

GUEST EDITORIAL

Translating progress in neuroimaging into clinical practice

Neuroimaging continues to be an exciting and rapidly evolving research field producing findings to inform clinical medical practice. Neuroimaging research has enabled a better understanding of *in vivo* structural, functional, and molecular neuropathology. Moreover, it has the potential to improve clinical care, where clinical assessment alone is sometimes insufficient to provide accurate diagnosis and prognosis. The future direction of neuroimaging is likely to focus on identifying imaging biomarkers suggestive of underlying preclinical disease, understanding the temporal progression from preclinical disease to overt clinical manifestation, and monitoring the therapeutic efficacy of potential disease-modifying agents.

A wide variety of brain imaging modalities have been utilized to investigate the most common mental disorders in the elderly, namely depression and dementia. Indeed, advanced brain imaging has been instrumental in elucidating similar patterns of structural and functional brain abnormalities between the two conditions (Jiang *et al.*, 2014). A key requirement for future research is to translate promising progress in these brain imaging studies into clinical practice, although integration of neuroimaging into clinical practice may be impeded by economic considerations and patient acceptability. Economic barriers to integration include the potential cost to healthcare systems of modern imaging modalities. Therefore, studies focused on determining the minimal number of imaging modalities to provide clinically meaningful information and the added value of each brain scan are needed to address this question. Moreover, the increasing sensitivity of imaging to detect abnormal findings with uncertain significance may be psychologically distressing to patients and reduce their willingness to undergo such investigation.

In this edition, in their paper entitled “The psychological impact of disclosing amyloid status to Japanese elderly: a preliminary study on asymptomatic patients with subjective cognitive decline,” Wake *et al.* (2017) explored the short-term psychological impact of disclosing Amyloid- β ($A\beta$) positron emission tomography (PET) results in 42 asymptomatic Japanese adults with subjective cognitive decline. Importantly, all participants

underwent pre-imaging counseling/education detailing the role of $A\beta$ in the evolution of cognitive decline and the interpretation of PET results. Out of the 42 participants, 10 had an $A\beta$ positive result and 32 had an $A\beta$ negative result; no between group differences were noted in measures of anxiety and depression at pre- and post-disclosure of amyloid neuroimaging status. Moreover, mean state anxiety and depression scores were below the normal limits in the pre- and post-disclosure in $A\beta$ positive and negative groups. Full disclosure of $A\beta$ positive status did not cause a greater change in anxiety and depression measures than negative results after a six-week period. This study attempts to address the psychological safety of full disclosure of positive neuroimaging results detected by advanced neuroimaging techniques, a concern that has become a major ethical issue due to the increasing application of amyloid imaging in disease-modifying clinical trials in Alzheimer’s disease (AD). These reassuring findings replicate earlier studies addressing this important question in cognitively normal older adults in the USA but do so in a cohort of participants from a different ethnic and cultural background to previous studies (Lim *et al.*, 2016). Furthermore, this is the first study to investigate this question among individuals with subjective cognitive decline, who may be potentially more anxious about their self-perceived risk of cognitive decline. This study suggests that clinicians may fully disclose positive amyloid scan results without inducing any negative psychological sequelae, providing the necessary groundwork of pre-scan explanation has been completed.

In an investigation addressing the important health economics question about the best use of limited healthcare resources and the value of additional neuroimaging to provide clinically meaningful information, Guinane and Ng (2017) recruited a convenience sample from their memory clinic. Specifically, they explored the beneficial role of additional MRI and/or SPECT brain imaging to routine diagnostic workup to improve diagnostic accuracy in a memory assessment encompassing a non-contrast CT brain. Over a 12-month period, 66 out of 253 patients were referred for additional imaging with participants undergoing MRI only ($n = 15$), SPECT ($n = 6$), and MRI and SPECT

($n = 29$), and 16 being excluded. The overall referral rate for additional MRI and/or SPECT in this study was modest at 26%, likely because participants had all had structural CT. Diagnostic amendments occurred in 11/44 (25%) of participants with MRI scan and 9/35 (26%) where SPECT was used. Those who were referred for additional imaging were significantly younger, more educated, and more likely to have a head injury. Previous studies have reported a higher referral rate for and a positive outcome rate using MRI and SPECT imaging in a clinical setting (Borghesani *et al.*, 2010). This study suggests that in selected cases there can be added value to such additional imaging but the scope to which this study is applicable to a clinical setting remains limited. However, it does highlight the need for further research in this area to inform future clinical guidelines for diagnostic imaging in the memory clinic.

