Collaboration between crucial proteins in signal transmission clarified

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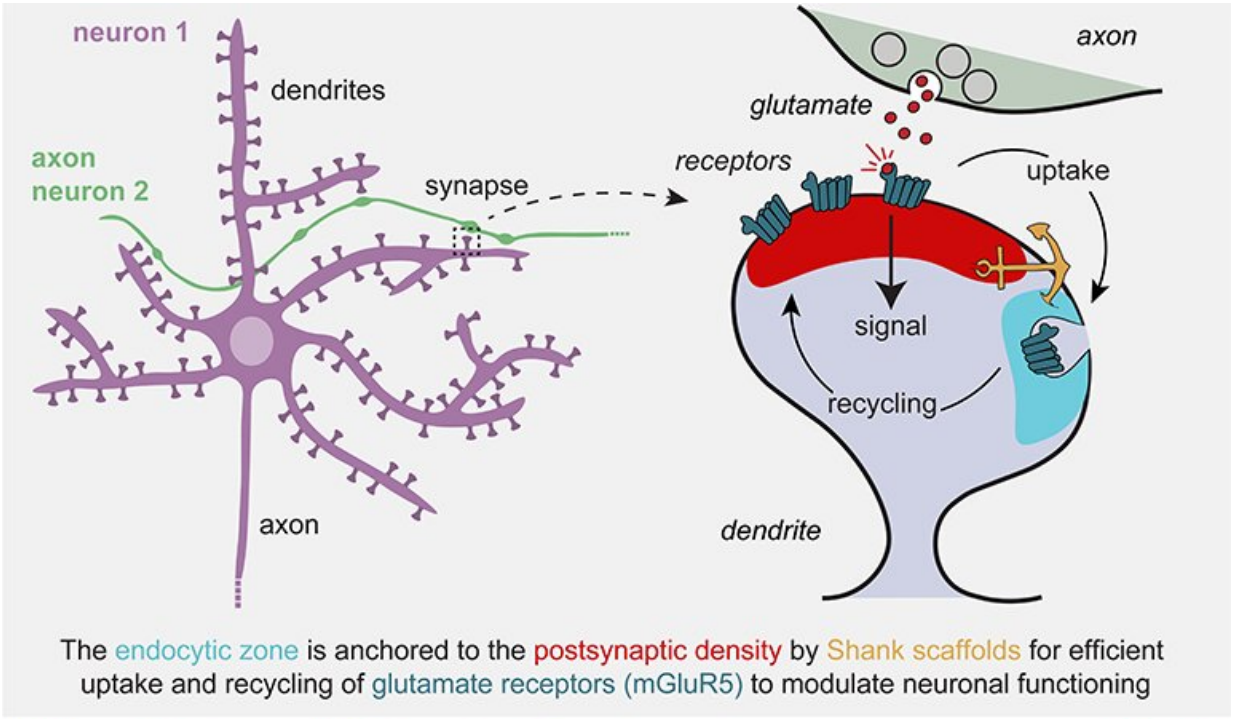
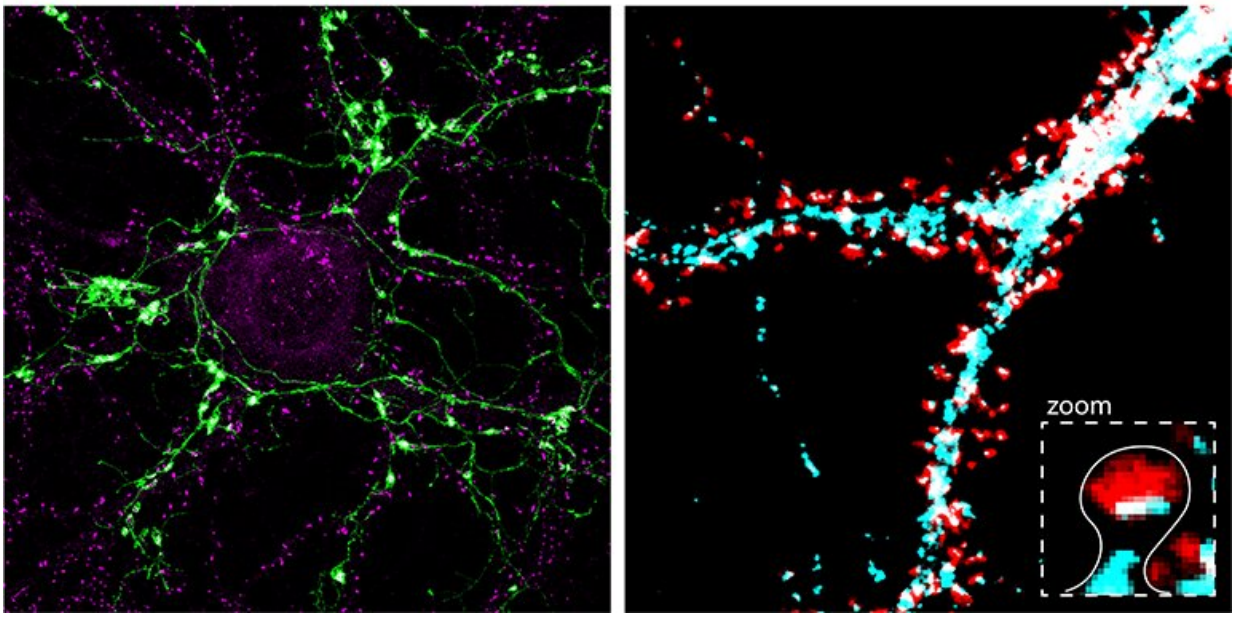




