Developmental Dysfunction of VIP Interneurons Impairs Cortical Circuits

Highlights
- VIP interneurons were dysregulated by early postnatal ERBB4 deletion
- Pyramidal neurons in mutants showed elevated firing rates and altered spike patterns
- Mutants showed impaired cortical visual responses and visual perceptual abilities
- Effects emerged in adolescence and were specific to cortical VIP cell disruption

Authors
Renata Batista-Brito, Martin Vinck, Katie A. Ferguson, ..., Karl Deisseroth, Michael J. Higley, Jessica A. Cardin

Correspondence
jess.cardin@yale.edu

In Brief
Batista-Brito et al. study the role of VIP interneurons in the postnatal development of cortical circuits. Deletion of the gene ErbB4 from cortical VIP interneurons causes long-term disruption of excitatory and inhibitory cortical neurons and impairs sensory processing and perception.
Developmental Dysfunction of VIP Interneurons Impairs Cortical Circuits

Renata Batista-Brito,1,2,7 Martin Vinck,1,2,3,7 Katie A. Ferguson,1,2 Jeremy T. Chang,1,2 David Laubender,1,2 Gyorgy Lur,1,2 James M. Mossner,1,2 Victoria G. Hernandez,1,2 Charu Ramakrishnan,4 Karl Deisseroth,4,5,6 Michael J. Higley,1,2 and Jessica A. Cardin1,2,8,*

1Yale University School of Medicine, Department of Neuroscience, 333 Cedar St., New Haven, CT, 06520, USA
2Kavli Institute of Neuroscience, Yale University, 333 Cedar St., New Haven CT, 06520, USA
3Ernst Strüngmann Institute (ESI) for Neuroscience in Cooperation with Max Planck Society, Deutschordenstraße 46, 60528 Frankfurt, Germany
4Department of Bioengineering
5HHMI
6Department of Psychiatry and Behavioral Sciences
Stanford University, Stanford, CA 94305, USA
7These authors contributed equally
8Lead Contact
*Correspondence: jess.cardin@yale.edu
http://dx.doi.org/10.1016/j.neuron.2017.07.034

SUMMARY

GABAergic interneurons play important roles in cortical circuit development. However, there are multiple populations of interneurons and their respective developmental contributions remain poorly explored. Neuregulin 1 (NRG1) and its interneuron-specific receptor ERBB4 are critical genes for interneuron maturation. Using a conditional ErbB4 deletion, we tested the role of vasoactive intestinal peptide (VIP)-expressing interneurons in the postnatal maturation of cortical circuits in vivo. ErbB4 removal from VIP interneurons during development leads to changes in their activity, along with severe dysregulation of cortical temporal organization and state dependence. These alterations emerge during adolescence, and mature animals in which VIP interneurons lack ErbB4 exhibit reduced cortical responses to sensory stimuli and impaired sensory learning. Our data support a key role for VIP interneurons in cortical circuit development and suggest a possible contribution to pathophysiology in neurodevelopmental disorders. These findings provide a new perspective on the role of GABAergic interneuron diversity in cortical development.

INTRODUCTION

GABAergic interneurons represent only a small fraction of all cortical neurons (~20%), but play critical roles in the establishment, maintenance, and function of cortical circuits. The diversity of inhibitory interneurons, which comprise a number of distinct classes with different intrinsic properties, morphology, synaptic targeting, and molecular markers, allows them to dynamically sculpt cortical activity during both development and mature function. Recent work has focused on three major interneuron populations: (1) cells that co-express the calcium binding protein parvalbumin (PV) and preferentially synapse on the cell bodies of excitatory neurons; (2) cells that co-express the peptide somatostatin (SST) and preferentially target the dendrites of excitatory neurons; and (3) cells that co-express vasoactive intestinal peptide (VIP) and preferentially target other interneurons (Kepecs and Fishell, 2014). Interneurons have been suggested to regulate early organizational activity patterns in the cortex and hippocampus (Alle` ne et al., 2008; Bonifazi et al., 2009; Picardo et al., 2011) and to control the expression of critical period plasticity by excitatory neurons (Takesian and Hensch, 2013). Recent work has further suggested complex developmental interactions between populations of inhibitory interneurons (Anastasiades et al., 2016; Marques-Smith et al., 2016; Tuncdemir et al., 2016). Developmental dysregulation of GABAergic cells is associated with pathophysiology underlying neurodevelopmental disorders including autism and schizophrenia, as well as epilepsy (Rossignol, 2011). However, the precise roles of the major interneuron classes in the postnatal development of cortical circuits remain poorly understood.

VIP-expressing interneurons (VIP-INs) have recently gained attention as important regulators of cortical function (Lee et al., 2013; Pi et al., 2013; Fu et al., 2014; Karnani et al., 2016). VIP-INs are preferentially found in superficial cortical layers and are innervated by local and long-range excitatory inputs as well as serotonergic and cholinergic afferents (Lee et al., 2013; Fu et al., 2014; Pröneke et al., 2015; Kamigaki and Dan, 2017). VIP-INs are strongly recruited by negative or noxious stimuli and arousing events such as the onset of motor activity (Lee et al., 2013; Pi et al., 2013; Fu et al., 2014). In turn, they regulate cortical excitatory activity and sensory response gain through inhibition of pyramidal neurons and other interneurons (Lee et al., 2013; Pfeffer et al., 2013; Pi et al., 2013; Fu et al., 2014; Garcia-Junco-Clemente et al., 2017). VIP-INs integrate into cortical circuits early in postnatal life (Miyoshi et al., 2015). However,
دریافت فوری متن کامل مقاله

امکان دانلود نسخه تمام متن مقالات انگلیسی
امکان دانلود نسخه ترجمه شده مقالات
پذیرش سفارش ترجمه تخصصی
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
امکان دانلود رایگان ۲ صفحه اول هر مقاله
امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
دانلود فوری مقاله پس از پرداخت آنلاین
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات