TOOLBOX

Suite of methods yields complex model of neuronal junctions

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Browser not compatible.

Researchers debuted a three-dimensional model of an average **synapse**, the point of connection between neurons, in the 30 May issue of *Science*[1].

The researchers analyzed proteins on the presynaptic side — the part of the synapse that sends signals to other neurons. This region is crowded with proteins that aid in releasing chemical messengers via tiny bubbles called vesicles.

Defects in **synaptic proteins have been implicated** in multiple disorders, **including autism**. But scientists have not had access to detailed information on the number of each protein type or their locations relative to each other.

The researchers isolated neuron endings from rat brains, focusing on the cortex — which is responsible for language, memory and consciousness — and the cerebellum, which is involved in movement and cognitive processes.

To determine the quantity of each type of synaptic protein, the researchers separated the proteins using gel electrophoresis and labeled them with antibodies,a method called quantitative immunoblotting.They also counted protein copies using mass spectroscopy.

To estimate the locations of proteins, the researchers used super-resolution fluorescence microscopy, a relatively new form of light microscopy that lets people see unprecedentedly small structures.They used electron microscopy to identify the general shape of the neuron endings.

With this suite of methods, the researchers found that there are considerably more copies of proteins involved in the release of synaptic vesicles than in the process by which the neuron takes up used vesicles again.

They speculate that there are so many protein copies related to synaptic vesicle release because it must happen reliably and quickly whenever a neuron fires. Recycling vesicles can happen at a more leisurely pace.The researchers are making similar models of synapses from smaller, more localized slices of the cortex, a first step in the longer process of figuring out how protein number and organization vary in synapses across the brain.

They are also modeling synaptic protein abundance and distribution in brains affected by Alzheimer's and Parkinson's diseases, and comparing these models to their own reference model of a healthy synapse.

REFERENCES:

1. Wilhelm B.G. *et al. Science* **344**, 1023-1028 (2014) **PubMed**