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Parvalbumin-Positive Basket Cells Differentiate among Hippocampal Pyramidal Cells

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SUMMARY

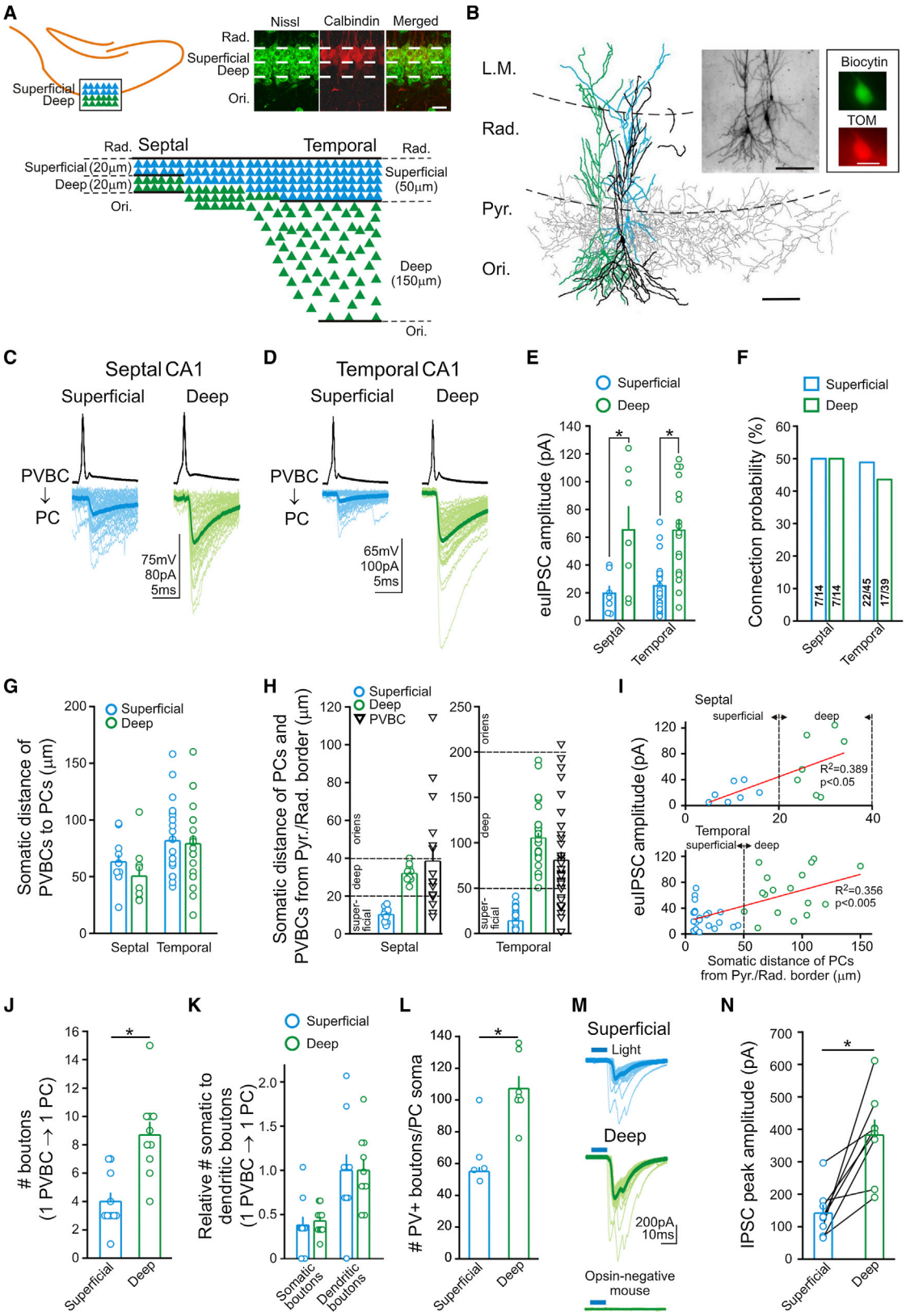
CA1 pyramidal cells (PCs) are not homogeneous but rather can be grouped by molecular, morphological, and functional properties. However, less is known about synaptic sources differentiating PCs. Using paired recordings in vitro, two-photon Ca^{2+} imaging in vivo, and computational modeling, we found that parvalbumin-expressing basket cells (PVBCs) evoked greater inhibition in CA1 PCs located in the deep compared to superficial layer of stratum pyramidale. In turn, analysis of reciprocal connectivity revealed more frequent excitatory inputs to PVBCs by superficial PCs, demonstrating bias in target selection by both the excitatory and inhibitory local connections in CA1. Additionally, PVBCs further segregated among deep PCs, preferentially innervating the amygdala-projecting PCs but receiving preferential excitation from the prefrontal cortex-projecting PCs, thus revealing distinct perisomatic inhibitory interactions between separate output channels. These results demonstrate the presence of heterogeneous PVBC-PC microcircuits, potentially contributing to the sparse and distributed structure of hippocampal network activity.

