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THE CLINICAL ROLE OF P-TAU 181 AND P-TAU217 IN BLOOD AND CSF AS BIOMARKERS FOR ALZHEIMER'S DISEASE

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ABSTRACT

Amyloid-BETA plaques and neurofibrillary tangles made of hyperphosphorylated tau are pathological features of Alzheimer's disease, the primary cause of dementia.phosphorylated tau at threonine 181 (p-tau-181) and threonine 217 (p-tau 217) are two tau isoforms that have become trustworthy fluid biomarkers for early diagnosis ,disease surveillance ,and distinguishing one neurodegenerative illness from another. Cerobrospinal fluid (CSF) assays have given robust diagnostic value, whereas recent improvements in ultrasensitive plasma–based assays now enable minimally invasive and scalable detection.P-tau217 has been shown to have better sensitivity and specificity than p-tau 181,and it has a stronger correlation with tau PET ,amyloid burden, and cognitive decline. P-tau indicators are increasingly seen as instruments for personalized and preventive therapy in addition to their diagnostic function. We suggest a digitally assisted, blood –first approach that incorporates plasma p-tau 217 with risk –tiered preventative treatments, remote cognitive monitoring, and two –cutoff triage techniques. This method makes it possible to identify at-risk persons earlier, lessens the need for intrusive CSF or expensive PET scans, and offers a target-to –target framework for therapeutic monitoring. Together,p-tau181 and p-tau 217 are transformational that have the potential to change AD prevention and precision care while also improving diagnostic accuracy.

Keywords: *Alzheimer's disease; p-tau181; p-tau 217; biomarkers; cerebrospinal fluid; plasma; phosphorylated tau; diagnosis; prevention; digital health; precision medicine.*

INTRODUCTION

The primary cause of dementia worldwide is Alzheimer's disease (AD), which places a tremendous burden on people, families, and healthcare systems due to its progressive cognitive deterioration. Both positron emission tomography (PET) and cerebrospinal fluid (CSF) analysis can identify the neuropathological hallmarks of AD, which include intracellular neurofibrillary tangles made of hyperphosphorylated tau and extracellular amyloid-β (Aβ) plaques. However, both techniques are invasive, expensive, and frequently unavailable for early screening in large populations [1-3]. Phosphorylated tau (p-tau) isoforms have become promising fluid biomarkers in recent years, especially those at threonine 181 (p-tau181) and threonine 217 (p-tau217). p-tau217 has continuously shown better diagnostic accuracy and dynamic range, even though CSF p-tau181 has long been established as a reliable indication of AD pathology [4].

For instance, Janelidze et al. found that CSF p-tau217 more accurately distinguishes AD from non-AD neurodegenerative illnesses than p-tau181 [4].it correlates more significantly with tau PET and amyloid load. When it comes to diagnosing AD and amyloid positive in plasma, p-tau217 performs better than p-tau181 (for example, plasma Aβ pathology AUC 0.91 vs. lower values) and exhibits consistent performance across a variety of cohorts [5-7]. In primary and secondary care settings, fully automated plasma p-tau217 tests can now achieve high accuracy (85–94%) thanks to recent technical advancements. This is especially true when employing a "two-cutoff" method to reduce intermediate or inconclusive results [8-9]. Additionally, combining digital cognitive tests with plasma p-tau217 enhances early detection, and distant cognitive performance enhances decline prediction on PACC or MMSE scales [10].

The prevailing clinical paradigm is still diagnostic or prognostic in spite of these advances. P-tau biomarkers are not widely used in frameworks for precision-based intervention or prevention. It is appropriate to investigate new routes where plasma p-tau217 serves as both a diagnostic and a preventative mechanism, given the growing trend towards the deployment of blood-based biomarkers (BBM) and digital health [9,10].

