Application Title: Quantitative oculomotor assessment in Late-Onset Tay-Sachs

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Late-Onset Tay-Sachs (LOTS) is a very rare, inherited, progressive neurodegenerative disorder resulting in progressive debilitation and with symptoms caused by reduced levels of the β-hexosaminidase A enzyme. In comparison to the infantile and juvenile forms of Tay-Sachs, LOTS symptoms generally start in early adulthood and is commonly misdiagnosed. There is progressive neurological deterioration and symptoms include walking difficulties, often requiring walking aids, due to a combination of weakness and ataxia (difficulty coordinating movements of the arms, legs, speech and eyes), speech and swallowing problems, cognitive decline and frequently associated with psychiatric illness. There are several potentially disease-modifying therapies and symptomatic treatments on the horizon for LOTS. However, for such trials, sensitive measures of disease (biomarkers) are urgently needed to both identify early signs of disease and to monitor subtle disease progression. Eye movements are abnormal and a discriminating feature in LOTS but have been little studied and are very common in the related cerebellar ataxias, often occurring before the onset of troublesome symptoms and have been suggested in studies as a potential clinical biomarker. We therefore plan to precisely measure eye movements in a lab setting, assess cognitive functioning and psychiatric symptoms, as well as perform a first study of subjective sleep quality in LOTS.

In this study, we will recruit patients with LOTS at different disease stages as part of an ongoing natural history study as well as individuals without the disease. We will ask patients about their LOTS test results, medical history, family history of neurological conditions, and about habits, as some of these can influence eye movements. Subjects will be evaluated with a neurological examination, using various disease-specific clinical scales and eye movements will be precisely measured using goggles to assess eye movements during different visual tasks. We will also assess cognition and psychiatric symptoms with novel scales specific to disorders with cerebellar involvement and sleep symptoms with dedicated assessment scales. We will compare the eye movement measurements to scales which assess the severity of clinical disease. These steps will enable us to see whether detailed assessment of eye movements can detect early signs of disease better than neurological examination, and whether eye movement testing can serve as an accurate measure of disease severity in LOTS and therefore be useful for upcoming clinical trials.