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Progressive supranuclear palsy finally has a clinically measureable τ abnormality

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Definitive biomarkers for both differentiating neurodegenerative diseases and monitoring their progression over time are sorely needed. This has become particularly crucial for the development of therapies targeting core disease mechanisms.[2] β-Amyloid (Aβ) and associated biomarkers have revolutionised current thoughts and theories on Alzheimer's disease (AD) with the hope that significant advances in clinical therapies can now be achieved.[2] The most significant change is their use to detect asymptomatic disease due to many disappointing clinical trials in definitively diagnosed symptomatic patients.[3] This change in thinking has only been possible in AD due to advances in imaging and peripheral biomarker research and their application in diverse population settings.[4] To date the identification of definitive biomarkers for other neurodegenerative diseases has been allusive.

The study by Wagshal *et al*[1] identifies a potential biomarker for patients with progressive supranuclear palsy (PSP). PSP deposits abnormal τ protein in the brain, and therefore is considered a primary tauopathy.[5] The τ protein also deposits in the brain of patients with AD and biomarker research for this disease has developed a range of tools for the detection of τ now recommended for clinical use.[4] The application of these tools to primary tauopathies has received less attention, but considering their disease processes differ from those of AD, further work in this area is particularly welcome. Unlike AD, PSP is characterised pathologically by τ deposition in astrocytes and other glia as well as in neurons,[5 6] and the location of this pathology produces heterogeneous clinical phenotypes of atypical parkinsonian syndromes[7 8] as well as frontotemporal dementia syndromes.[6] This clinical diversity of PSP affects knowledge on the true prevalence and risk factors for PSP, with no treatments for any of its phenotypes. Further research on how to find and treat its core pathology is a priority.

Wagshal *et al*[1] show that cerebrospinal fluid (CSF) analysis of τ using ELISAs can differentiate patients with PSP from normal controls and patients with AD, as patients with PSP have reduced measures of CSF τ levels. This was apparent even in a small sample (24 with PSP, 37 with AD and 26 controls) suggesting that the technique may be applicable to individuals in a clinical setting. If replicable, these findings of a different biomarker signature for the core pathology of PSP from that of AD could be used in a similar way to the Aβ and τ biomarkers proposed for AD[4] and significantly advance knowledge of this diverse clinical condition. Additionally, this difference in CSF τ between PSP and AD confirms the significantly different disease mechanisms underlying these disorders, a clinical finding which can now be researched further and followed longitudinally. As τ therapies are already in clinical trials largely although not exclusively targeting AD,[9–11] the potential differences between the disease mechanisms affecting τ in PSP versus AD may indicate the need for separately focused therapeutic development. Importantly, the majority of preclinical develop has occurred using τ animal models similar to those for PSP[9 10] and therefore may be most appropriate for patients with pathological PSP. Regardless, the identification of reduced τ levels in PSP gives a clear target for any restorative treatments for this disorder, and the impact of this finding on therapeutic treatment development should not be underestimated.

The hunt for objective biomarkers for neurodegenerative disorders is starting to pay dividends, with a reduction rather than increase in CSF τ levels identified by Wagshal *et al*[1] in patients with progressive supranuclear palsy (PSP).

Competing interests None.

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