Deciphering brain connections between amyotrophic lateral sclerosis and frontotemporal dementia

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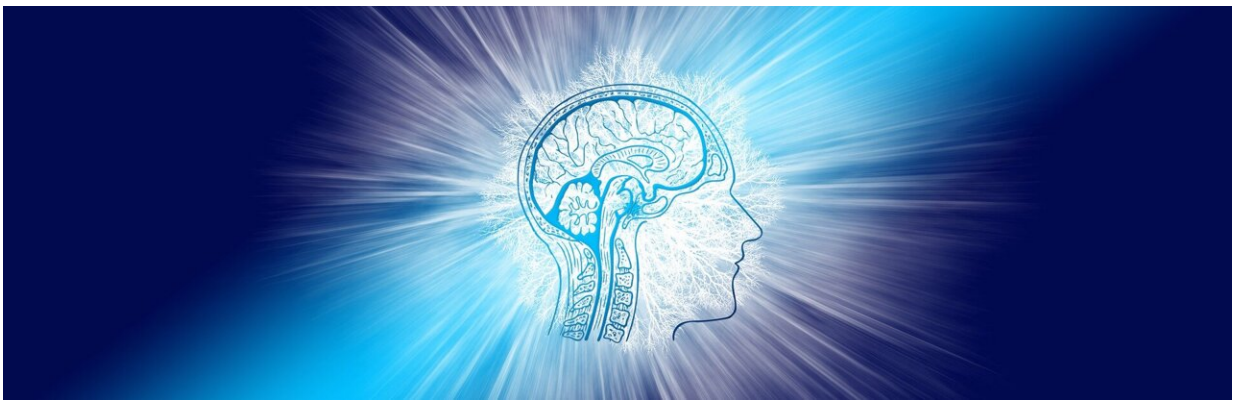

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A group of scientists from various hospitals and research centers in Catalonia have published a study in the journal *Brain* that reveals connections between two devastating brain diseases: amyotrophic lateral sclerosis (ALS) and frontotemporal dementia.

Led by Drs. Álvaro Carbayo and Ricard Rojas, researchers from the Neuromuscular Diseases Group at the Sant Pau Research Institute, in collaboration with Dr. Sergi Borrego-Écija and Dr. Ellen Gelpi from the Alzheimer's Disease and other Cognitive Disorders Group and the Neurological Tissue Bank of IDIBAPS, the study examines the

relationship and the full spectrum of these two neurodegenerative diseases, which share more similarities than initially thought.

ALS, a disease affecting motor neurons, and frontotemporal dementia, characterized by cognitive and behavioral problems, exhibit a common but highly heterogeneous clinical, genetic, and pathological spectrum, as explained by Dr. Ricard Rojas, researcher at IR Sant Pau and head of the Neurodegenerative Diseases Unit at the Neurology Service of Sant Pau Hospital.

Clinical studies revealed that up to 50% of ALS patients may develop cognitive and behavioral symptoms, with 10 to 15% specifically meeting diagnostic criteria for frontotemporal dementia.

Now, through neuropathological examination of a large series of ALS cases, it has been discovered that the actual figure may be much higher: 35.5% of cases also presented pathological features of frontotemporal dementia.

Findings show that the pathological aggregation of the TDP-43 protein was present in 93.6% of ALS cases and was more extensive in those with the coexistence of frontotemporal dementia pathology.

While it is known that most cases share the presence of TDP-43 protein aggregates, the study highlights the marked heterogeneity of neuropathological characteristics, suggesting possible different pathophysiological mechanisms. It's important to note that, currently, the identification of these proteins is done post-mortem, in the absence of a precise biomarker.

"Neuropathological studies and correlation with clinical characteristics help us expand our knowledge of the basis of diseases such as ALS and frontotemporal dementia, opening doors to future studies on biomarkers

and specific therapies," says Dr. Carbayo, the study's lead author.

The research included all cases that met the neuropathological criteria for frontotemporal dementia from the Neurological Tissue Bank of the FRCB-IDIBAPS-Clinic Hospital of Barcelona between 1994 and 2022, regardless of their final clinical diagnosis.

Clinical and neuropathological data were retrospectively reviewed, allowing analysis of the main clinical, genetic, and pathogenic characteristics, comparing patient groups with and without pathological changes of frontotemporal dementia, attempting to define specific subgroups.

"We have observed astonishing heterogeneity in the clinical presentation and pathological and genetic characteristics of patients, with a higher frequency of frontotemporal dementia than described in other series," says Dr. Carbayo.

From his perspective, these results emphasize the importance of interdisciplinary collaboration between ALS and frontotemporal dementia professionals and units.

"It is crucial that we work together to better understand this spectrum of neurodegenerative diseases and to better care for our patients. In fact, at Sant Pau, we have been working with this structure for six or seven years," concludes Dr. Carbayo.

More information: Álvaro Carbayo et al, Clinicopathological correlates in frontotemporal lobar degeneration: motor neuron disease spectrum, *Brain* (2024). DOI: 10.1093/brain/awae011

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