



Application number/Title: 30544 - Diet, body fat and brain health: a multi-organ imaging study in the UK Biobank

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Keywords provided by the Applicant PI to describe the research project:

Brain-health, diet, obesity

Application Lay Summary:

The aim is to investigate how diet interacts with obesity to influence susceptibility to neurodegenerative brain processes that contribute to later-life dementia.

Specific aims are to:

- 1) Examine relations between total and regional body fat distribution (abdominal, liver, pancreatic and muscle fat) and risk of cognitive impairment
- 2) Examine associations between dietary patterns, total and regional body fat compartments and MRI-measured brain structures and functions
- 3) Determine whether associations are influenced by other lifestyle behaviours, socio-demographic factors (age, gender, race, socioeconomic status), disease risk (depression, cardiovascular disease, metabolic and inflammatory disease) and genetic risk factors

This study fulfils the purpose of UK Biobank to support a diverse range of research intended to improve the prevention, diagnosis and treatment of illness, and the promotion of health throughout society. Given that brain changes of dementia accumulate years before cognitive impairment becomes apparent, understanding the influence of diet-related obesity on brain structure and function across the life-course is important for prevention strategies. The study findings will inform design of future dietary interventions aimed at enhancing cognition and preventing or delaying dementia and will allow interventions to be targeted towards those who are likely to benefit most. We will investigate associations between diet, body fat and MRI measures of brain structure (total, grey matter, and white matter volume, mean diffusivity, fractional anisotropy) and brain

function (resting and task functional measures). We will consider factors e.g. lifestyle, disease (metabolic, vascular, inflammatory, cognitive impairment) and available genetic risk factors associated with obesity and dementia. We will examine obesity phenotypes and dietary patterns that are associated with brain structure and function, then test how effects are modified by other lifestyle, disease and genetic factors and vice-versa. We will use statistical procedures such as linear/logistic multivariate regression modelling.

1) Full cohort with dietary analysis, whole body DXA and cognitive function to examine relations between diet, obesity and cognitive impairment

2) Full cohort MRI abdomen and brain MRI (IDPs) to examine body fat and brain measures (~10,000) initially, aiming to utilise the full cohort (~100,000) to explore our hypotheses when available

3) Subsample (GWAS) specific SNPs of interest - genotyping at ApoE, FTO rs9939609, DRD2/ANKK1 rs1800497, OPRM1 rs1799971, COMT rs4680, MC4R rs17782313 to examine interactions with genetic risk factors

4) Full cohort Biochemical markers - inflammation, metabolic syndrome and insulin resistance (CRP, HbA1c, lipids) when available