



Application number/Title: 41127 - Using MRI imaging to investigate how cardiac shape and function effect dementia-associated brain lesions and what genes and health factors underlie these changes.

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

GWAS, big data, brain imaging, cardiac imaging, health biomarkers, white matter lesions

Application Lay Summary:

A diagnosis of dementia can mean a significantly diminished quality of life for those affected as well as their family and carers. As our population ages it is more important than ever that we seek a more complete understanding of the underlying causes of this disease. While there are undoubtedly many contributing factors, not least just getting older, evidence that changes in the shape and function of the heart may directly affect the brain, are gaining traction.

On brain images from particular MRI scans there are bright white patches that increase in older individuals. Interestingly, these same patches are often linked to dementia and cognitive decline. While there are different kinds of dementia, the most well-known and the one which affects the most people is Alzheimer's disease, "certain signs are invariably present. Prominent amongst these is a change to the blood flow in the vessels that provide oxygen and nutrients to the brain cells that are changed by the dementia. What then, causes these changes to the blood flow? We think it may have something to do with the way the heart is operating and uniquely, UK Biobank, offers the opportunity to investigate this link as of the approximately half-million individuals in the study, up to 100,000 will have scans of both their brain and their heart.

If we can establish a link between the heart and brain we would like to explore if there is something in the genes of these individuals that contributes to this. Once again, UK Biobank is an exceptionally rare resource in that the genetic code for each of the individuals with heart and brain images has also been mapped. This

will allow us to understand something about the genetic switch that causes these changes, and knowing this, can help in the search for potential treatments.

If there are certain kinds of genes responsible, then additional information in UK Biobank such as levels of blood pressure, cholesterol, obesity and other health measures that are routinely taken in hospitals and GP surgeries can be tested for an association to those genes. If the gene switches are causing these health measures to change, which in turn are altering the heart function, that is in turn causing changes in the brain leading to dementia, then we have made a small step in understanding the processes that cause distress to so many.