Tau imaging is an exciting research area, and in addition to enlightening the early stages and progress of the tauopathy of AD, this imaging modality will inform us about other forms of tauopathy. In their paper, Takaya *et al.* (2017) examined two patients with frontotemporal lobe degeneration (FTLD) associated with different types of aphasia. They used ^{18}F -THK-5351 PET to identify tau deposits in two participants with variants of primary progressive aphasia (PPA) who had also had negative amyloid imaging assessed using Pittsburgh compound B (PiB). Both participants also underwent MRI imaging and FDG-PET imaging, demonstrating frontotemporal atrophy and concomitant cortical hypometabolism consistent with frontotemporal dementia-related PPA. Based on current diagnostic criteria, one patient was diagnosed as semantic variant of PPA, a subtype of FTLD and the other as logopenic PPA.

Previous studies on late-life depression have identified widespread functional connectivity alterations (Kenny *et al.*, 2010), and in this edition of *International Psychogeriatrics*, Zhu *et al.* (2018) advanced our understanding by applying a graph theoretical approach to assess the role of the default mode network (DMN). Specifically, they examined whether resting-state functional magnetic resonance imaging (fMRI) could detect alternations in functional connectivity and topological organization of the default-mode network (DMN) in patients with remitted geriatric depression (RGD) compared with healthy controls. In comparison to the 31 healthy controls, the 33 RGD showed reduced functional connectivity in the posterior regions of the DMN and abnormal global topology of the DMN. Neuropsychological measures of processing speed and executive function correlated

with network abnormalities noted on fMRI. Longitudinal studies have previously shown the patients with RGD have an increased risk of cognitive decline (Jiang *et al.*, 2014). Given the correlation between neuropsychological measures and resting-state fMRI measures of the DMN, these network measures could be used as a potential biomarker of cognitive impairment in RGD.

Vasudev *et al.* (2017) assessed the role of ventromedial prefrontal cortex (vmPFC) in regulating emotional control in late-life depression as assessed using emotional valence to blood oxygenation level-dependent (BOLD) fMRI and the burden of total brain white matter hyperintensities (WMH). This study differed from prior studies in this field by examining the role of the vmPFC in both genders and by using a combination of structural and functional brain imaging. In this small cross-sectional study, 16 participants with mild to moderate late-life depression were compared to 14 aged-matched healthy controls. As expected WMH volume was greater in the late-life depression group than in the health controls. There was no difference in BOLD activation between groups in terms of emotional valence contrast but interestingly, a gender difference was noted with female participants with late-life depression (LLD) having both more WMH volume and reduced BOLD activation in the vmPFC than controls. The results of this study concord with a prior work with female LLD patients showing reduced activation of the vmPFC to negatively valenced word in an fMRI task (Brassen *et al.*, 2008). The findings of this study are intriguing and require confirmation in a larger study.

In conclusion, the five papers outlined above illustrate the increasing capabilities of sophisticated brain imaging techniques and reassure that disclosure of imaging findings after appropriate patient education is not detrimental to the psychological well-being of patients. Advanced imaging techniques are capable of uncovering the relationships between cognitive impairment, depression, gender, and brain network alterations. Brain network alterations in the DMN have the potential to be a biomarker of cognitive dysfunction among RGD patients. Reduced activation of the vmPFC among female patients with LLD is an interesting finding that needs to be explored in a larger sample size. In the clinical setting, there may be added value of MRI and/or SPECT to current diagnostic work-up in a memory clinic, but further studies in field would be required, and the application of tau imaging among the rarer clinical phenotypes of dementia has much potential. While these studies show some of the opportunities, the translation of research findings into routine clinical

care will be a painstaking process and progress will continue to be incremental.

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