A NEUROIMAGING PARADIGM FOR EXPLORING AGEING, ANXIETY, AND COGNITION

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BACKGROUND
Anxiety disorders represent notable disease burden and impact both quality of life and overall cognition. They are the most prevalent mental disorders and will affect up to 33.7% of the population within their lifetime (Bandelow and Michaelis, 2015). Despite reductions in rate of incidence with older age, a substantial proportion (12%) of people aged 55 and older still present with anxiety disorders (Byers et al., 2010). With the steadily aging population in Australia, there is a need to assess how aging interacts with late-life anxiety disorders.

Pathological worry is a central feature of anxiety psychopathology. Worry is a hallmark characteristic of Generalised Anxiety Disorders (GAD; APA, 2013) and describes repetitive and uncontrollable thoughts intended to prepare for or prevent possible future threats (Heimberg et al., 2004). It strongly predicts overall disability and disease severity, serves as a proxy for the severity of anxiety, and is also strongly predictive of psychopathology (Hoyer et al., 2009; Newman et al., 2013).

Worry induction paradigms rely on priming, visualisation, affective stimuli, or personalised cues to induce neural representations of worry. They are well-represented in the current literature and have demonstrated reliability and repeatability, both in the general and older populations. We have drawn from existing work to produce a modified paradigm for probing both the immediate and residual effects of worry in older adults.

Aims
1. Investigate differences in resting state dynamics caused by worry through fMRI observation
2. Investigate differences in neural correlates of worry across healthy and anxious older adult cohorts
3. Compare differences in network connectivity elicited by worry across healthy and anxious older adult cohorts
4. Probe physiological correlates of worry using heart rate variability as a measure
5. Investigate behavioural correlates of worry using behavioural and cognitive assessments

Outcomes
Existing literature on anxiety in older adults points to a complex interplay with elements such as learned coping strategies, deteriorating executive control, and degradation of interoceptive awareness with age. These elements may mask the recognition of the physiological and cognitive manifestations of pathological worry. A greater understanding of the correlates of worry (as a proxy for anxiety) within older adults could present alternative biomarkers for the objective diagnosis and assessment of anxiety, while also indicating new avenues for investigation or novel treatment modalities.

Experimental Paradigm
This presentation is bookended by two rest blocks of 8 minutes each; the latter rest block is designated as the reset block. This block is intended to probe residual effects of worry.

Worry task
The entirety of the task will be concurrent with functional magnetic resonance imaging (fMRI). As part of a modified worry induction paradigm (adapted based on previous work by Paulesu et al. 2010, Andreescu et. al. 2015, and Mohlman et. al. 2017; the latter two in geriatric cohorts), anxious and healthy older participants (n=25 per cohort) will be presented with verbal personalised worry cues in 4 2-minute blocks. Each block will present a novel cue of increasing severity, alternating with 2 minute blocks of a neutral (i.e. no affective engagement) condition requiring the listing of household objects.

Heart rate variability
Concurrent heart rate variability measurements via in-scanner pulse oximetry will provide data on heart rate variability as a proxy for the integrity of autonomic regulation of arousal.

Structural imaging
Anatomical and vascular integrity will be assessed by diffusion tensor imaging and structural MRI.

Behavioural and cognitive assessments
An extensive assessment battery encompassing working memory, attention, processing speed, verbal reasoning, visuospatial reasoning, and executive function. Measures of quality of life and social function will also be administered.