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Molecular mechanisms and biomarkers in frontotemporal dementia

Frontotemporal dementia (FTD), the second most common cause of dementia in under 65-year-olds, belongs to a large group of heterogenous neurodegenerative syndromes leading to degeneration in the frontal and temporal areas of the brain. Clinical symptoms in FTD patients may vary from changes in personality, behavior, and executive function, problems in understanding or producing speech, and motor dysfunction to psychiatric symptoms, which complicate differential diagnostics of FTD from other brain diseases, especially in the early phases of the disease. Almost half of the FTD cases can be caused by different genetic mutations, such as those in MAPT, GRN, and C9orf72. The C9orf72 hexanucleotide repeat expansion (C9-HRE) is an exceptionally common genetic cause of FTD in Finland. Our studies in mouse neurons expressing the C9-HRE have shown that these neurons have significant changes in synaptic structures and function. Examinations of potential synaptic changes in induced pluripotent stem cell-derived neurons from C9-HRE-carrying and non-carrying FTD patients are presently undergoing. We have also found in Finnish patient cohorts that blood-based measurements of neurofilament light and glial fibrillary acidic protein may offer possibilities for differential diagnostics of FTD patients from patients with a psychiatric disease. In this presentation, potential mechanisms related to synaptic dysfunction and promising biomarkers for differential diagnostics in FTD will be discussed.