

## **Behavioral subphenotypes and their anatomic correlates in neurodegenerative disease**

Ashlin R. K. Roy, Samir Datta, Emily Hardy, Virginia E. Sturm, Joel H. Kramer, William W. Seeley, Katherine P. Rankin, Howard J. Rosen, Bruce L. Miller, David C. Perry

Patients with neurodegenerative disorders experience a range of neuropsychiatric symptoms and the neural correlates have been explored for many individual behaviors, such as apathy or disinhibition. Atrophy patterns have been associated with broadly-recognized syndromes that bring together multiple symptoms, such as the behavioral variant of frontotemporal dementia. However, there is substantial heterogeneity of symptoms, with partial overlap of behavior and affected neuroanatomy in dementia subtypes. It is not well established if there are anatomically-distinct behavioral subphenotypes in neurodegenerative disease. The objective of this study was to identify shared behavioral profiles in frontotemporal dementia-spectrum and Alzheimer's disease-related syndromes and determine the neural correlates of these symptom clusters.

Two hundred and eighty-one patients diagnosed with one of seven different dementia syndromes, in addition to healthy controls and individuals with mild cognitive impairment, completed a 109-item assessment capturing the severity of a range of clinical behaviors. A principal component analysis was used to capture distinct clusters of related behaviors. Voxel-based morphometry analyses were used to identify regions of volume loss associated with each component.

Seven components were identified and interpreted as capturing the following behaviors: Component 1 - emotional bluntness, 2 - emotional lability and disinhibition, 3 - irritability and anxiety, 4 - rigidity and impatience, 5 - indiscriminate consumption, 6 - psychotic behaviors, and 7 - Geschwind Syndrome-related behaviors. Correlations with structural brain volume revealed distinct neuroanatomical patterns associated with each factor, including after controlling for diagnosis.

Localized neurodegeneration can lead to the development of behavioral symptom clusters across various dementia syndromes.

### **Conflicts of interest**

N/A