huang Z J (2012). GABA signaling promotes synapse elimination and axon pruning in developing cortical inhibitory interneurons. J Neurosci, 32(1): 331–343

Yang J W, Hanganu-Opatz I L, Sun J J, Luhmann H J (2009). Three patterns of oscillatory activity differentially synchronize developing neocortical networks *in vivo*. J Neurosci, 29(28): 9011–9025

Yang J W, Reyes-Puerta V, Kilb W, Luhmann H J (2016). Spindle Bursts in Neonatal Rat Cerebral Cortex. Neural Plast, 2016: 3467832

Yozu M, Tabata H, Konig N, Nakajima K (2008). Migratory behavior of presumptive interneurons is affected by AMPA receptor activation in slice cultures of embryonic mouse neocortex. Dev Neurosci, 30(1-3): 105–116

Zeisel A, Muñoz-Manchado A B, Codeluppi S, Lönnerberg P, La Manno G, Juréus A, Marques S, Munguba H, He L, Betsholtz C, Rolny C, Castelo-Branco G, Hjerling-Leffler J, Linnarsson S (2015). Brain structure. Cell types in the mouse cortex and hippocampus revealed by single-cell RNA-seq. Science, 347(6226): 1138–1142

Zhang Z, Sun Q Q (2011). Development of NMDA NR2 subunits and their roles in critical period maturation of neocortical GABAergic interneurons. Dev Neurobiol, 71(3): 221–245