THE UNDERLYING PATHOPHYSIOLOGY OF TAU PHOSPHORYLATION IN ALZHEIMER'S DISEASE

1. Tau and Phosphorylation Regulation's Normal Function

Tau is a microtubule-associated protein that is essential for maintaining axonal transport and stabilizing neuronal microtubules. Its ability to bind microtubules is modulated by reversible phosphorylation under physiological conditions. This is most noticeable during development, when tau is strongly phosphorylated, as opposed to lower levels in adults [11].

2. Aggregation and Hyperphosphorylation of Tau

Tau's affinity for microtubules is reduced in Alzheimer's disease (AD) due to aberrant hyperphosphorylation at multiple serine/threonine sites, particularly those followed by proline. Tau detachment, misfolding, and aggregation result in the formation of neurofibrillary tangles (NFTs) and paired helical filaments (PHFs) [12].

3. The Kinases That Drive the Phosphorylation of Tau

Tau phosphorylation occurs at several disease-relevant locations, such as Ser202, Thr231, Ser396, Ser404, and Thr217 [11,13], and is caused by a variety of proline-directed kinases, including GSK-3β, CDK5, MARK, and MAPKs, as well as non-PDPKs, including PKA, CaMKII, and casein kinases I/II.

4. Phosphatase Impairment in AD

Serine/threonine phosphatases PP1, PP2A, PP2B, and PP2C are the main enzymes responsible for tau dephosphorylation; PP2A is responsible for around 70% of this activity. PP2A activity is significantly decreased (by about 20–40%) in AD brains, which leads to persistent tau hyperphosphorylation [14].

5. External Factors: Inflammation, Oxidative Stress, and Aβ

Tau phosphorylation and aggregation can be caused or worsened by toxic Aβ species, oxidative stress, and neuroinflammation. Aβ can increase tau phosphorylation, which accelerates the formation of NFTs and neuronal death, whereas oxidative changes such as nitration and disulfide formation encourage misfolding and hyperphosphorylation [15].

6. Cytoskeletal and Synaptic Dysfunctions Induced by Tau

Hyperphosphorylated tau detachment affects synaptic function, destabilizes microtubules, and interferes with axonal transport. It contributes to progressive cognitive impairment through synaptic degeneration caused by mislocalized tau within dendrites and synapses [16].

TECHNIQUES FOR ANALYZING P-TAU181 AND P-TAU217

Phosphorylated tau species, particularly p-tau181 and p-tau217, must be accurately detected in biological fluids such as blood and cerebrospinal fluid (CSF) in order to diagnose and track Alzheimer's disease (AD) early. To measure these biomarkers, a number of precise and sensitive analytical methods have been developed and improved.

1. P-tau in CSF has traditionally been measured using immunoassays, such as enzyme-linked immunosorbent assays (ELISAs). These methods have demonstrated dependable detection of p-tau181 with modest sensitivity and employ antibodies specific to phosphorylation sites [17,18]. Conventional ELISAs, however, might not have sufficient sensitivity to identify trace amounts of p-tau species in plasma.
2. Ultrasensitive assays such as single-molecule array (Simoa) technology, which provides femtomolar sensitivity for plasma p-tau181 and p-tau217 detection, have been developed to overcome this issue [19,20,21]. These indicators can be accurately measured in blood samples using Simoa-based immunoassays, which have also been linked to AD pathology and CSF levels [22,23].
3. An alternative is offered by mass spectrometry (MS)-based methods, which enable multiplexed detection and precise quantification of tau isoforms and phosphorylation sites. High-specificity, site-specific measurement of p-tau181 and p-tau217 has been made possible by methods such as liquid chromatography-tandem mass spectrometry (LC-MS/MS) [24,25,26].
4. Although high-throughput clinical settings are less suitable for MS approaches due to their significant sample preparation requirements, they provide unparalleled precision and the capacity to differentiate tau post-translational modifications, including phosphorylation patterns [27,28].
5. More recently, tau proteins can be enriched from plasma or CSF prior to MS analysis using immunoprecipitation combined with mass spectrometry (IP-MS), which improves the detection limits for p-tau species [29,30].
6. For the measurement of p-tau181, electrochemiluminescence (ECL) assays have also been used. Compared to conventional ELISAs, these assays improve dynamic range and sensitivity by combining the sensitivity of immunoassays with electrochemiluminescence signal detection [31].

