**Project Title:** A multidisciplinary study looking at neural correlates of cognitive function and health variability across the lifespan: Towards a better understanding of neurodegeneration.

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**Level:** PhD

**Background to the project:**
With increased longevity and the rise in the prevalence of dementia, there is a need to identify potential neurological, lifestyle, nutritional, environmental and individual difference variables that maintain healthy cognitive ageing and functional independence for longer. The current study will adopt a lifespan approach to examine cognition in healthy ageing and to identify patterns of change that are indicative of the early signs of neurodegeneration such as Mild Cognitive Impairment (MCI) and Alzheimer’s Disease (AD) and to identify the impact of the factors listed above on these conditions. There are structural and functional changes in the brain with healthy ageing (Bishop et al., 2010) which may be responsible for normal changes in cognition. There is a need to understand more fully what reflects normal and abnormal changes. Although there has been an abundance of research into AD, this has not produced a better understanding of its causes or effective treatments (Wolf et al., 2013). There is a need for interventions for dementia to be more ecologically valid and based on a sound theoretical model of cognitive ageing (Hampstead et al., 2014). This study will attempt to build a comprehensive model of cognitive function across the lifespan which looks at factors that promote healthy cognitive ageing, while at the same time outlining potential predictors of cognitive decline and AD, to our knowledge this has not been done previously in this multidisciplinary approach.

Healthy ageing is not just the absence of disease and disability, according to the World Health Organisation (2015), it is “the process of developing and maintaining functional ability that enables well-being in old age”. Maintaining cognitive function is thought to be essential to healthy ageing (Horvat et al., 2016), and involves the interaction between physical, social and psychological functioning, which will be closely examined in the current project. This is supported by research that suggests chronic conditions such as heart disease, diabetes and stroke are associated with cognitive decline (Basu et al., 2015). There is a need to understand more fully the role of lifestyle factors such as diet and physical activity in cognitive function across the lifespan, as this potentially could mediate healthy ageing (Chatterji et al., 2015).

This study will consider a range of factors that may contribute to the development of cognitive degeneration in later life in conjunction with behavioural (CANTAB) and neurological (MEG/EEG) measures of memory. This will be used to develop a model of cognition across the lifespan. Early diagnosis of those at risk of dementia would provide early intervention, a possible slowing of the disease progression, early support
for family carers, better quality of life and reduced disability for those affected (Gualtieri, 2004). This would also contribute to the Department of Health’s policy on “Improving Care for People with Dementia” (2013). This multi-disciplinary study will involve researchers within The Psychology Research Institute, The Northern Ireland Centre for Food and Health (NICHE), The Intelligent Systems Research Centre and a consultant Clinical Psychologist within The Northern Health and Social Care Trust.

Methods

Design & Sample: This will be a cross sectional study of community dwelling healthy adults across the life span employing strata sampling by age and sex: 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, with 20 males and 20 females within each age range. In a second aspect of the study, a clinical sample of participants with in the early stages of MCI and other dementias (25 MCI, 25 AD, 25 Lewy Body and 25 Vascular dementia) will also be recruited. Power Calculations were performed using GPOWER 3.0 (Faul et al., 2007). Specified as an A x B factorial analysis of variance with age (6 levels - 20-29, 30-39, 40-49, 50-59, 60-69, 70-79 years) and gender (2 levels) as independent factors, Cohen’s (Cohen, 1988) effect size conventions for such a design are given as (small =.10, medium = .25, large =.40). With α= 0.05, a sample size of 240, the study would have sufficient power (.8) to detect effect sizes of .235, .182 and .235 for the respective between subject’s main effects of age, gender and age x gender.

Measures:

Screening: Only those participants who are deemed to be in good mental and physical health will be recruited into the cross sectional study of health ageing. This will be assessed using the General Health Questionnaire-28 (Goldberg, 1978) a screening measure of psychiatric morbidity and the Mini Mental Health Examination (Folstein, Folstein, & McHugh, 1975) a screening measure of cognitive decline. The MCI and dementia groups will be identified by a consultant clinical psychologist (Dr Frances Duffy) working with dementia patients within the Northern Health and Social Care Trust.

