Analysis and modeling of functional connectome and tau burden in Alzheimer's disease

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Abstract

Accumulation of intraneuronal tau-tangles is a hallmark of Alzheimer's Disease (AD). Tau proteins aggregate in the neurons in form of tangles, affecting neuronal function and leading to neuronal death. Whereas the tau-tangles in the brain of AD patients has been known for more than a century, only recently information has been collected indicating that they may travel from one neuron to another, inducing tangles in neighboring neurons in a prion-like fashion. Gaining further evidence on tau-pathology in AD along brain networks is essential to better understand disease pathomechanisms and to predict the future course of disease.
For the analysis of the complex interplay between tau burden and the complexity of brain networks, we apply in [WB] a graph-theoretical approach similar to [C]. Brain regions and their functional connections are modeled as weighted graph and network architecture is described using graph metrics such as weighted degree and weighted participation coefficient. By this, densely connected hub regions can be identified and analyzed in view of tau-pathology. Furthermore, a comparison to healthy network architecture investigates possible effects of tau burden on network connectivity.
Our results reveal a positive correlation between pathology and weighted degree suggesting that high connectivity is associated with increased tau pathology. Hence the trans-neural spread mechanism is supported by our analysis. This spread mechanism now justifies the modeling of disease propagation as network diffusion process.

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References

[C] T. E. Cope et al., Tau burden and the functional connectome in Alzheimer's disease and progressive supranuclear palsy, Brain (2018), p.550-567. https://doi.org/10.1093/brain/awx347.

[WB] A.Weller, G. Bischof, P. Schlüter, N. Richter, J. Kukolja, B. Neumaier, A. Drzezga, A. Kunoth, Y. Shao, T. van Eimeren. *Graph theoretical analysis of tau burden and the functional connectome in Alzheimer's disease.* Poster presented at 2nd Molecular Imaging of Neurodegeneration in Cologne Symposium, Cologne, Oct. 2018.