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Biomarker-Based Stratification For Alzheimer’s Disease Diagnosis

Alzheimer’s disease (AD) and 4-repeat tauopathies (4RTs) represent two distinct types of neurodegenerative diseases characterised by abnormal tau protein aggregation. While advances in biomarker research have revolutionised AD diagnosis, there remains a significant challenge in accurately diagnosing 4RTs, such as progressive supranuclear palsy (PSP) and corticobasal syndrome (CBS). The recent study titled “Combining cerebrospinal fluid and PI-2620 tau-PET for biomarker-based stratification of Alzheimer's disease and 4R-tauopathies” proposes an innovative biomarker-based algorithm for better distinguishing these diseases. The study discusses how cerebrospinal fluid (CSF) and tau-PET imaging are utilised for differentiating AD from 4RTs, the significance of tau protein distribution patterns, and the potential implications for improving diagnostic workflows and clinical trials.

Biomarkers in Alzheimer’s Disease

The presence of tau and amyloid plaques in the brain is one of the hallmark features of Alzheimer’s disease. Biomarker studies focusing on amyloid and tau proteins have enabled in vivo detection of AD, making it possible to stratify patients more precisely based on their molecular pathology. Recent advancements in positron emission tomography (PET) imaging and cerebrospinal fluid (CSF) analysis allow for early detection of tau aggregates and their progression, helping in staging the disease according to the Amyloid/Tau/Neurodegeneration (ATN) model. In Alzheimer’s disease, tau aggregates primarily in the cortical regions, contributing to cognitive impairments characteristic of the condition. These biomarkers, particularly CSF p-tau181 and total tau (t-tau), exhibit elevated levels in AD patients, distinguishing them from other tauopathies.

Challenges in Diagnosing 4R-Tauopathies

In contrast to Alzheimer’s disease, the diagnosis of 4-repeat tauopathies (4RTs) such as progressive supranuclear palsy (PSP) and corticobasal syndrome (CBS) has been largely dependent on clinical criteria and imaging studies, with no definitive biomarkers being widely available. These diseases are characterised by abnormal aggregation of tau isoforms in the brainstem and subcortical regions. Patients with 4RTs exhibit symptoms such as motor dysfunction and cognitive impairments, yet their tau protein aggregates are mainly confined to the basal ganglia. While tau-PET imaging has shown promise in detecting these tau aggregates, the lack of well-established biomarkers has hindered the effective stratification of these patients in clinical settings. Introducing the PI-2620 tau-PET tracer, which can bind specifically to 4R-tau deposits, provides an exciting avenue for improving in vivo diagnosis.

Combining CSF and Tau-PET for Better Diagnosis

The novel approach proposed in the study emphasises the importance of combining cerebrospinal fluid biomarkers with 18F-PI-2620 tau-PET imaging to differentiate between Alzheimer’s disease and 4R-tauopathies. The study found that elevated CSF p-tau181 and tau binding in cortical areas were characteristic of AD, while normal CSF p-tau181 with increased subcortical tau binding was more indicative of 4RTs. This distinction is crucial because it allows for more accurate diagnoses, particularly when clinical symptoms overlap between the two conditions. Additionally, the research demonstrated that posterior cortical hypoperfusion could be used as an additional biomarker of neuronal injury in AD, further aiding in disease stratification. Integrating both CSF and PET data enables a more refined biomarker-guided algorithm that could lead to more personalised patient treatment plans.

Conclusion

The findings presented in the study highlight the potential of combining cerebrospinal fluid biomarkers and tau-PET imaging in enhancing the diagnostic accuracy for Alzheimer’s disease and 4R-tauopathies. By identifying specific patterns of tau distribution in the brain, the biomarker-based algorithm offers a significant improvement over traditional clinical methods, enabling more precise differentiation between these diseases. This approach not only advances diagnostic workflows but also holds promise for facilitating the development of disease-modifying treatments

through improved patient stratification in clinical trials. Future research should focus on validating these biomarkers in larger, longitudinal studies to assess their performance over time and explore their utility in tracking disease progression.

Source: **Alzheimer's And Dementia**

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