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Research Report

Visual thalamocortical circuits in parvalbumin-deficient mice

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ABSTRACT

The dorsal lateral geniculate nucleus (dLGN) is considered as the visual gateway to the visual cortex (VC) and sends collaterals to the thalamic reticular nucleus (RTN) that in turn receives collaterals of the corticofugal feedback projections. At all levels of this thalamocortical circuit there are GABAergic neurons expressing the calcium-buffer parvalbumin (PV). The present study reports for the first time the analysis of in vivo extracellular electrophysiological recordings performed simultaneously in dLGN, RTN and VC of anesthetized wild-type (WT) and parvalbumin-deficient (PVKO) mice. The firing rates of VC and RTN cells were increased in PVKO during spontaneous activity as well as in the presence of a photic stimulation (strobe flash at 2.5 Hz). Interestingly, dLGN cells in PVKO did not show significant changes in the rate of firing in comparison to WT. dLGN responses to the light flashes were characterized by ripples of inhibition and phasic excitation/rebound. We have analyzed the pattern of functional interactions between pairs of neighboring cells in VC, dLGN and RTN and across these areas in simultaneously recorded thalamocortical triplets, with one neuron from each area. We found that in PVKO the strength of the interactions tended to decrease locally, between neighboring cells, but tended to increase across the areas. The combination of these analyses provides new evidence on the important role played by PV-expression in regulating information processing in the central visual pathway suggesting that the ability to process information along parallel channels is decreased in the thalamocortical pathway of PV-deficient mice.

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1. Introduction

Parvalbumin (PV) is a Ca^{2+}-binding protein that can act as an endogenous Ca^{2+} buffer and is localized in fast-contracting muscles, where its levels are highest, and in the brain and some endocrine tissues (Schwaller, 2010, 2012a). PV is characterized by a slow-onset Ca^{2+} binding that generally does not affect the initial amplitude of Ca^{2+} transients, but then accelerates the decay phase, thus often converting a monoexponential $[Ca^{2+}]_i$ decay into a bi-exponential one

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(Collin et al., 2005; Lee et al., 2000). The acceleration of the early phase of $[Ca^{2+}]_i$ decay associated to PV activity limits or slows down the buildup of residual $[Ca^{2+}]_i$ in presynaptic terminals, thus affecting short-term plasticity (Caillard et al., 2000; Vreugdenhil et al., 2003). Several observations indicate that a decrease in the expression of PV is likely to lead to behavioral and neurochemical alterations that have been associated to epileptic seizure susceptibility (Marco et al., 1997; Schwaller et al., 2004; Farré-Castany et al., 2007), schizophrenia (Pinault, 2011; Lewis et al., 2012) and autism spectrum disorder (Oblak et al., 2011). The hypothesis is that elimination of PV produces alterations of brain development during specific periods of pre or postnatal life (Heizmann and Braun, 1992). Nowadays PV knockout (PVKO) mice represent an essential animal model to study the effects of absence of PV (Schwaller, 2012b).

Parvalbumin is highly expressed in GABAergic neurons (Celio, 1990) and the reactivity for the perineuronal net marker around GABAergic neurons confirmed that GABAergic neurons are still viable in PVKO mice (Schwaller et al., 2004). Specific parvalbumin immunoreactivity (PV-ir) was identified within subpopulations of ganglion and amacrine cells of the mouse retina (Endo et al., 1986; Sanna et al., 1993; Kim and Jeon, 2006). However, the study of the functional properties of the visual pathway of mice has attracted limited attention by the neurophysiologists in the past probably because of the poor visual acuity of this species (Prusky et al., 2000). In mice, less than 3% of the entire retinofugal pathway projects ipsilaterally (Dräger and Olsen, 1980), and the number of retinal ganglion cells viewing a point in binocular space is 9 times smaller for the ipsilateral than for the contralateral retina (Dräger and Olsen, 1980). Despite such disparity in retinofugal projections the contralateral-to-ipsilateral ratio of visually evoked responses is only 2 times smaller for the ipsilateral than for the contralateral retina at the level of the primary visual cortex (Coleman et al., 2009).

