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PRESS RELEASE

Secret structure in the wiring diagram of the brain

Researchers discover a hidden order in seemingly random connections between neurons

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Bonn, October 14, 2022 - In the brain, our perception arises from a complex interplay of neurons that are connected via synapses. But the number and strength of connections between certain types of neurons can vary. Researchers from the University Hospital Bonn (UKB), the University Medical Center Mainz and the Ludwig-Maximilians-University Munich (LMU), together with a research team from the Max Planck Institute for Brain Research in Frankfurt, as part of the DFG-funded Priority Program "Computational Connectomics" (SPP2041), have now discovered that the structure of the seemingly irregular neuronal connection strengths contains a hidden order. This is essential for the stability of the neuronal network. The study has now been published in the journal "PNAS".

Ten years ago, connectomics, that is the creation of a map of the connections between the approximately 86 billion neurons in the brain, was declared a future milestone of science. This is because in complex neuronal networks, neurons are connected to each other by thousands of synapses. Here, the strength of the connections between individual neurons is important because it is crucial for learning and cognitive performance. "However, each synapse is unique and its strength can vary over time. Even experiments that measured the same type of synapse in the same brain region yielded different values for synaptic strength. However, this experimentally observed variability makes it difficult to find general principles underlying the robust function of neuronal networks," says Prof. Tatjana Tchumatchenko, research group leader at the Institute of Experimental Epileptology and Cognitive Research of the UKB and at the Institute of Physiological Chemistry of the University Medical Center Mainz, explaining the motivation to conduct the study.

Mathematics and laboratory combined purposefully

In the primary visual cortex (V1), the visual stimuli transmitted by the eye via the thalamus, a switching point for sensory impressions in the diencephalon, are first recorded. The researchers took a closer look at the connections between the neurons that are active during this process. To do this, the researchers measured experimentally the joint response of two classes of neurons to different visual stimuli in the mouse model. At the same time, they used mathematical models to predict the strength of synaptic connections. To explain their lab-recorded activities of such network connections in the primary visual cortex, they used the so-called "stabilized supralinear network" (SSN). "It is one of the few nonlinear mathematical models that offers the unique possibility to compare theoretically simulated activity with actually observed activity," says Prof. Laura Busse, research group leader at LMU

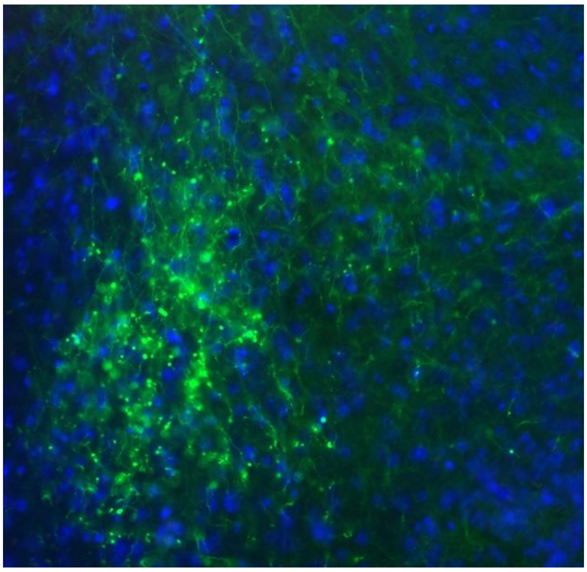
Neurobiology. "We were able to show that combining SSN with experimental recordings of visual responses in the mouse thalamus and cortex allows us to determine different sets of connection strengths that lead to the recorded visual responses in the visual cortex."

Sequence between the connection strengths is the key

The researchers found that there was an order behind the observed variability in synapse strength. For example, the connections from excitatory to inhibitory neurons were always the strongest, while the reverse connections in the visual cortex were weaker. This is because the absolute values of synaptic strengths varied in the modeling - as they had in the earlier experimental studies - but nevertheless always maintained a certain order. Thus, the relative ratios are crucial for the course and strength of the measured activity, rather than the absolute values. "It is remarkable that analysis of earlier direct measurements of synaptic connections revealed the same order of synaptic strengths as our model prediction based on measured neuronal responses alone," says Simon Renner, Ph.D., of LMU Neurobiology, whose experimental recordings of cortical and thalamic activity allowed characterization of the connections between cortical neurons. "Our results show that neuronal activity contains much information about the underlying structure of neuronal networks that is not immediately apparent from direct measurements of synapse strengths. Thus, our method opens a promising perspective for the study of network structures that are difficult to access experimentally," explains Nataliya Kraynyukova, Ph.D., from the Institute of Experimental Epileptology and Cognitive Research of the UKB and Max Planck Institute for Brain Research in Frankfurt. This study is the result of an interdisciplinary collaboration between the lab of Prof. Busse and Prof. Tchumatchenko, who worked closely together, building on the computational and experimental expertise of their labs.

Publication: Nataliya Kraynyukova*, Simon Renner*, Gregory Born, Yannik Bauer, Martin Spacek, Georgi Tushev, Laura Busse*, and Tatjana Tchumatchenko* [* shared first author; ** shared senior author]: In vivo extracellular recordings of thalamic and cortical visual responses reveal V1 connectivity rules; PNAS; https://doi.org/10.1073/pnas.2207032119

Visuals:



Caption: Neurons in the mouse visual system:
Green: genetically labeled inhibitory neurons. The aim of the published work was to use a mathamatic model of neuronal networks and the responses of neurons to visual stimuli to determine the connections between neuronal cell types.

Photo credit: UKB & LMU / Dr. Nataliya Kraynyukova; Dr. Simon Renner

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To the University Hospital Bonn:
In the UKB, around 500,000 patients are cared for each year, 8,800 staff are employed and the balance sheet total amounts to 1.5 billion euros. In addition to the more than 3,300 medical and dental students, a further 580 women and men are trained each year in numerous healthcare professions. The UKB is ranked first among university hospitals in NRW, has the third highest case mix index in Germany and was the only one of the 35 German university hospitals to increase its performance in the Corona years 2020 and 2021.

To the Ludwig Maximilian University of Munich (LMU):
LMU is one of the leading universities in Europe with a tradition of more than 500 years. It offers a broad spectrum of all fields of knowledge - the ideal basis for outstanding research and a challenging range of courses. It ranges from the humanities and cultural studies to law, economics and social sciences, medicine and the natural sciences. 18 percent of the 50,000 students come from abroad - from a total of 130 nations. The know-how and creativity of its scientists form the basis for the university's outstanding research record. LMU's success in all three phases of the Excellence Competition and its permanent promotion as an "Excellence University" impressively document the research strength of Munich University.

About the University Medical Center of the Johannes Gutenberg University Mainz
The University Medical Center of the Johannes Gutenberg University Mainz is the only medical institution of supra-maximum supply in the German state of Rhineland-Palatinate and an internationally recognized science location. Medical and scientific specialists at more than 60 clinics, institutes and departments work interdisciplinarily to treat more than 320,000 patients per year. Highly specialized patient care, research and teaching are inseparably intertwined. More than 3,500 medicine and dentistry students as well as around 700 future medical, commercial and technical professionals are trained in Mainz. With a workforce of approximately 8,700 colleagues the University Medical Center Mainz is one of the largest employers in the region and an important driver of growth and innovation. Find more information online at www.unimedizin-mainz.de/?L=1.