Progress Report

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Title of Project: Left ventricular hypertrophy, amyloid and tau deposition in patients with type 2 diabetes mellitus

Summary: (approximately 1,000 words)

Summary of aims

In this sub-study, we sought to establish whether people with type 2 diabetes mellitus (T2DM) and left ventricular hypertrophy have a higher amyloid and/or tau burden in their brains, compared to people with T2DM, but without left ventricular hypertrophy (LVH). We also sought to establish whether amyloid and tau levels are associated with brain volume and thinking skills in these two groups. Our goal was to complete amyloid and tau PET scans in 30 T2DM participants already enrolled in the Diabetes & Dementia (D2) study at 2-years post-baseline.

Progress to date and plan

We encountered two major challenges in 2019, which has meant that we are yet to begin scanning participants in this PET imaging sub-study. The challenges are summarised below:

- Delays in participant recruitment for the larger D2 study. In response, we have expanded recruitment to other sites in Melbourne (e.g., St Vincent's Hospital). This has meant that all staff members involved in the D2 study have been focused on participant screening and recruitment.
- Delays in price negotiations with the Molecular Imaging and Therapy Department of Austin Health for the amyloid and tau PET scans. The Austin Nuclear Medicine department has undergone changes, including requiring new machinery and turnover of senior staff members. The world-wide lack of technetium has also affected their throughput. However, despite all this, negotiations have progressed and we are now ready to scan participants.

Importantly, we have made progress in the larger D2 study and we are now better placed to carry out the PET imaging sub-study. We have recruited 141 of the 168 participants required; 123 participants have completed their baseline MRI scans and

cognitive assessments; and 34 participants have completed their 2-year review sessions.

We have finalised the amyloid 18F-NAV4694 and tau 18F-MK6240 tracer PET scanning protocols in collaboration with the Molecular Imaging and Therapy Department of Austin Health.

We have submitted our ethics application to the Austin Health Office for Research, with approval expected by January 2020. Our aim is to scan our first participant in late February 2020, and the larger group of 30 participants, by September 2020. We will complete the analyses in October 2020 and report the findings of the study in November.

We believe this timeline is realistic. One-hundred and ten participants will complete their 2-year review sessions between January and September 2020. Our prior experience suggests that 26% of participants will agree to take part in a PET imaging sub-study[1].

We apologise for the unanticipated delays with the project. We are confident that we can carry out the aims of the project by November 2020.

Hypothesis vs Findings

This research project aims to address two main hypotheses:

1. People with type 2 diabetes and LVH have a higher burden of Aβ and tau accumulation compared to diabetes patients with no LVH;
2. Higher Aβ and tau load is associated with poorer cognitive function and magnetic resonance imaging (MRI) markers of structural brain ageing (e.g. lower cortical thickness, total brain volume, and hippocampal volume and greater white matter hyperintensity volume).

As discussed, we expect to have answers to these hypotheses in November 2020.

Unanswered Questions
As above.

What these research outcomes mean
As above.

Please include any appropriate photos or diagrams.

N/A.

References

Rowe, CC., Ellis, KA., Rimajova, M., Bourgeat, P., Pike, KE., Jones, G., Fripp, J., Tochon-Danguy, H., Morandeau, L., O'Keefe, G., Price, R., Raniga, P., Robins, P., Acosta, O., Lenzo, N., Szoeke, C., Salvado, O., Head, R., Martins, R., Masters, CL., Ames, D., & Villemagne, V. (2010). Amyloid imaging results from the Australian Imaging, Biomarkers and Lifestyle (AIBL) study of aging. *Neurobiology of aging*, *31*(8), 1275-1283.