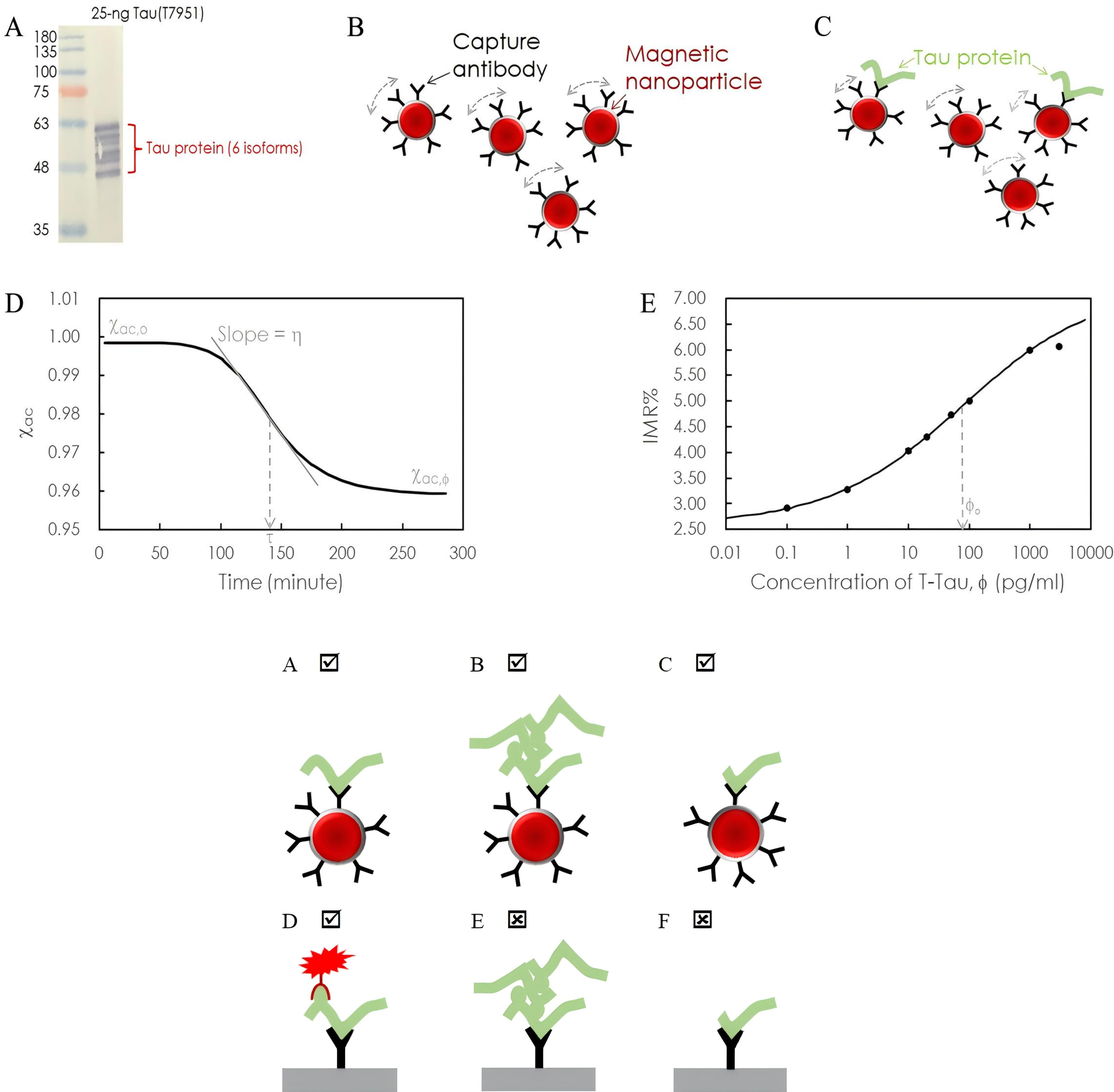


INTRODUCTION

Tau protein stabilizes neuronal microtubules; its hyperphosphorylation and aggregation drive Alzheimer's disease (AD) and related tauopathies. Cerebrospinal fluid (CSF) tau measurement, though diagnostically validated, is limited by lumbar puncture invasiveness. Blood-based alternatives demand extraordinary sensitivity to detect picogram-per-milliliter concentrations—a challenge met by emerging platforms like immunomagnetic reduction (IMR). This review synthesizes forty-five studies (2013–2025) examining IMR's technical foundations and clinical performance in plasma total tau (T-Tau) quantification across the neurodegenerative spectrum.

