Minding the gap: International team defines spaces through which nerve cells communicate

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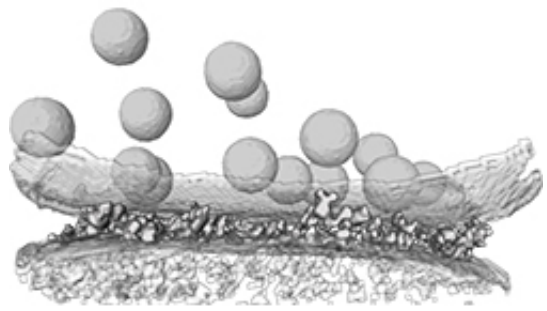

Intricate network of proteins that connects synapses, the sites of communication in the brain. Credit: Nikolas Schrod and Vladan Lucic, Max Planck Institute of Biochemistry

In a report published in the journal *Neuron*, an international team of researchers defined the makeup of the cellular structures through which nerve cells communicate with each other. These "synaptic clefts" are the small gaps between nerve cells (neurons) that relay information in the brain. Synapses, including the synaptic clefts, are formed rapidly shortly before and after birth. Mutations in the proteins that make up the cleft increase vulnerability to developmental disorders, notably autism spectrum disorders.

The research team set out to identify the molecular and structural organization of the synaptic cleft and the role of proteins that adhere to each other to hold the cleft together. To gain insight on the molecular level, the team examined the synaptic clefts in mice by studying two of the synapse-organizing proteins. They employed an array of the most advanced imaging techniques available including tomography and imaging below the diffraction limit of light.

"By illuminating how nerve cells are connected to each other, we are closer to understanding what organizational steps go awry in synaptic disorders that impair brain development," said senior author Thomas Biederer, Ph.D., from the Department of Neuroscience at Tufts University School of Medicine. He is also a member of the program faculties in Cell, Molecular & Developmental Biology, Cellular & Molecular Physiology, and Neuroscience at the Sackler School of Graduate Biomedical Sciences at Tufts.

This work is the first study to quantitatively define the macromolecular organization of the synaptic cleft. Taken together, the results support the novel concept that the synaptic cleft is comprised of structurally and molecularly diverse sub-compartments, and that its components can be dynamic.

"What surprised me most was the cloud-like formations of synaptic adhesion complexes at the perimeter of the cleft," said Biederer. "These proteins form quite beautiful structures at synapses that have never been seen before. Given that there are genetic mutations in synaptic adhesion proteins that are linked to autism, these findings enable research into how these mutations change the structure and hence the function of synapses."

Among the behavioral alterations that the researchers suspect may be related to the structure and dynamics of the synaptic cleft is the ability to learn and access memory, as well as an increased risk for drug addiction.

More information: Perez de Arce et al., Topographic Mapping of the Synaptic Cleft into Adhesive Nanodomains, *Neuron* (2015), dx.doi.org/10.1016/j.neuron.2015.11.011

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