Receptor uptake and reclycling. Credit: Nicky Scheefhals/ Utrecht University

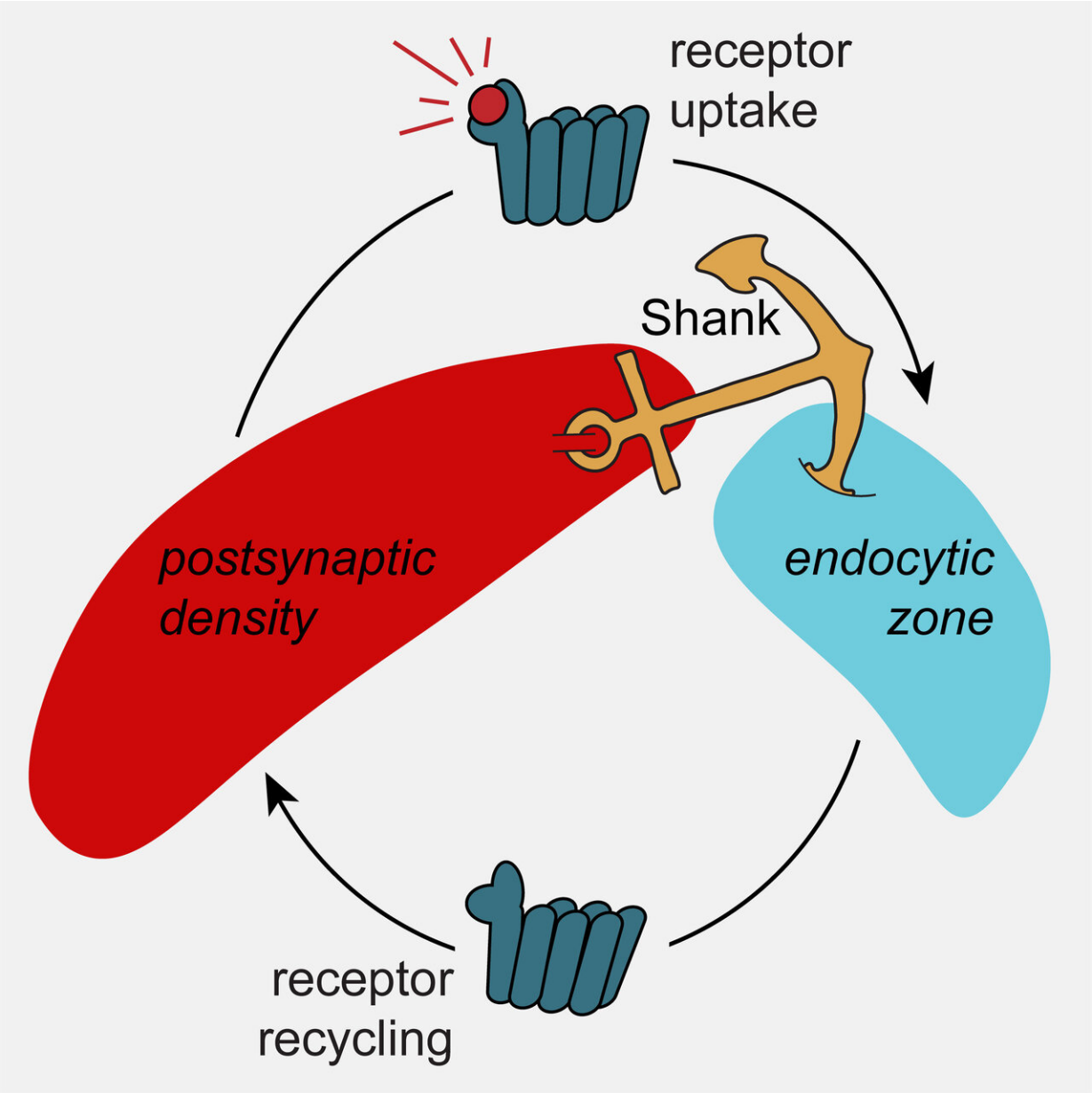
Researchers from Utrecht University have clarified the function of proteins that play a role in signal transmission between neurons. Without

