Picher *et al.: Intrinsic Activity*, 2019; **7**(Suppl.1):A3.37
doi:10.25006/IA.7.S1-A3.37
published online: 11 September 2019

Joint Meeting of the Austrian Neuroscience Association (16th ANA Meeting) and the Austrian Pharmacological Society (25th Scientific Symposium of APHAR)

Innsbruck, 25–27 September 2019

MEETING ABSTRACT

A3.37

Intracellular characterization of CA3 PN activity during spatial navigation

Magdalena PICHER, Xiaomin ZHANG and Peter JONAS*

Institute of Science and Technology Austria (IST Austria), Klosterneuburg, Austria

Background: The hippocampal CA3 region plays an important role in episodic memory retrieval. Synapses between CA3 pyramidal neurons (PNs) are thought to be endowed with Hebbian synaptic plasticity to support the reactivation of neuronal ensembles during partial input stimuli, a phenomenon referred to as pattern completion [1]. However, the classical view of a homogeneous pyramidal neuron population that uniformly contributes to diverse cognitive functions of the hippocampus has been challenged recently [2]. The main arguments include an anatomical gradient in terms of functional properties and connectivity from dentate gyrus (DG), entorhinal cortex and CA3 interconnection along the proximo–distal axis within CA3 [3,4]. Moreover, a novel type of CA3 PNs was described, which lacks the input from DG granule cells and was proposed to be involved in sharp-wave generation [5]. However, the exact behavioral implication of the described CA3 PN heterogeneity *in vivo* and their role during cognitive functions remains enigmatic.
Methods: To shed light on cellular mechanisms and intrinsic parameters involved in CA3 PN activity, we combine intracellular patch-clamp with local-field-potential recordings in head-fixed mice navigating on a linear treadmill apparatus. While the animals run for a water reward, a series of somatosensory cues is presented, which allows the recording of sequential place-field activity. In order to correlate the anatomical position and morphological properties of CA3 PNs with their network and behavioral function, recorded neurons are filled with biocytin for *post hoc* morphological analysis.
Results: In a sample of 7 morphologically identified CA3 PNs, highly heterogeneous activity patterns were observed. Sub-threshold and supra-threshold activity include silent CA3 PNs receiving only sub-threshold EPSPs, spikelets, single spikes, short bursts of 3–4 APs with prolonged membrane potential (V_m) ramps, and complex spikes without preceding V_m ramps. In a subset of CA3 PNs (6 out of 20 cells), running induced hyperpolarization and converted bursting into single-spike activity (2 out of 20 cells). In another subset of CA3 PNs (4 out of 20 cells), locomotion mildly increased the mean action potential frequency. Finally, in 2 out of 20 cells, firing was unchanged.
Discussion: CA3 PNs in awake, running mice exhibit a wide range of subthreshold and suprathreshold activity patterns and are heterogeneously modulated during locomotion. This heterogeneity in V_m dynamics might suggest a differential role of CA3 PNs in pattern completion and other cognitive functions.
Acknowledgements: This project is funded by the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement no. 692692) to P.J.
Keywords: hippocampus – CA3 – spatial memory – *in vivo*

References

1. Guzman SJ, Schlögl A, Frotscher M, Jonas P: **Synaptic mechanisms of pattern completion in the hippocampal CA3 network.** *Science,* 2016; 353(6304):117–1123. doi:10.1126/science.aaf1836
2. Cembrowski MS, Spruston N: **Heterogeneity within classical cell types is the rule: lessons from hippocampal pyramidal neurons.** *Nat Rev Neurosci,* 2019; 20(4):193–204. doi:10.1038/s41583-019-0125-5
3. Sun Q, Sotayo A, Cazzulino AS, Snyder AM, Denny CA, Siegelbaum SA: **Proximodistal Heterogeneity of Hippocampal CA3 Pyramidal Neuron Intrinsic Properties, Connectivity, and Reactivation during Memory Recall.** *Neuron,* 2017; 95(3): 656–672.e3. doi:10.1016/j.neuron.2017.07.012
4. Kowalski J, Gan J, Jonas P, Pernía-Andrade AJ: **Intrinsic membrane properties determine hippocampal differential firing pattern in vivo in anesthetized rats.** *Hippocampus,* 2016; 26(5):668–682. doi:10.1002/hipo.22550
5. Hunt DL, Linaro D, Si B, Romani S, Spruston N: **A novel pyramidal cell type promotes sharp-wave synchronization in the hippocampus.** *Nat Neurosci,* 2018; 21(7):985–995. doi:10.1038/s41593-018-0172-7

*Corresponding author e-mail: *peter.jonas@ist.ac.at*