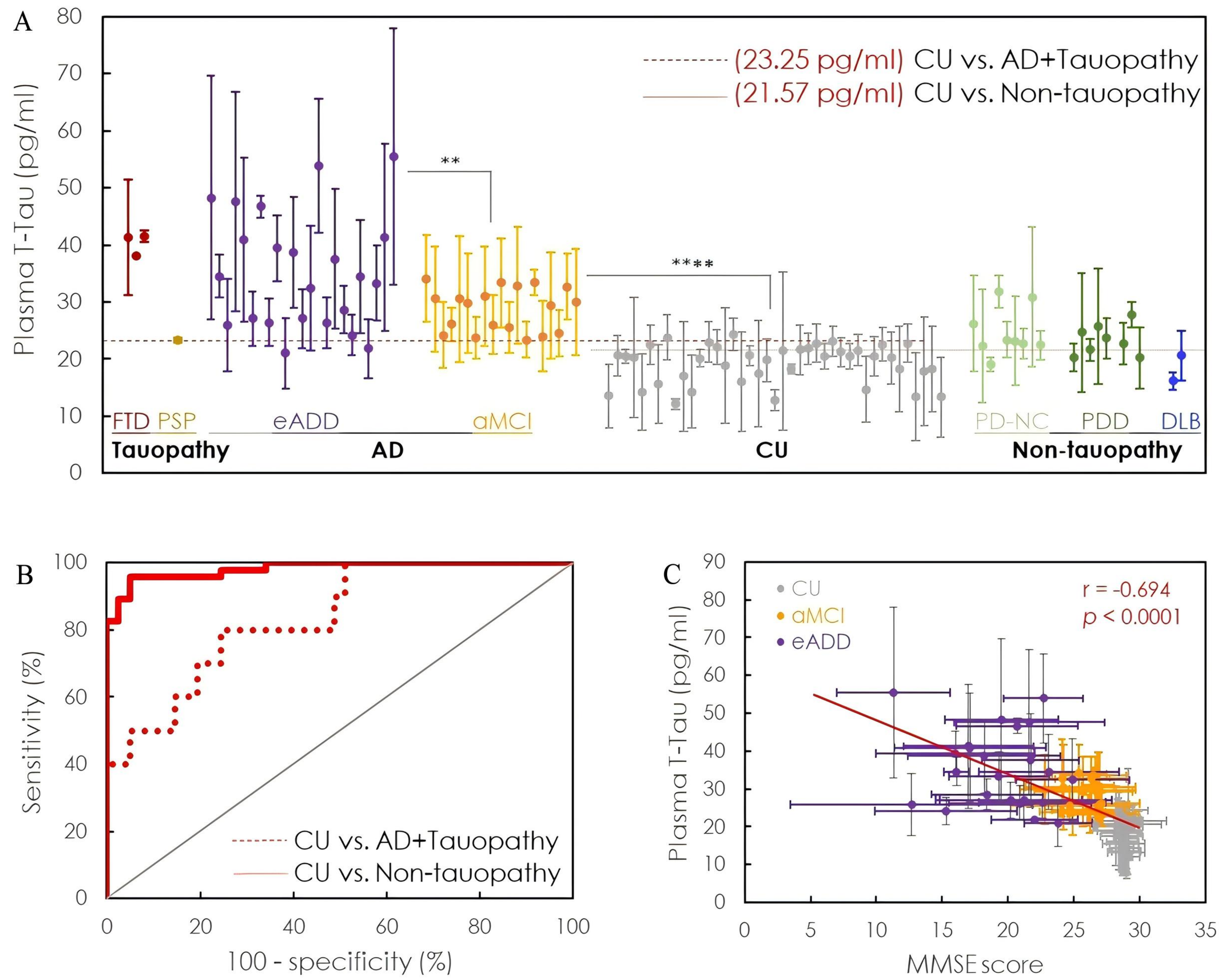
METHODS

This review synthesizes forty-five clinical studies published between 2013 and 2025 that employed IMR for plasma total tau (T-Tau) quantification. We examine the technological foundations of IMR—including its nanoparticle-based signal amplification and superconducting quantum interference device (SQUID) magnetometry—and evaluate clinical performance across four domains: diagnostic differentiation, structural brain correlates, cognitive tracking, and therapeutic monitoring.



RESULTS

IMR achieves a limit of quantification of ~ 89 fg/mL, enabled by 3.6×10^{12} nanoparticles per assay (342 cm² binding area) and ultra-low-noise SQUID detection. Plasma T-Tau levels in cognitively unimpaired individuals ranged from 12.12–24.33 pg/mL across forty-one studies (coefficient of variation = 17.98%), demonstrating superior inter-study consistency compared with single molecule array (45.78%). For discriminating AD and tauopathies (progressive supranuclear palsy, frontotemporal dementia) from controls, IMR yielded an area under the curve of 0.983 (sensitivity 0.957, specificity 0.951) at a cutoff of 23.25 pg/mL. Plasma T-Tau correlated significantly with hippocampal volume ($r = -0.47$ to -0.57), gray matter atrophy, and cognitive measures (Mini-Mental State Examination: $r = -0.694$). Longitudinal studies confirmed that rising T-Tau tracks cognitive decline ($r = -0.93$), and intervention studies demonstrated T-Tau reductions following olfactory stimulation.



CONCLUSIONS

IMR-based plasma T-Tau measurement bridges the gap between CSF biomarker accuracy and routine clinical practicality. Its ultra-sensitive detection of disease-relevant tau conformations, robust structural and cognitive correlations, and utility in monitoring therapeutic interventions position it as a transformative tool for neurodegenerative disease diagnosis, prognosis, and treatment evaluation. Regulatory approval in Taiwan and Europe signals its transition from research platform to clinical reality.