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## Current themes and issues in neuroimaging of aging processes: Editorial overview to the special issue on imaging the nonpathological aging brain

Aging is a ubiquitous phenomenon that, for the general population, ultimately results in some degree of subjectively noticeable functional decline. This reduction in everyday capabilities can be an annoyance at best, but it is also common that this weakening in function is a contributing factor to reduced quality of life. Compounded by concerns of abnormal neurodegenerative processes such as Alzheimer's disease, older adults can experience significant distress, even when they are performing optimally for their age. It is therefore critical to define mechanisms that contribute to variation in function among older adults and particularly to describe this range within individuals considered to be cognitively healthy and without obvious signs of abnormal conditions such as neurodegenerative disease.

Neuroimaging has provided critical insights into changes that occur in the brain with typical aging. Age-associated alterations in brain function have been described since the 1940s via electroencephalography (EEG) and novel insights into the consequences of brain aging continue to this date. Recently, studies of brain aging have often been the first tests of novel brain imaging procedures, in part due to the fact that the investigators have general access to older adults without the absolute need for a physician referral and the fact that often significant alterations in brain structure and function can be expected when compared to a younger cohort. The older population therefore provides a critical test-bed to assess the performance of new procedures outside of the population for which the procedures were developed. This accessibility however, has also resulted in effects reported in less well characterized populations that potentially include individuals suffering from a range of abnormal medical conditions—a potential confound to data interpretation even in research on well characterized cohorts.

In this Special Issue of *Neuroimage*, we aimed to curate a range of studies applying advanced neuroimaging procedures to the study of 'nonpathological' brain aging. The simple definition of nonpathological in this context was that we intended to exclude studies with an obvious focus on the manifestations of abnormal neurodegenerative processes. Of course, one of the major conclusions from decades of brain imaging older adults is that there is a very unclear line between what can be considered 'pathological', ranging from obvious cognitive and behavioral impairment such as dementia, to less clear cognitive risk states such as mild cognitive impairment, or alternatively genetic and/or imaging indicators of preclinical risk, such as beta-amyloid deposition. Here we primarily omitted manuscripts that focused on a diagnosed patient population or focused on groups with defined abnormal performance. We aimed in the spirit of pioneering neuroimaging studies to include studies applying cutting-edge techniques and procedures and the Special Issue includes contributions describing structural, functional, and stimulation

techniques from several corners of the neuroimaging world spanning multiple substantive areas of study, as evidenced by the word cloud in Fig. 1.

### 1. Overview of the special issue

In the following, we provide a brief overview of the topics covered in this Special Issue with a particular focus on trending neuroimaging techniques and issues important to the study of aging. As a measure of the zeitgeist of the study of the aging brain, one can explore the popularity of various neuroimaging techniques being employed, with this special issue as a small proxy for the current field. In that vein, these collected 26 articles utilize neuroimaging techniques spanning brain structure (molecular, microstructural, and macrostructural), brain function, and brain stimulation. Techniques to measure aspects of brain function include functional magnetic resonance imaging (fMRI) BOLD methods including both task-evoked (Berghuis et al., 2019; Fernandez et al., 2019; Keller et al., 2019; Kennedy et al., 2018; West et al., 2019; n = 7) and resting state (Abdellande-Perez et al., 2019; Cassady et al., 2019; Fountain-Zaragoza et al., 2019; Kumral et al., 2019; Li et al., 2019; li et al., 2019; Salami et al., 2018; Viviano et al., 2019; Zonneveld et al., 2019; n = 9), as well as functional near infra red spectroscopy (fNIRS; Wagshul et al., 2019; n = 1) and magnetoencephalography (MEG; Wiesman and Wilson, 2019; n = 1). Brain structural methods are also well-represented including diffusion weighted imaging (including magnetic transfer, tensor-based, and high angular resolution sequences), and other white matter imaging techniques (including those to assess white matter hyperintensities, enlarged perivascular spaces, and microbleeds) (Badji et al., 2019; Brown et al., 2019; Dubost et al., 2019; Fan et al., 2019; Guerri et al., 2019; Langen et al., 2019; Williams et al., 2019; n = 7). Two studies used magnetic relaxation properties to assess iron content in the aging brain via R2\* mapping (Daugherty et al., 2019; Salami et al., 2018), one study utilized spectroscopy to assess GABA (Cassady et al., 2019), and four studies utilized PET imaging of various radioligands to assess beta-amyloid and tau (Dong et al., 2019; Li et al., 2019; Kennedy et al., 2019; Properzi et al., 2019). Finally, the special issue contains two articles on the topic of non-invasive brain stimulation methods, one review paper (Tan et al., 2019) and one empirical study (Abellaneda-Perez et al., 2019).

As would be anticipated, there were numerous submissions (n = 10) utilizing a multimodal neuroimaging approach, including two or more imaging techniques (Abellaneda-Perez et al., 2019; Brown et al., 2019; Cassady et al., 2019; Dong et al., 2019; Fan et al., 2019; Kennedy et al., 2018; Langen et al., 2019; Li et al., 2019; Salami et al., 2018; Wagshul

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special issue is the importance of yoking differences in brain properties with aging back to some outcome measure of cognition or function. A gratifyingly large number of the special issue submissions placed their neuroimaging findings into a cognitive context. Indeed, at least 16 of the 26 submissions contained a cognitive, behavioral, or performance measure of some type. This practice is especially important as the field seeks out which brain alterations are most associated with cognitive consequences, and is a practice to be lauded and encouraged for all future aging and brain studies. Where the aging and brain field continues to fall short, and this special issue is no exception, is the persistence of solely cross-sectional designs and the use of extreme age group comparisons. Of the 26 studies included, almost all were cross-sectional in design (excepting Brown et al., 2019; Williams et al., 2019), and those that contained a longitudinal component, tended to utilize baseline-change association investigations rather than change-change associations. The difficulties associated with longitudinal aging research are non-trivial, yet this research design is needed to gauge actual change in brain and cognition with age. The editors hold great hope that the next instantiation of a special issue on the aging brain will contain many longitudinal studies, or ideally, even comprise the whole issue!

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