INTRODUCTION

The mammalian hippocampus plays a critical role in learning and memory processes, by transforming input from associative neocortical regions and sending output primarily through long-distance projecting pyramidal cells (PCs) in the CA1 region. These outputs target a number of brain areas, including the medial prefrontal cortex (mPFC), medial entorhinal cortex (MEC), and amygdala (AMG) (Cenquizca and Swanson, 2007), potentially coordinating the interactions among brain areas during mnemonic functions (Maren and Quirk, 2004; Fanselow and Poulos, 2005). Heterogeneity across the CA1 PC population is recognized along the radial axis (superficial to deep), marked by differential expression of the neurochemical markers (e.g., calbindin and zinc; Figure 1A), and in long-range projection patterns (Baimbridge and Miller, 1982; Slomianka et al., 2011). Whereas the CA1 region as a whole is known to be the general output of the hippocampus proper, how the heterogeneous PCs integrate into the CA1 circuit remains unknown.

In particular, it is unclear what the nature of the relationship is between heterogeneity of PCs (Bannister and Larkman, 1995; Mizuseki et al., 2011; Deguchi et al., 2011; Graves et al., 2012) and the well-known diversity of local GABAergic hippocampal interneurons (Soltesz, 2005). Specifically, given the heterogeneous structural and functional properties of PCs in CA1, the question arises if all PCs are regulated by essentially identical local GABAergic circuits or whether hippocampal interneurons nonuniformly target specific subpopulations of CA1 PCs. The issue of heterogeneity in target selection by cortical interneurons is controversial. Some reports suggest that local GABAergic microcircuits in various cortical areas can be selective for different postsynaptic populations (Fariñas and DeFelipe, 1991; Yoshimura and Callaway, 2005; Bodor et al., 2005; Otsuka and Kawaguchi, 2009; Varga et al., 2010; Gittis et al., 2010; Viviani et al., 2011; Lee et al., 2014; for a review, see Krook-Magnuson et al., 2012). In contrast, others reported a lack of preference in target selection for a variety of neocortical interneurons, including parvalbumin- (Packer and Yuste, 2011) and somatostatin-positive interneurons (Fino and Yuste, 2011). The lack of clear evidence for or against the differential regulation of distinct subpopulations of CA1 PCs by local inhibitory circuits limits our understanding of hippocampal network operations.

Among local microcircuits of the hippocampus, the interactions between PCs and perisomatic-targeting, fast-spiking, parvalbumin-expressing basket cells (PVBCs) (Figure 1B) have been extensively studied and inexorably linked to hippocampal rhythmogenesis (for a review, see Buzsáki and Wang, 2012). The importance of these interneurons is also highlighted by the fact that PVBCs have been implicated, both within and outside the hippocampus, in local circuit operations, learning and memory, sensory processing, and critical period plasticity; aberrant PVBC activities may also be mechanistically linked to



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