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Title of Project: Determining the influence of objectively measured sleep quantity and quality on cognitive function, blood and neuroimaging biomarkers of Alzheimer's disease.

Progress Report Summary:

Relatively sparse information is currently available regarding sleep quality and quantity as a preventative approach to decrease the risk of cognitive (memory and thinking) decline leading to Alzheimer's disease (AD). It is therefore essential that further focused research is undertaken to identify which aspects of sleep are the strongest contributors to such cognitive decline (and associated AD pathology) and consequently may be most promising for subsequent intervention. In order to achieve this goal, this study sought to address the following aims:

To assess the association between objectively-determined sleep quantity and quality and cognitive function, brain amyloid load, brain glucose utilisation, brain volume and AD-related blood and cerebrospinal fluid biological markers over 12 months.

Hypotheses

1) Poorer sleep quantity and quality will predict greater decline on cognitive tasks over 12 months;

2) Poorer sleep quantity and quality will be associated with greater brain amyloid burden and accumulation over 12 months;

3) Better sleep quantity and quality will be associated with greater brain glucose utilisation and attenuated age-related decline in brain structure volumes over 12 months;

4) Poorer sleep quantity and quality will be associated with higher levels of AD-related blood and cerebrospinal fluid biomarkers over 12 months.

Findings to Date

At the time of writing, cognitive assessment, FDG-PET (to determine brain glucose utilisation), blood samples and objective sleep data have been obtained for 74 participants aged over 60 (mean age = 72.1±5.8 years). Whilst data collection is not yet complete, interim analyses are yielding highly promising results.

Partial correlations controlling for age reveal that more favourable sleep (e.g., less time awake after falling asleep, better sleep efficiency) is associated with greater cerebral glucose metabolism (indicated by overall neocortical Standardised Uptake Value Ratio (SUVR) '*r*' values ranging from 0.23-0.29) particularly in the prefrontal

cortex, with the strongest relationships found in the dorsolateral, orbitofrontal and anterior cingulate cortices (‘*r*’ values ranging from 0.20-0.35). Moreover, increased Wake After Sleep Onset is associated with increased apathy, disinhibition and executive dysfunction, as well as poorer performance on measures of visuospatial functioning, visual memory and simple processing speed.

Unanswered Questions

AD-related blood biomarkers will be measured once all samples have been collected. Brain imaging and cognitive data will also be reanalysed once data collection is complete.

What these research outcomes mean

Whilst currently only interim analyses have been undertaken, the results certainly appear to suggest that ‘better sleep quality’ is associated with both better cognitive performance and increased brain glucose metabolism in older adults.

These data have been pivotal in leveraging additional funding from other sources in order to commence a pilot study examining cognitive measures and brain imaging biomarkers following an intervention aimed at *improving* sleep parameters.