7. There are still analytical issues to be resolved, such as assay standardization, antibody specificity, and variations in pre-analytical factors such as sample handling that can affect p-tau readings. As a result, continuous efforts focus on creating reference standards and validating assay repeatability [17,19,28].
8. Comprehensive biomarker panels for differential diagnosis are anticipated with the introduction of multiplex immunoassays that can concurrently detect various tau phosphorylation sites (p-tau181, p-tau217, p-tau231), in addition to additional AD biomarkers [20,22,31].
9. Although they are currently mostly in the research stages, novel techniques that make use of nanotechnology and biosensors are being studied to increase sensitivity, decrease sample volume, and enable point-of-care testing [30,31].
10. Finally, a strong platform for p-tau biomarker identification is provided by the combination of ultrasensitive immunoassays and MS methods, which aids in early diagnosis, disease monitoring, and the assessment of therapy response in AD [18,23,29].

CLINICAL EVIDENCE FOR P-TAU181 AND P-TAU217 IN CEREBROSPINAL FLUID (CSF)

Cerebrospinal fluid (CSF) contains phosphorylated tau species, particularly p-tau181 and p-tau217, which have become important biomarkers for diagnosing Alzheimer's disease (AD), tracking its course, and distinguishing it from other neurodegenerative diseases.
1. As a biomarker of tau pathology in AD, CSF p-tau181 has been thoroughly validated. It correlates with neurofibrillary tangle burden post-mortem and exhibits higher levels in patients than in cognitively normal controls [32,33].
2. Research indicates that CSF p-tau181 levels rise early in the course of the illness, even in preclinical stages of AD, and can be used to predict cognitive loss and the transition from mild cognitive impairment (MCI) to AD dementia [34,35].
3. The Connection to Amyloid-β
P-tau181 is a useful marker for differential diagnosis against non-AD dementias since it exhibits superior pathophysiological relevance and higher specificity for AD when compared to total tau (t-tau) [36,37].
4. According to recent studies, p-tau217 is a better biomarker than p-tau181, and it can differentiate AD from other tauopathies and frontotemporal lobar degeneration with greater diagnostic accuracy [38,39].
5. Compared to p-tau181, CSF p-tau217 levels show better associations with tau positron emission tomography (PET) imaging, more accurately reflecting tau accumulation [40,41].
6. According to longitudinal research, CSF p-tau217 tracks neurodegeneration and cognitive loss more sensitively than p-tau181 and gradually rises with disease severity [42,43].
7. Compared to conventional CSF biomarkers, the combination of CSF p-tau217 and the amyloid-β42/40 ratio enhances early AD detection and clinical progression prediction [44,45].
8. Additionally, elevated CSF p-tau217 has been connected to genetic forms of AD, including autosomal dominant mutations, confirming its function in tracking the development and course of the illness [46].
9. CSF p-tau217 is being used increasingly in clinical trials as an endpoint metric to evaluate how well treatments improve tau pathology [39,42].
10. When established procedures are followed, the levels of p-tau181 and p-tau217 in CSF are repeatable biomarkers that remain consistent across several analytical platforms [32,37,44].
11. Less invasive biomarker techniques are supported by the high correlation between CSF p-tau species and plasma p-tau assays [33,41].
12. The clinical usefulness of CSF p-tau217 has been improved by the proposal and validation of diagnostic cut-offs across a variety of cohorts [38,43].
13. According to recent meta-analyses, CSF p-tau217 performs better than p-tau181 in terms of sensitivity and specificity for the diagnosis of AD [40,45].
14. In addition, it has been demonstrated that in asymptomatic people at risk for AD, increased CSF p-tau217 levels might predict future neurodegeneration [42,46].
15. In order to enhance early and precise Alzheimer's disease identification, clinical evidence generally supports the inclusion of CSF p-tau181 and p-tau217 in standard diagnostic panels [34,36,39].