these proteins, it is more difficult to pass on nerve stimuli, which may play a role in neurological disorders such as autism. The researchers will publish their findings in *Cell Reports* on 8 October.

Neurons communicate with one another via synapses, the contact site between two neurons where the signal is transferred from the axon to the receiving dendrite. The axon sends the signal by releasing synaptic vesicles filled with the neurotransmitter glutamate. The neurotransmitters then activate the receptors at the postsynaptic density on the receiving dendrite. With this, the signal is transferred and initiates a signal cascade in the receiving neuron. However, in order to prevent overstimulation in the receiving neuron, it is important that the activated receptors are rapidly deactivated.

Recycling

Researchers in Utrecht have now published an article in *Cell Reports* explaining how this process works. The deactivation of the receptors takes place in the endocytic zone, an area for the uptake and recycling of glutamate receptors (mGluR5). The protein Shank plays a crucial role in this process. "Shank works like an anchor that holds together the postsynaptic density and the endocytic zone", explains first author Nicky Scheefhals of Utrecht University. "When we remove Shank, the recycle centre is disconnected, resulting in the mis-sorting of receptors and fewer receptors are recycled to the postsynaptic density." As a result, it is more difficult to transfer nerve stimuli.



Receptor uptake and reclycling. Credit: Nicky Scheefhals/ Utrecht University

Autism

The balance in the uptake and recycling of receptors is crucial for the proper communication between neurons. "If there are too many or too

few receptors, then it could result in neurological disorders", says last author Harold MacGillavry of Utrecht University. The protein Shank had already been associated with autism, but scientists previously thought that Shank formed an 'anchor' in another way than the researchers demonstrate in this research. Until now, medicines that bind to the receptors have had only limited success. "Clarifying the precise mechanism is vital for the development of medicines that intervene in this process. And thanks to this research, we're now a step closer towards reaching this goal."

More information: Nicky Scheefhals et al. Shank Proteins Couple the Endocytic Zone to the Postsynaptic Density to Control Trafficking and Signaling of Metabotropic Glutamate Receptor 5, *Cell Reports* (2019). DOI: 10.1016/j.celrep.2019.08.102

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