Researchers discover mechanism that allows rapid signal transmission between nerve cells

December 14 2017

Researchers at Charité's NeuroCure Cluster of Excellence have successfully identified the mechanism behind rapid signal transmission. Their work, published in the current issue of *Nature Neuroscience*, shows that bridging by a specific protein is responsible for this high speed of transmission.

The manner in which individual nerve cells communicate is fundamental to human brain function. Signal transmission occurs via highly complex contact points called synapses. Here, incoming signals effect the release of transmitters from stores known as vesicles, which fuse with the adjoining cell membranes in order to transmit the signal. This fusion is only possible once vesicles and membranes have been brought into close enough proximity; here, speed is everything.

"In short, the distance between the synaptic vesicle and the membrane is a major barrier to rapid fusion," explains the article's corresponding author, Prof. Dr. Christian Rosenmund of the Institute of Neurophysiology and the NeuroCure Cluster of Excellence. While the protein synaptotagmin had been known to play an important role in determining the speed of signal transmission, the nature of the underlying mechanism had previously remained unclear. "We have now found that synaptotagmin is capable of pulling the synaptic vesicles closer to the membrane within a matter of milliseconds. It does this by acting like a double-sided sticky tape, forming a bridge between the vesicle and the membrane," says Prof. Rosenmund, further explaining that fusion can only occur once this bridge has been formed.

The electron microscopy-based method developed by Prof. Rosenmund was integral to this research, as it allowed researchers to break down in slow motion processes that normally last only milliseconds. The findings themselves were purely coincidental. Dr. Shuwen Chang, a researcher at the Rosenmund Lab and the study's first author, was meant to use the new electron microscopy-based method for the direct visualization of the vesicle-membrane fusion process. "As it all happens so quickly, we were looking for ways to slow down the process of fusion," says Dr. Chang. The team decided to reduce the speed of fusion by removing synaptotagmin from the equation. They were surprised to find that this not only slowed the process of fusion, but also resulted in vesicles and membranes remaining farther apart.

There are a number of neurological diseases known to develop as a result of mutations affecting the synaptotagmin protein. The researchers are planning to conduct further experiments in the hope of establishing whether these mutations also affect the speed of vesicle fusion and, consequently, the speed at which nerve cells communicate.

More information: Shuwen Chang et al, Synaptotagmin-1 drives synchronous Ca2+-triggered fusion by C2B-domain-mediated synaptic-vesicle-membrane attachment, *Nature Neuroscience* (2017). DOI: 10.1038/s41593-017-0037-5

Provided by Charité - Universitätsmedizin Berlin