Study presents new insights in the search for treatments for neurological diseases

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A team of researchers led by professor Patrik Verstreken (VIB/KU Leuven) has exposed the fine details of a mechanism that provides more insight in the communication between neurons. The research has clarified how damaged synapses - the connection points between neurons - are repaired to keep communication between neurons at an optimal level. Disturbances in these mechanisms are believed to play a role in the development of neurodegenerative diseases, such as dementia, ALS or Parkinson's disease.

The results have been published in leading neuroscience journal *Neuron*.

Our brains are made up of billions and billions of nerve cells or neurons that gather and transmit signals via so-called synapses. These synaptic connections between neurons transmit 'electrical firings' via chemical messengers (neurotransmitters). Synapses thus contribute to numerous bodily functions, including speech, thoughts and voluntary actions.

Disruption of synaptic transmission

Prof. Patrik Verstreken (VIB/KU Leuven): "Synapses are the active part of neurons, and this activity causes some damage in the long term. Fortunately, synapses are capable of breaking down and 'recycle' damaged cellular components. Our study has largely revealed the process behind this. It is quite a significant discovery, especially when you consider that many neurological diseases, such as Parkinson's, ALS or

dementia, but also speech or motion disorders for instance, are caused by the disruption of synaptic transmission."

Cellular debris

Prior research revealed that several different proteins play a role in neuronal communication. However, these same proteins can also cause disruptions. This happens, for instance, when proteins split, causing their particles to stick together and clump. This 'cellular debris' then disrupts synaptic transmissions and may contribute to the development of neurodegenerative diseases.

The importance of 'microautophagy'

Prof. Patrik Verstreken (VIB/KU Leuven): "We studied the proteins involved, both in vitro and in vivo and, in doing so, exposed a mechanism called 'synaptic microautophagy'. This mechanism helps 'clean up' cellular debris at the synapse, by engulfing the debris in a membrane and then removing it, for instance. It ensures that the cellular debris is isolated from the rest of the synapse. We found that synaptic communication slows down when microautophagic activity is reduced (i.e. when the cellular debris is not broken down) and that it speeds up when microautophagic activity increases (when more cellular debris is broken down). This discovery therefore represents an important advance in the search for treatments for neurodegenerative diseases, such as Alzheimer's - which are caused by clumped together cellular debris."

Pathways for further research

The study conducted by prof. Verstreken and his team once again emphasizes the need for ongoing research into neuronal communication. Such research could examine substances that may counteract the

progress of neurodegeneration in neurons. This would aid the search for potential drug treatments for neurological diseases, such as Alzheimer's.

More information: Hsc70-4 deforms membranes to promote synaptic protein turnover by endosomal microautophagy, Uytterhoeven et al., *Neuron* 2015

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