BLOOD P-TAU181 AND P-TAU217: A DEVELOPMENT IN PERIPHERAL BIOMARKERS

The identification of phosphorylated tau isoforms in blood, specifically p-tau181 and p-tau217, is a significant step forward for the non-invasive diagnosis and tracking of AD.
1. It was initially shown that blood-based p-tau181 could accurately differentiate AD patients from controls, and it had a strong correlation with both tau PET imaging and CSF p-tau181 [47,48].
2. It is a useful method for early identification because subsequent research has shown that plasma p-tau181 levels increase early in the disease, especially in preclinical and mild cognitive impairment (MCI) phases [49,50].

3. When it comes to distinguishing AD from other neurodegenerative illnesses, including frontotemporal dementia and Lewy body dementia, plasma p-tau181 performs exceptionally well as a diagnostic tool [51,52].
4. In distinguishing AD from non-AD tauopathies, p-tau217 has lately emerged as an even more sensitive and specific plasma biomarker, surpassing p-tau181 [53,54].
5. The accurate measurement of p-tau181 and p-tau217 in plasma at femtomolar quantities has been made possible by analytical advancements, including mass spectrometry and ultrasensitive immunoassays (Simoa) [55,56].
6. Compared to p-tau181, plasma p-tau217 levels have a better correlation with tau PET and amyloid PET imaging, more accurately indicating disease pathology [57,58].
7. Longitudinal measures of plasma p-tau217 track disease progression and cognitive decline more accurately than plasma p-tau181, supporting its promise as a monitoring biomarker [59,60].
8. Studies on the general population show that plasma p-tau indicators can forecast the transition from cognitively normal status to AD dementia years before symptoms appear [61,50].
9. Blood p-tau181 and p-tau217 measurements are useful in clinical and research contexts because they are inexpensive, minimally invasive, and appropriate for repeated sampling [47,51].
10. Their use in extensive screening initiatives may revolutionize early AD diagnosis and allow for prompt treatment [52,55].
11. Despite their potential, ensuring test reproducibility across laboratories still requires standardization of pre-analytical and analytical procedures [48,56].
12. Disease staging and diagnostic accuracy are enhanced when plasma p-tau indicators are combined with additional blood biomarkers, such as neurofilament light chain (NfL) and amyloid-β peptides [49,57].
13. A growing number of clinical trials use plasma p-tau217 as an endpoint to evaluate how well disease-modifying treatments work [59,60].
14. Point-of-care testing is made possible by sensors that increase sensitivity [55,61]
15. All things considered, plasma p-tau181 and p-tau217 have transformed the development of peripheral biomarkers and offer enormous potential for Alzheimer's disease prognosis, early diagnosis, and therapeutic monitoring [47,53,58].

COMPARISON OF P-TAU181 AND P-TAU217: ADVANTAGES AND DISADVANTAGES

Although both phosphorylated tau species, p-tau181 and p-tau217, are important biomarkers for Alzheimer's disease (AD), their clinical usefulness, pathological associations, and diagnostic capabilities vary.

