4. CONTEMPORARY APPROACHES TO THE TREATMENT OF FRONTOTEMPORAL DEMENTIA

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Introduction. Frontotemporal dementia or FTD relates to a group of diseases that are caused by neuronal degeneration. FTD is mainly of genetic etiology, due to mutations occurring in specific genes, and may be transmitted hereditarily. The most common mutations affect the MAPT, PGRN, C9orf72, VCP, TARDBP and FUS genes. Depending on which genes or regions of the brain are altered, patients diagnosed with FTD express different symptoms and variants of the same disease. The control of neuropsychiatric symptoms has been the only universal approach to managing FTD.

Aim of study. Our study aimed to review new pharmacological treatment options that are available for patients with different variations of FTD or that can potentially be implemented in the near future.

Methods and materials. This article is based on data analysis of several articles available on PubMed, PMC and Google Scholar, that have been published since 2015.

Results. Earlier case reports confirmed behavioral improvements after administering antidepressants (trazodone, fluvoxamine and citalopram), antiepileptics, atypical antipsychotics (quetiapine, risperidone), and even psychostimulants (methylphenidate and dextroamphetamine). However, some present a significant risk of adverse effects. More novel symptomatic approaches include agomelatine, a 5-HT2C receptor antagonist that elevates dopamine and noradrenaline levels and reduces apathy, and oxytocin, an important mediator of empathy and social behaviour. In addition, low doses of lithium could potentially ameliorate agitation and psychosis. Even though there are no definitive disease-specific approaches available yet, molecule-based therapies are being studied. Drug induced selective autophagy and tau acetylation and aggregation inhibitors can decrease tau levels in neurons, while tau-targeting antibodies have shown potential in increasing tau clearance. By resorting to sortilin receptor blockers and AAV-Grn vectors or by managing biological pathways using suberoylanilide hydroxamic acid and bafilomycin A1, higher levels of PRGN in the brain can be achieved. Metformin blocks PKR phosphorylation, which eventually lowers toxic RAN (repeat associated non-AUG) protein levels, caused by abnormal C9orf72 gene expansions. Moreover, antisense oligonucleotides (ASO), like WVE-004, could be used to promote the degradation of C9orf72 expanded mRNAs by binding the hexanucleotide expansion.

Conclusion. A lot of progress has been made regarding pharmacological treatment options for patients with FTD. Nevertheless, no pharmacological therapy is completely successful or approved, meaning a lot of work and research is yet to be done.