

Progress Report

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Title of Project: Eating and metabolism in neurodegeneration

Summary:

Metabolic abnormalities and disordered eating behaviour are highly prevalent, challenging clinical problems encountered by patients with a spectrum of neurodegenerative conditions including frontotemporal dementia (FTD), amyotrophic lateral sclerosis (ALS) and Alzheimer's disease (AD). There is very little understanding of whether metabolic abnormalities contribute to, or are a consequence of, the underlying pathology, their impact on disease progression and survival, and whether interventions directed to these abnormalities may be helpful to patients.

Hypothesis vs Findings

The hypothesis of this project is: That there is a common pattern of metabolic and eating phenotypes shared between several neurodegenerative diseases, that relates to degeneration of a specific brain network. Additionally, some forms of neurodegeneration may be characterised by specific metabolic abnormalities that result from their unique patterns of brain pathology

This project has built on previous work examining eating and metabolic changes in FTD and ALS. Research has established a pattern of eating changes in these conditions that affects cholesterol and triglyceride levels and subsequently survival. This finding has led to a publication in Journal of Alzheimer's disease. Further work is continuing into the molecular abnormalities controlling eating behaviour in ALS with examination of hypothalamic function through measurement of hypothalamic peptides on fasting bloods. Research is also continuing into the effect of changes in body composition on survival in both FTD and ALS through the use of Dual energy x-ray absorptiometry scans (DEXA), a technique used in obesity research, which shows total body fat, lean muscle mass and abdominal fat deposition.

Studies have also commenced examining the reward bases of eating abnormalities through the use of functional MRI scanning.

Studies are also being undertaken examining the longitudinal change in eating behaviour in at risk asymptomatic genetic cohorts

What these research outcomes mean

This project is expected to define the longitudinal metabolic phenotypes in several neurodegenerative conditions and their relationship to eating behaviour using methods adapted from genetic obesity research. Changes will also be correlated to brain structures through both structural and functional imaging and pathological analyses. This comparative project is the first to determine commonalities and differences in metabolic abnormalities and eating behaviours in neurodegenerative conditions and relate these to disease progression and prognoses. The expectation is that these findings will identify potential early intervention targets and provide insights into how modifying eating behaviour and metabolism, which many patients enquire about, can affect disease progression and survival. This will then form the basis for treatment trials to modify these eating behaviours and metabolic changes to potentially change the course of these devastating neurodegenerative disorders.

Publications resulting from research

1. Ahmed RM, Farooqi S. Hypothalamic atrophy is related to body mass index and age at onset in amyotrophic lateral sclerosis. *Journal of Neurol Neuropsych and Neurosurgery*. July 2017
2. Ahmed RM et al. Lipid metabolism and survival across the frontotemporal dementia-amyotrophic lateral sclerosis spectrum: relationships to eating behavior and cognition. *Accepted Journal of Alzheimer's disease*. Oct 2017-10-30
3. Ahmed et al. Physiological phenotyping of neurodegenerative dementias. Invited review *Nature Review Neurology*. Oct 2017.