1. P-tau181 has been extensively researched and established as a robust biomarker for AD, with high associations with tau pathology and cognitive decline. As such, it is a trustworthy indication of the onset and course of the illness [62,63].
2. In contrast, p-tau217 has lately drawn interest because of its exceptional sensitivity and specificity in differentiating AD from other tauopathies and neurodegenerative illnesses [64,65].
3. According to comparative research, p-tau217 reduces false-positive diagnoses by better distinguishing AD from frontotemporal dementia (FTD) and other non-AD neurodegenerative diseases than p-tau181 [66,67].
4. Compared to p-tau181, p-tau217 exhibits a stronger correlation with tau PET imaging and post-mortem tau burden, indicating that it more correctly represents tau disease [68,69].
5. P-tau217 exhibits a steeper rise and superior discriminative power in preclinical and mild cognitive impairment stages, even if both markers increase early in the illness course [70,71].
6. P-tau181 analytical detection is more well-established, with standardized assays available and substantial clinical cohort validation, in contrast to the ongoing optimization and standardization of p-tau217 tests [72,73].
7. The clinical acceptance of p-tau181 tests is facilitated by their increased availability and repeatability across many platforms and laboratories [74,75].
8. In contrast, the lower quantity of this isoform in p-tau217 tests, especially in plasma, necessitates the use of ultrasensitive methods such as mass spectrometry or Simoa [73,76].
9. The expense and technical difficulty of p-tau217 tests may prevent their widespread use, particularly in low-resource settings [72,74].
10. Although p-tau217 has been proposed to be more closely associated with amyloid-induced tau phosphorylation, both p-tau181 and p-tau217 exhibit strong associations with amyloid-β disease [68,70].
11. Changes in p-tau217 may be more helpful for clinical trials since longitudinal studies show that it better tracks disease progression and therapeutic response than p-tau181 [65,71].
12. In contrast to p-tau181, fewer extensive longitudinal and demographic studies are available for p-tau217 due to its relative novelty [72,75].
13. Diagnostic accuracy is increased beyond that of either marker alone when p-tau181 and p-tau217 are combined with additional biomarkers, such as neurofilament light chain (NfL) and amyloid-β [62,66].

14. Because of its defined cut-offs and assay maturity, p-tau181 is still a useful and validated biomarker in clinical contexts, even with the benefits of p-tau217 [63,74].
15. In conclusion, research is being conducted to combine the two for the best AD diagnosis and monitoring. While p-tau181 provides a more widely accepted and accessible biomarker, p-tau217 shows promise for improved specificity and early detection [64,67,73].

FUNCTION IN DIFFERENTIAL NEURODEGENERATIVE DISEASE DIAGNOSIS

In order to distinguish Alzheimer's disease (AD) from other neurodegenerative diseases that have similar clinical symptoms, phosphorylated tau isoforms-in particular, p-tau181 and p-tau217-have become crucial diagnostic tools.

1. To differentiate AD from frontotemporal lobar degeneration (FTLD), Lewy body dementia (LBD), and other non-AD dementias, elevated levels of CSF and plasma p-tau181 and p-tau217 are highly suggestive of AD pathology [1,2].
2. In separating AD from FTLD, where tau pathology varies in isoform composition and phosphorylation locations, studies show that p-tau217 has better selectivity than p-tau181 [3,4].
3. P-tau levels, particularly p-tau217, are low or normal in patients with clinically confirmed dementia with Lewy bodies (DLB), which helps distinguish them from AD, where higher p-tau is usual [5,6].
4. Similarly, p-tau biomarker levels are lower in Parkinson's disease dementia (PDD) than in AD, which supports the use of these markers in clinical differential diagnosis [7,8].
5. Amyloid-β pathology, which is either nonexistent or very weak in non-AD neurodegenerative disorders, is highly correlated with elevated p-tau biomarkers in CSF and plasma, offering biochemical distinction [9,10].
6. Despite atypical clinical characteristics, p-tau181 and p-tau217 aid in confirming AD pathology in atypical AD presentations, such as posterior cortical atrophy or logopenic variant primary progressive aphasia [11,12].
7. To differentiate them from AD, tauopathies such as corticobasal degeneration (CBD) and progressive supranuclear palsy (PSP) usually show low or normal levels of p-tau181 and p-tau217 [13,14].
8. In complex situations with overlapping clinical and imaging characteristics, p-tau biomarkers combined with amyloid-β42/40 ratios and neurofilament light chain (NfL) improve diagnostic accuracy [1,15].
9. According to a number of studies, plasma p-tau217 improves clinical decision-making by having a stronger discriminative ability than p-tau181 in distinguishing AD from other neurodegenerative illnesses [3,6].
10. Compared to CSF-based tests, the ability to assess these indicators in blood provides less invasive and more accessible tools for differential diagnosis [2,7].
11. Using p-tau181 and p-tau217 in conjunction with neuroimaging biomarkers such as tau PET enhances disease staging and differential diagnosis [8,10].
12. Elevated p-tau biomarkers in patients with mild cognitive impairment (MCI) help with early diagnostic accuracy by predicting progression to AD dementia rather than other dementias [4,11].
13. Function in Differential Neurodegenerative Disease Diagnosis

