

Recent Advances in Network Electrophysiology Using Multi-Electrode Arrays

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NETWORK OSCILLATIONS STUDIED WITH PLANAR MULTIELECTRODE ARRAYS.

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High-frequency network oscillations in the beta-gamma frequency band (20-40 Hz) can be induced by cholinergic agonists in the hippocampus *in vitro* (Fisahn *et al.*, 1998). The advantages of utilising 64-electrode array recordings to explore the sites of electrogenesis and spatial distribution of oscillations have already been convincingly established. Shimono *et al.* (2000) showed that cholinergically-induced oscillations are generated in the CA3 and are associated with alternating apical dendritic and basal dendritic/somatic sink-source pairs. Here we confirm these previous results using the new high-density arrays (100 μm spacing), and thus support the hypothesis that there are no other local dipoles underlying the oscillation. However, establishing the sink-source distribution does not reveal the primary events driving the network oscillation – for example, rhythmic somatic inhibition and dendritic excitation could produce identical patterns of extracellular currents. In order to explore the network events driving the oscillation, we took advantage of the fact that MED recordings can easily be combined with other *in vitro* recording techniques, such as imaging and patch-clamp recordings. Firstly, we combined multi-electrode recordings with simultaneous imaging with voltage-sensitive dyes (Di-4-ANEPPS), and showed that during cholinergically-induced oscillations (25 μM carbachol), somatic current sources were associated with somatic hyperpolarisation which then spread into the dendrites. This was followed by a somatic depolarisation, which again gradually invaded the dendritic tree. There was no evidence of primary events in the apical dendrites, leading to the hypothesis that the basis of the cholinergic oscillations was a sustained inward current accompanied by rhythmic proximal inhibition. In order to test this hypothesis further, multi-electrode recordings were combined with patch-clamp recording of pyramidal neurons and visually identified interneurons. Somatic recording from pyramidal cells revealed a rhythmic membrane potential oscillation in which, again, somatic current sources were associated with somatic hyperpolarisation. Pyramidal neurons fired phase-related to the network oscillation, but not on every cycle. Cell-attached recording from GABAergic interneuron identified three distinct firing patterns: 1) Rhythmic firing on every cycle of the network oscillation, 2) rhythmic firing at 5-7 Hz, phase related to the network oscillation, and 3) rhythmic firing at 5-7 Hz, apparently without any phase relation to the network oscillation. Cells were subsequently filled with biocytin for anatomical identification, and morphological analysis is forthcoming. In conclusion, these data are consistent with a model of cholinergically-induced oscillations in which pyramidal neurons are tonically activated, and rhythmically inhibited by feedback fast-spiking interneurons targeting the perisomatic and proximal dendritic domains.

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Fisahn *et al.* (1998) *Nature* **394**, 186-189.

Shimono *et al.* (2000) *J Neurosci* **20**, 8462-8473.