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TRR 295 ReTune

Electrophysiological classification of human layer 2-3 pyramidal neurons reveals subtype-specific synaptic interactions.

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Understanding how large-scale brain signals emerge from underlying cellular activity remains a central challenge when translating neuron level mechanisms into therapeutic strategies. While human recordings in patients, such as LFP, ECoG or MEG, provide powerful access to network-level dynamics, the cellular and microcircuit mechanisms that generate these signals are still poorly understood. In this context, the present study by Planert et al. provides a fundamental contribution by resolving the functional diversity and synaptic connectivity principles in human cortical neurons.

Using high-throughput multineuron patch-clamp recordings in human temporal cortex, the authors characterized more than 1,400 neurons and over 1,400 synaptic connections. They identify four distinct electrophysiological subtypes of layer 2–3 pyramidal neurons, each defined by specific intrinsic properties, morphology, and connectivity patterns. Crucially, these subtypes form structured synaptic subnetworks with subtype-specific connectivity. This work demonstrates that pyramidal neurons in the human cortex are not homogeneous but are composed of functionally specialized neuron subtypes that differentially integrate and communicate information. For example, some subtypes preferentially receive many inputs and may act as integrators, whereas others form sparse but strong and short-term depressing synapses, suggesting roles in selective signal propagation. At the same time, synaptic properties exhibit substantial variability, indicating a rich parameter space for flexible computation within a structured framework. In a separate study on the same dataset, the authors have also identified directed and acyclic network properties of this network which can support more complex network computations (Peng et al., Science 2024). These studies show that neuronal diversity and structured connectivity directly translate into distinct computational properties within human cortical circuits.

From a ReTune perspective, this study provides a critical bridge across scales. The diversity of cellular subtypes and their synaptic interactions form the mechanistic substrate from which mesoscopic signals such as LFPs and macroscopic signals such as EEG or ECoG emerge. Understanding these cellular and synaptic principles is essential for interpreting patient recordings and for linking observed oscillatory patterns, such as beta or gamma activity, to underlying circuit mechanisms. Ultimately, this work lays a foundation for mechanistic models of cortical computation in humans. By revealing how specific neuron types contribute to circuit dynamics, it advances our ability to translate between cellular physiology and the network-level signals that could guide future brain-computer-interfaces and neuromodulation therapies such as deep brain stimulation.

Dr. Henrike Planert & Franz Mittermaier. They are two co-first authors of the study and use the multi-patch approach to study principles of synaptic physiology in human brain slices. Henrike Planert is a postdoctoral researcher, and Franz Mittermaier is a medical doctorate candidate with neurosurgical training, both at the Institute of Neurophysiology at the Charité.

Dr. Yangfan Peng & Prof. Jörg Geiger Peng & Geiger have co-led this study at the Institute of Neurophysiology, Charité Berlin. Geiger is the director of the Institute of Neurophysiology. Peng is a Emmy Noether group leader within the Movement Disorders and Neuromodulation Unit and the Institute of Cell and Neurobiology at Charité. He focus is on translating principles of cortical microcircuits across species and link those to in vivo population dynamics recorded using high-density electrodes.

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