Crucially, the specificity of p-tau217 in plasma improves the reliability of AD diagnosis in clinical settings by lowering false positives in populations with mixed diseases [5,14].

14. The use of p-tau biomarkers for differential diagnosis is becoming more widely acknowledged in clinical recommendations, which incorporate them into biomarker-based diagnostic criteria for AD and associated diseases [9,12].
15. In general, p-tau181 and p-tau217 are crucial biomarkers that increase the accuracy of diagnosing neurodegenerative diseases and enable more precisely focused treatment approaches [13,15].

ADAPTATION TO CLINICAL PRACTICE: OBSTACLES AND PROSPECTS

Although there are many obstacles to overcome and strategic developments are needed to optimize their potential impact, the incorporation of p-tau181 and p-tau217 as biomarkers for Alzheimer's disease (AD) into standard clinical practice offers enormous promise.

1. Standardizing test procedures across platforms and laboratories to guarantee reliable and consistent measurements of plasma and CSF p-tau biomarkers is a significant problem [1,2].
2. For dependable clinical application, strict procedural harmonization is required because pre-analytical factors such as sample collection, handling, and storage conditions have a substantial impact on p-tau levels [3,4].
3. Variability in p-tau181 and p-tau217 cut-off values between studies complicates clinical interpretation and emphasizes the need for generally recognized thresholds, despite promising diagnostic performance [5,6].
4. To verify the generalizability of p-tau biomarkers, clinical validation in diverse groups, including those with varying ethnicities and concomitant illnesses, is necessary [7,8].
5. Widespread clinical usage is now constrained by the expense and accessibility of ultrasensitive assay methods, such as mass spectrometry and Simoa, particularly in areas with limited resources [9,10].

6. To maximize decision-making, integration with current diagnostic procedures, such as neuroimaging and cognitive tests, necessitates the creation of precise clinical algorithms and guidelines [11,12].
7. To increase diagnostic confidence and improve patient management, healthcare personnel must receive training on how to understand and interpret p-tau biomarker results [13,14].
8. In order to facilitate the clinical application of blood-based p-tau tests and their integration into standard testing panels, regulatory approval and reimbursement policies must evolve [1,15].
9. To assess how p-tau biomarker alterations relate to treatment outcomes and disease progression in real-world clinical settings, longitudinal research is required [4,7].
10. By combining p-tau biomarkers with other newly discovered indicators, including neurofilament light chain (NfL) and amyloid-β ratios, personalized medicine techniques may be guided, and diagnostic accuracy and prognostic value may be improved [5,10].
11. Digital health platforms and point-of-care testing technologies have the potential to enhance patient access to early AD diagnosis and streamline biomarker monitoring [8,11].
12. Careful policy development and patient counseling techniques are necessary due to ethical concerns surrounding early diagnosis and biomarker disclosure to asymptomatic patients [13,14].
13. To capture diverse AD pathology, future research should concentrate on improving test sensitivity and specificity, reducing costs, and expanding biomarker panels [2,9].
14. To speed up biomarker standardization, validation, and clinical adoption, cooperation between academia, business, and healthcare systems is essential [3,15].
15. Ultimately, despite the enormous promise of p-tau181 and p-tau217 biomarkers, their successful clinical integration hinges on resolving logistical, ethical, legal, and technical issues through interdisciplinary methods [1,6,12].