Lifestyle: A self-report Health and Lifestyle questionnaire, adapted from the EPIC study (Simpson et al., 2005) will be administered to look at socio-demographic variables (age, sex, marital status, education level and social class) socioeconomic status (SES), physical activity, dietary habits and status will be assessed as these factors have been found to influence cognition. The EPIC Food Frequency Questionnaire (Bingham et al., 1997) will be used to further assess dietary intake.

Cognitive function: CANTAB (Cambridge Automated Neuropsychological Test Battery, Morris et al., 1986), is a reliable and well validated computerised test battery, which measures various aspects of cognitive function, including working memory, verbal memory, attention, and visual recognition memory. These are reported to be sensitive to normal cognitive ageing (Robbins et al., 1994) and neurodegenerative changes in brain function (Fray and Robins, 1996; Rabbitt and Lowe, 2000). All of the tests have brain to behaviour reliability (Luciana and Nelson, 2002), and activate specific areas of the brain that may be affected by changes in the central nervous system with age and neurodegeneration (Robbins et al., 1994). More recently CANTAB batteries have been developed to assess changes in Alzheimer’s Disease (AD) and Mild Cognitive Impairment (MCI).
Neurological measures of memory: Either MEG or EEG will be completed in a subsample of participants, (use of MEG will be dependent on obtaining additional external funding). MEG: Magneto encephalography (MEG) is a functional neuroimaging technique for mapping brain activity, this may be used to establish differences in underlying neurological mechanisms in healthy and non-health cognitive ageing and how this is related to cognitive performance on CANTAB tests. To assess memory usage, the event-related desynchronisation/synchronization (ERD/ERS) phenomena can be utilised, whereby spectral information relative to the oscillatory nature of the EEG components pre/post and during stimulus can be compared. ERD is a spectral amplitude attenuation of certain EEG rhythms during stimulus processing, e.g., during memory retrieval/recall. ERS is an amplitude enhancement of certain EEG rhythms when cortical areas are not specifically engaged in a given mode of activity at a certain instant of time (Pfurtscheller, 1998). ERD/ERS is a process for studying the differences in cognition/memory in different age groups and potentially for identifying indicators of declination in these processes (Karrasch et al, 2005). Studies have indicated that there are statistically conclusive differences in the oscillatory responses of individuals, even between normal and MCI, and that this information may be used for early stage identification of MCI and dementia (Leocani & Comi, 2006; Karrasch et al, 2005).

**Statistical analysis:** For the healthy volunteer sample (N=240) a series of ex post facto (6 x 2) ANOVA’s will be used to provide descriptions of mean differences on all outcome variables by age group and sex. Differences between the MCI and dementia groups and healthy controls (cross sectional study) will also be investigated using ANOVA and multi-level modelling to identify factors that predict MCI/dementia vs Non-MCI/dementia.

**Resources needed**
The student will have access to the School of Psychology Psychology Test library where we hold measures of health and lifestyle, cognitive function and psychological well-being. They will have access to CANTAB a computerised cognitive test battery, and training on how to select, administer and interpret tests. The student will have access to a Brain Analyser available within the School of Psychology, and in collaboration with the School of Computing and Intelligence Systems, to assess changes in EEG with age and cognitive function. The student may also have the opportunity to work in the state of the art Functional Brain Mapping facility at UUM, using MEG imaging, but this will be dependent on additional external funding.

**Objectives of the research:**
- To determine differences in lifestyle factors (socio-demographic information, smoking, alcohol intake, dietary habits, physical activity and sedentary behaviour) across the age groups and the clinical dementia groups.
- To establish differences in behavioural (CANTAB) and neurological (MEG/EEG) measures of memory in healthy adults and clinical dementia groups.
- To determine predictors of healthy versus unhealthy cognitive function.
- To use the information provided above to develop a model of cognitive ageing.

**Skills required of applicant:**
- Ability to perform scientific literature searches
- Good communication skills
- Good report writing skills
- Ability to work independently and as part of a team
- Experience of databases and SPSS
- Experience of carrying out research projects. Preferably some experience of memory testing but not essential as training will be given for CANTAB and MEG/EEG testing.
- Experience of working with older adults would be preferred but not essential

References:
Department of Health (2013). Improving Care for People with Dementia. Available at: https://www.gov.uk/government/policies/improving-care-for-people-with-dementia


