New aspects of globular glial tauopathy could help in the design of more effective drugs

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Dr. Isidre Ferrer. Credit: Isidre Ferrer

Tauopathies are a group of neurodegenerative diseases characterized by the accumulation of phospho-tau—in other words tau associated to phosphate groups. Globular Glial Tauopathy, as well as Alzheimer's, are members of this large group. It is characterized by the accumulation of phospho-tau in neurons and by the formation of protein inclusions in glial cells astrocytes or oligodendrocytes. The majority of these kinds of tauopathies are spontaneous, but some of them are caused by specific mutations.

This study published in *Acta Neuropathologica* journal, was led by Dr. Isidre Ferrer, from Bellvitge Biomedical Research Institute (IDIBELL), Medicine and Health Science Faculty from Barcelona University (UB) and Bellvitge Hospital (HUB), with the collaboration of Dr. José Antonio del Río from Institute for Bioengineering of Catalonia (IBEC) and Biology Faculty from UB, both of them are members of Neuroscience Institute (UBNeuro) from UB. They studied several cases of patients with various kinds of tauopathy, genetic or spontaneous. The study shows that the addition of phosphate groups is not specific to tau—many other proteins are abnormally phosphorylated. This hyperphosphorylation induces protein disfunction and accumulation, which generates cell damage. Navarra Hospital also participates in these observations performing the proteomic and phosphorylation analysis.

Another relevant aspect of the study is that protein accumulation not only affects neurons but glial cells associated with them are also impaired, specifically astrocytes and oligodendrocytes. Glial cell affectation could promote the loss of some neural connections. Moreover, these inclusions can travel neuron to neuron or glial cell to glial cell, which facilitates the damage spreading to other cerebral regions.

These findings provide new information for the design of new drugs that stop disease progression. Firstly, new drugs must act in other proteins apart from tau since tau is not the only protein with increased phosphorylation. On the other hand, a new player has emerged on the scene: glial cells that not only are interfering in the cerebral damage, but also participate in the spreading of protein inclusions. Finally, new drugs that stop cellular transmission of protein inclusions could be an interesting target for this disease.

More information: Isidro Ferrer et al, Familial globular glial tauopathy linked to MAPT mutations: molecular neuropathology and seeding capacity of a prototypical mixed neuronal and glial tauopathy, *Acta Neuropathologica* (2020). DOI: 10.1007/s00401-019-02122-9

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