EARLY INTERVENTION PATHWAY ANCHORED BY P-TAU217 (WITH DIGITAL MONITORING)

Early Intervention Pathway Anchored by p-tau217 (with Digital Monitoring)

Justification: With the FDA-approved Lumipulse G p-tau217/β-amyloid 1-42 ratio assay and clinic-grade performance, plasma p-tau217 is now able to help with diagnosis, paving the way for population-level triage and preventive intervention before symptoms. According to recent research, p-tau217 can substitute two-cutoff procedures for many LP/PET confirmations, predicts future tau spread and cognitive deterioration, and is being incorporated into practice guidelines.

The Suggested Course of Action (Creative Contribution)

Step 1: Triage in the Community (Blood First):

Use a two-cutoff system with plasma p-tau217 (or, if available, the FDA-approved p-tau217/Aβ42 ratio):

- **Low (rule-out):** lifestyle regimen plus regular follow-up.
- **Intermediate:** retake the test in three to six months and add the baseline for digital cognition.
- **High (rule-in/confirm):** only move on with targeted confirmatory PET/CSF when therapy decisions call for it.

In memory-clinic procedures, this method can minimize LP/PET by around 60–85% while optimizing NPV/PPV.

Step 2: Home-Based Digital Phenotyping

To identify minor changes early and monitor continuously—scalable even in low-resource settings—complement blood results with remote cognitive composites and wearable/smartphone signals (sleep regularity, activity, and reaction-time tasks).

Step 3: Bundle of Risk-Tiered Prevention

- **Low tier (rule-out):** depression treatment, vascular risk reduction, and precision lifestyle (aerobic activity, Mediterranean diet, and sleep optimization); check in every 12 months.
- **Intermediate tier:** increase cognitive training and cardiometabolic control; retest p-tau217 three to six months later to verify trajectory.
- **High tier (biomarker-positive):** use the p-tau217 drop as a pharmacodynamic marker in conjunction with clinical results; validate AD pathology if medication is being investigated; and start disease-modifying therapy when qualified.

Step 4: "Treat-to-Target" Longitudinally

Monitor Δ p-tau217 (and NfL) every three to six months; adjust the level of intervention based on trends in digital cognition and biomarkers.

P-tau217 is a dynamic biomarker of development and response that is supported by newly emerging longitudinal evidence.

Notes on Implementation (Friendly to India)

Start with secondary-care memory clinics; incorporate AI-assisted triage dashboards; and use brand-agnostic, performance-based cutoffs in accordance with the Alzheimer's Association CPG. To cut down on travel expenses and increase reach, use remote assessments (smartphone tasks, caregiver-reported function).

CONCLUSION

Phosphorylated tau isoforms, specifically p-tau181 and p-tau217, have revolutionised the way Alzheimer's disease (AD) is diagnosed. While p-tau217 has better sensitivity and specificity, stronger associations with amyloid and tau PET imaging, and greater accuracy in differentiating AD from other neurodegenerative illnesses, p-tau181 has long been established as a reliable biomarker. Reliable plasma-based detection is now possible thanks to developments in ultrasensitive assays, such as mass spectrometry and single-molecule array (Simoa), which lessen the need for expensive positron emission tomography (PET) and invasive cerebrospinal fluid (CSF) analysis. Even with these developments, the majority of applications are still diagnostic in nature. P-tau biomarkers need to be included into precision-based and preventive approaches in order to reach their full potential. Plasma p-tau217 is used in a two-cutoff triage paradigm as part of a suggested "blood-first, digitally supported prevention pathway," which also includes risk-tiered lifestyle or therapy interventions and remote cognitive monitoring. Neurofilament light chain (NfL) and Δp-tau217 longitudinal monitoring provides a treat-to-target approach for illness progression and therapy response. In summary, p-tau181 and p-tau217 are catalysts for a paradigm shift in dementia care rather than just indicators of AD pathology. When paired with digital health tools and preventive strategies, their incorporation into clinical workflows has the potential to shift the field away from managing Alzheimer's disease in its advanced stages and towards proactive, patient-centered prevention, which will ultimately improve outcomes and lessen the disease's worldwide burden.

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