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Title of project: A Novel Biomarker to Assess Presence and Progression of Diabetic Neuropathy

ABSTRACT

Diabetic neuropathy (DN) is the most common late complication of diabetes. At present, the diagnosis of DN generally awaits nerve fiber dysfunctions being measurable by simple bedside examinations reflecting late-stage disease and without a clear consensus on the clinical definition of this complication. A biomarker for DN could provide a valuable tool for early detection and follow-up of DN to monitor the natural course of the disease and provide an objective intermediate outcome measure that could simplify the evaluation of interventions across different study populations and accelerate the development of future treatments for DN. A novel neuronal axonal cytoskeletal protein; neurofilament light chain (NfL) has emerged as a potential candidate biomarker for DN. NfL is abundant in neurons of the central and peripheral nervous system and released to the cerebrospinal fluid and blood upon decay of nerve fibers. Whereas solid evidence exists for NfL as a sensitive and broad marker of central nervous system diseases, the evidence for its use in the peripheral nervous system is sparse. Yet, recent studies have reported serum NfL levels to reflect presence and severity of inherited and certain acquired peripheral neuropathies.
We aim to investigate the biomarker potential of NfL in DN in this project using three different cohorts of people with diabetes. First, we will evaluate NfL levels longitudinally from the time of screen-detected type 2 diabetes in participants of the ADDITION-Denmark trial and align these data with the extensive DN measures obtained in nearly 600 participants at the clinical 13-year followup examination of this cohort. Second, we will quantify the association between NfL levels and the presence of painful diabetic polyneuropathy (DPN) as well as the severity of DPN in nearly 500 people from the English PiNS cohort. Lastly, we will measure longitudinal NfL levels in 200 people with diabetes attending the Steno Diabetes Center Aarhus outpatient clinic to understand the association between levels of NfL and presence, severity and progression of active diabetic foot ulcers.