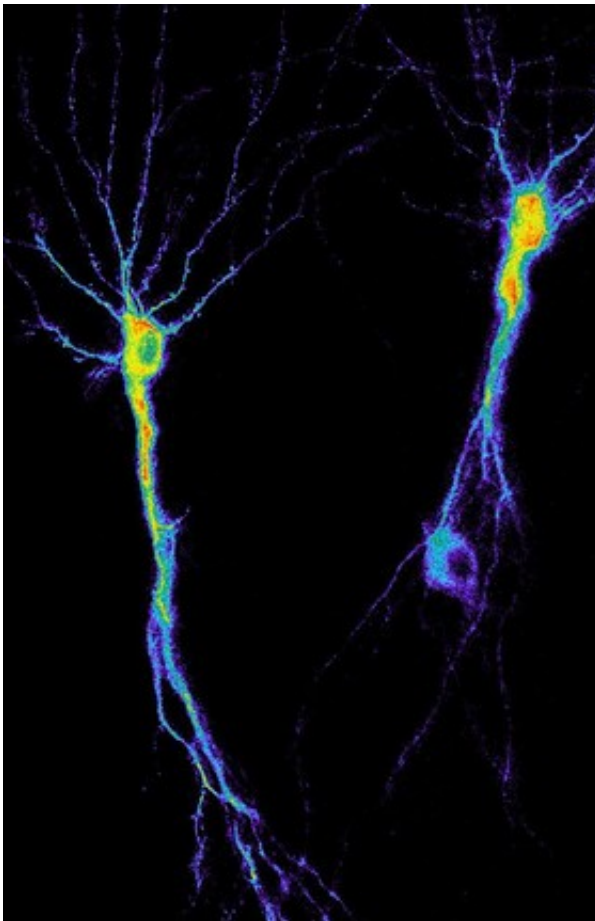


Aberrant Tau proteins put neuronal networks to sleep

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The current study shows that Tau aggregates attenuate neuronal activity. In the above image two neurons are depicted. Credit: DZNE/Frank Dennissen

The brain could easily be compared to the internet. In both networks

information is transmitted from one unit to the next with numerous units making up the network. Unlike computers, neurons are interconnected by axons, thin biological wires which can be as long as one meter. A protein called Tau normally helps in maintaining axonal integrity by stabilizing the tracks which are necessary to transport cellular components within the axon. However, Tau goes astray in multiple neurodegenerative diseases like Alzheimer's and other "tauopathies". Here it starts to aggregate into tiny fibers or clumps, which can corrupt neuronal function. However, the underlying mechanisms are poorly understood and there is therefore no effective treatment.

Now, researchers at the DZNE and the caesar research center led by Eva-Maria and Eckhard Mandelkow shed new light on the pathological processes that involve Tau proteins. As they report in the *Proceedings of the National Academy of Sciences (PNAS)*, under pathological conditions, small aggregates of Tau accumulate in the axons. As a result, [neuronal activity](#) is attenuated but neurons do not die and do not seem to be seriously ill. The aggregates only let neurons, so to say, doze off. However, the researchers also found a potential antidote: A drug called "Rolofylline". It re-establishes neuronal activity despite of the production of pathological Tau. Rolofylline works by enhancing signal transmission and reception which strengthens the communication between nerve cells. Consequently, Rolofylline alleviates learning and memory deficits in mice that express the aberrant Tau protein, as the scientists have revealed.

Rolofylline was originally devised to treat renal dysfunction in human heart failure patients. The drug binds to a subset of cellular sensors called "adenosine A1 receptors". Thereby, signal pathways are blocked, that otherwise would down-regulate neuronal network activity. Patients with [neurodegenerative diseases](#) might benefit from this. "Our results suggest that Rolofylline could potentially be useful to treat neuronal dysfunctions that occur in tauopathies. This makes the drug a hot

candidate for further studies. As an analogy, the Tau aggregates resemble a concrete wall in the middle of the room which blocks a WiFi signal. Rolofylline seems to work as a WiFi booster that can re-establish the connection despite of the obstruction", says Frank Dennissen, a member of the Mandelkow Lab and first author of the current paper.

More information: Frank J. A. Dennissen et al, Adenosine Areceptor antagonist rolofylline alleviates axonopathy caused by human Tau Δ K280, *Proceedings of the National Academy of Sciences* (2016). [DOI: 10.1073/pnas.1603119113](https://doi.org/10.1073/pnas.1603119113)

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