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TRR 295 ReTune

Directed and acyclic synaptic connectivity in the human layer 2-3 cortical microcircuit.

Peng Y, Bjelde A, Aceituno PV, Mittermaier FX, Planert H, Grosser S, Onken J, Faust K, Kalbhenn T, Simon M, Radbruch H, Fidzinski P, Schmitz D, Alle H, Holtkamp M, Vida I, Grewe BF, Geiger JRP.
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Studying the properties of human neurons is an emerging field that is powered by the rare access to human tissue and aims to understand the unique computational capabilities of the human neocortex. One major determinant of computation in a neuronal network is its underlying synaptic connectivity. While long-range connections between brain regions are well established, the principles governing synaptic connectivity between neighboring neurons in the human brain is unknown.

Our previous understanding of synaptic connectivity in the neocortex is mostly based on findings from rodent studies. Those have shown that local excitatory neurons are strongly recurrently connected. This means that similarly tuned neurons prefer to connect to each other through reciprocal connections, going back and forth between them. These reciprocal connections also tend to be stronger, forming "Hebbian assemblies" with clustered connectivity. We discovered fundamental wiring principles of the human cortical microcircuit that contrast and go beyond these previous observations in rodents.

In this study, we characterized monosynaptic connections via multi-neuron patch-clamp recordings from acute human cortical brain slices. The tissue was obtained from anterior temporal lobectomy performed on temporal lobe epilepsy patients (n = 23). The unique access to this tissue for research was facilitated through the close collaboration between the Departments of Neurology, Neurosurgery, Neuropathology, Neuroanatomy and Neurophysiology at the Charité Berlin. The tissue was collected from the surgical theatre for immediate preparation and kept alive for up to 48 hours. We developed a semi-automated multi-neuron patch-clamp approach to simultaneously record up to ten neurons for high-throughput analysis. In total, we recorded 7,200 potential synaptic connections between 1,170 pyramidal neurons. In contrast to rodents, we found that reciprocal connectivity was not more common than expected in a random network. Instead, connections tend to be acyclic and directed. Through anatomical analyses we found that part of this directionality arises from spatially asymmetric connectivity, where neurons preferably connected onto deeper neurons. Such a directed connectivity implies feed-forward information flow within the layer 2-3 of the human cortex. Another striking difference to rodents was the independence of connection density and connection strength.

To explore the implication of these network features for neural activity and computation, we simulated different neural network models and trained them on machine learning tasks. Overall, our analytical and simulation results suggested that the identified principles increase the network state space and allow higher dimensional representations of local neuronal activity. This would provide an increased information capacity and the ability to process information on a longer timescale. To which extent these properties underlie the unique cognitive abilities of humans or represent a more general principle beyond the human temporal L2-3 cortex remains to be determined. ▪

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Yangfan Peng has performed the study as a postdoctoral researcher at the Institute of Neurophysiology, Charité Berlin. He is currently member of the Movement Disorders and Neuromodulation Unit at Charité Berlin. His research focuses on cortical microcircuits and cellular level understanding of population dynamics during movement.

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