Inputs from the retina are sent from the ascending retinal ganglion cells via the optic tract to the dorsal lateral geniculate nucleus (dLGN), which serves as the obligatory pathway for visual information transfer from the retina to neocortex. Mouse dLGN has recently emerged as a model system in the study of thalamic circuit development (Linden et al., 2009; Bickford et al., 2010). The vast majority, approximately 80%, of the neurons of dLGN are thalamocortical (TC) neurons, also referred to as relay neurons, as they relay information from the retina to the cortex. Although clear morphological differences were reported among relay cells, TC cells are not PV-ir and an analysis of their electrophysiological properties did not reveal any additional distinguishing characteristics (Krahe et al., 2011). The remaining neurons of mouse dLGN are PV-ir GABAergic interneurons, whose density may be as low as 10–20% (Arcelli et al., 1997; Jaubert-Miazza et al., 2005) as recently confirmed by the analysis of the ultrastructure of synaptic profiles (Bickford et al., 2010). Excitatory projections from dLGN to the visual cortex send collaterals to the visual sector of the reticular thalamic nucleus (RTN) (Rafols and Valverde, 1973; Baldauf, 2010). In return the RTN, which is rich in PV-ir neurons (Jones and Hendry, 1989; Tanahira et al., 2009), sends GABA-mediated inhibitory projections back to the thalamus. The visual cortex sends glutamatergic excitatory projections back to dLGN with collaterals to RTN (Alexander et al., 2006; Petrof et al., 2012; Jurgens et al., 2012). A comprehensive, morphological study of the adult mouse visual cortex shows that PV-ir cells account for approximately 40% of GABAergic cortical interneurons (Gonchar et al., 2008). The two main types of cortical PV-ir interneurons are axon initial segment-targeting chandelier cells and soma-targeting large basket cells (del Río et al., 1994).

The geniculate relay cells can alter the retinocortical transfer of information changing their firing pattern between two modes, tonic and burst, with burst firing postulated to serve as a 'wakeup call' for the cortex (Sherman and Guillery, 2011). This firing mode is controlled by a T-type calcium channel that produces a voltage- and time-dependent I_T current (Zhan et al., 2000; Parajuli et al., 2010). The burst firing mode occurs during visual stimulation more often than in spontaneous activity in the mouse dLGN under halothane and nitrous oxide anesthesia (Grubb and Thompson, 2005). In behaving mice, dLGN bursting occurs more frequently during the inactive state, when cortex is in fact less responsive to the visual stimuli (Niell and Stryker, 2010). These findings show the complexity of the inhibitory mechanisms involving distinct roles of local dLGN interneurons and RTN GABAergic cells, thus suggesting that PV's role in dLGN is more complicated than simple calcium buffering (Augustinaite et al., 2011). In the visual cortex, inhibition appears to have a critical role in influencing the receptive field properties and the response gain of the neurons (Dräger, 1975; Hübener, 2003; Métin et al., 1988; Liu et al., 2010; Smith and Häusser, 2010). Different studies show the importance of PV in the mouse visual cortex for cortical information processing (Cardin et al., 2009; Chattopadhyaya et al., 2007) and how corticothalamic processing is regulating the activity in dLGN and RTN (Augustinaite et al., 2011; Jurgens et al., 2012).

The aim of the present work is to study the changes in activity of in vivo visual thalamocortical circuits produced by the deficiency of PV. We investigate the firing properties of dLGN, RTN and visual cortex neurons in anesthetized wildtype (WT) and PVKO mice by means of simultaneous extracellular recordings during spontaneous activity and photic stimulation by stroboscopic flashes. We report here for the first time electrophysiological results simultaneously recorded in dLGN, RTN and visual cortex neurons. However, the small size of the mouse brain makes such in vivo cellular recordings very difficult to perform and we collected only limited amount of data. Thanks to the combined study of the firing pattern, local functional interaction and functional interactions across the thalamocortical circuit, we provide new evidence on the important role played by PV-expression in regulating information processing in the central visual pathway.

2. Materials and methods

2.1. Mice

PV-deficient (PVKO) mice were originally generated on a mixed C57Bl/6J × 129/OlaHsd genetic background (Schwaller et al., 1999) and backcrossed to C57Bl/6J for 10 generations