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Editorial article

Frontotemporal Dementia and the Therapeutic Void: Bridging the Gap in Drug Development for FTD

Running Title: Bridging the Therapeutic Gap in FTD

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Abstract

Frontotemporal dementia (FTD) is a progressive and early-onset neurodegenerative condition, and there are no approved disease-modifying therapies. Despite growing insight into its molecular pathology and the development of biomarkers and genetic stratification tools, drug development for FTD remains limited. Significant challenges include the clinical and pathological heterogeneity of the disease, difficulties in early diagnosis, and limited commercial incentives due to its relative rarity. This editorial highlights the urgent need for coordinated translational research efforts, international collaboration, and robust funding mechanisms to accelerate therapeutic innovation. While the scientific groundwork is promising, overcoming the current therapeutic void requires sustained and strategic global initiatives.

Keywords: Frontotemporal Dementia; Drug Development; Therapeutic Gap; Neurodegeneration; Biomarkers; Translational Research; Precision Medicine.

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Introduction

Frontotemporal dementia (FTD) is a progressive neurodegenerative disorder characterized by atrophy of the frontal and temporal lobes, leading to profound changes in personality, behavior, language, and executive function. Unlike Alzheimer's disease, which predominantly affects older adults, FTD often emerges in individuals between 45 and 65 years of age, creating a unique set of personal, social, and economic challenges. Despite its significant burden, FTD remains one of the most under-recognized and under-treated forms of dementia (1).

Currently, there are no disease-modifying therapies explicitly approved for FTD. Symptomatic treatments are limited, and many commonly used medications, such as antipsychotics or SSRIs, are prescribed off-label with variable efficacy (2). This therapeutic void is primarily due to the complex and heterogeneous nature of FTD, which encompasses multiple clinical syndromes, including behavioral variant FTD and primary progressive aphasia, as well as a diverse range of underlying pathologies, including tauopathies and TDP-43 proteinopathies (3).

The landscape of FTD research is evolving. Advances in neuroimaging, fluid biomarkers, and genetics—such as the identification of pathogenic mutations in MAPT, GRN, and C9orf72—are enabling more precise disease stratification (4). These developments hold promise for targeted drug development, especially as biomarker-driven clinical trials become increasingly feasible. However, despite scientific progress, the pipeline of FTD-specific therapeutics remains relatively sparse.

Challenges in FTD drug development include small and heterogeneous patient populations, difficulties in early and accurate diagnosis, and the lack of standardized outcome measures. Moreover, the rarity of the disease compared to other neurodegenerative conditions may limit commercial incentives for pharmaceutical companies to invest in high-cost, high-risk drug development programs (5).

Bridging this gap will require coordinated efforts across the academic, clinical, regulatory, and pharmaceutical sectors. Collaborative international consortia, public–private partnerships, and increased funding for translational research are essential to accelerate the discovery and validation of effective treatments. Early-phase trials should continue to explore repurposed compounds, novel biologics, and gene-based approaches, while also prioritizing patient-reported outcomes and the unique ethical considerations specific to this population.

As our understanding of FTD's pathobiology deepens, the opportunity to translate scientific discoveries into therapeutic innovations is within reach. While significant hurdles remain, the current trajectory of research provides cautious optimism. A sustained and focused effort toward filling the therapeutic void in FTD could ultimately lead to interventions that not only alleviate symptoms but also modify disease progression—offering hope to patients and families who, for too long, have faced this disease with few options.

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