SynaDeg

Prediagnostic early synaptic disturbances in neurodegenerative diseases

Frontotemporal dementia (FTD) and dementia with Lewy bodies (DLB) are neurodegenerative disorders, which show overlapping clinical symptoms with other types of dementia, especially in the early phases, complicating their accurate diagnosis. In addition, disease-modifying therapies, specific biomarkers, and fundamental understanding of disease mechanisms are so far lacking. Synaptic disturbances have been suggested as the earliest pathological changes in neurodegenerative diseases.

SynaDeg consortium, formed by internationally renowned experts in clinical, translational, and preclinical research of neurodegenerative diseases, postulates that it is possible to identify early disease-specific synaptic alterations combined with measurable physiological disturbances, easily monitorable even at home (e.g., altered behaviour and autonomic functions), that could be feasibly implemented to clinical practice for improved early diagnostics of FTD and DLB. SynaDeg brings together a synergistic and innovative research ecosystem with a joint aim to generate novel, non-invasive diagnostic tools and clarify disease mechanisms underlying the early synaptic or other physiological disturbances in FTD and DLB patients to be utilised in accurate and timely diagnostics and personalised medicine. SynaDeg efficiently utilises already existing data and samples from large, exceptionally well-characterised patient cohorts (altogether ~1000 patients) at different partner sites, containing clinical data, biofluid and neuropathological samples, and induced pluripotent stem cell (iPSC) lines from FTD and DLB patients to assess neurotransmitter and synaptic deficits and physiological alterations. The existing cohorts and sample collections will be supplemented with newly identified individuals suspected to have a prodromal or early-phase neurodegenerative disease and their samples during the study.

Specific aims of SynaDeg are:

1) Identification of early physiological and synaptic changes, which could improve the early diagnosis of FTD and DLB by i) pinpointing specific clinical symptoms and signs related to physiological disturbances (e.g., altered behaviour and autonomic functions, like gastrointestinal complaints, heart rate variation, sleep, physical and social activity), which can be easily monitored at home, and ii) detecting neurotransmitter system alterations predicting synaptic dysfunction and neurodegeneration using a beyond-state-of-the-art non-invasive transcranial magnetic stimulation;
2) Discovering new cerebrospinal fluid and blood-based biomarkers indicating synaptic dysfunction;
3) Characterisation of specific pathological and functional alterations underlying synaptic dysfunction and neurodegeneration and their mechanisms in brain samples and iPSC-neurons from genetic and sporadic FTD and DLB patients;
4) Strengthening collaboration between research community and patient organisations (POs) to promote efficient dissemination of SynaDeg results to scientific community, health care professionals, and lay audience, establish ethical and best practices for patient recruitment for neurodegenerative disease research, and share knowledge on management of these diseases in the health service systems. SynaDeg endeavours are expected to yield new disease-specific fluid biomarkers and therapeutic targets, and clinical and physiological assessment tools to aid early identification and treatment of FTD and DLB patients. This will save societal expenses in the management and diagnostics of FTD and DLB due to earlier accurate diagnoses and shortened diagnostic paths. Finally, communication between the general public and health care professionals, and dissemination of SynaDeg results.

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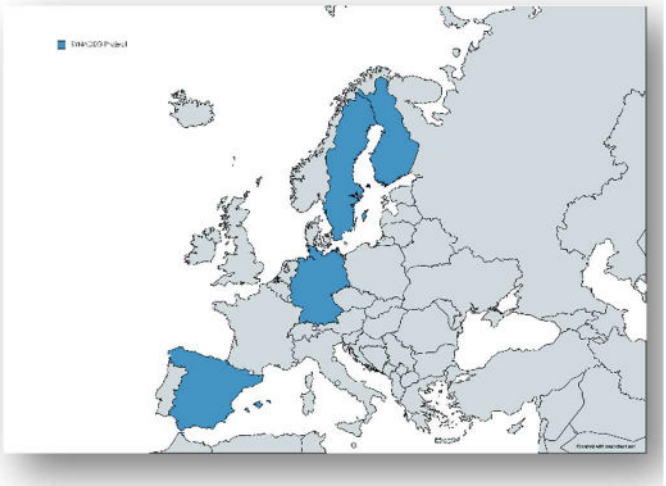

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