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Preface

Preface for the special issue of imaging brain aging and neurodegenerative disease ☆

Nearly 10,000 people a day turn 65 in the United States, and as the percentage of the population who are elderly continues to rise, increasing numbers of individuals will be at risk for dementia. The high costs of caring for seniors with cognitive decline call for better evidence-based health recommendations and treatments. These improved measures will require a greater understanding of the brain mechanisms that distinguish between normal aging and dementia. At present, dementia remains a clinical diagnosis. However, over the past decade, neuroimaging research has yielded important new information that promises to sharpen and better support clinical diagnosis. Objective neuroimaging biomarkers may be of particular importance if they can identify early dementia states, when emerging interventions are most likely to be successful. In keeping with this view, newly proposed criteria for Alzheimer's disease (AD) support the use of neuroimaging to identify cognitively normal individuals who are at imminent risk for the future development of AD (http://www.alz.org/research/diagnostic_criteria/).

In this special issue of BBA Molecular Bases of Disease on 'Imaging brain aging and neurodegenerative disease', leading experts review patterns of neural decline that characterize normal aging and some of the most common forms of dementia. The majority of articles will focus on Alzheimer's disease (AD) because it is the most prevalent form of dementia. However, neuroimaging profiles associated with other common dementias such as frontotemporal dementia (FTD) and vascular dementia will also be reviewed. Each of these dementias is likely to involve multiple pathologies, causing multiple forms of neurodegeneration. These different forms of neurodegeneration and underlying pathologies can be optimally appreciated by specific neuroimaging techniques. Thus, a key focus of the present special issue is to highlight how the use of specific neuroimaging techniques has improved our knowledge about patterns of neurodegeneration associated with aging and various forms of dementia.

The most readily apparent change affecting the aging brain is cortical atrophy resulting from synaptic and neuronal loss, which can be quantified with volumetric magnetic resonance imaging (MRI). Another visibly apparent structural change is the appearance of lesions within white matter. These present as hyperintense patchy or confluent areas on FLAIR images that reflect vascular effects, some of which may compromise cognition or processing speed [1]. The recent development of several other neuroimaging sequences has enabled assessment of age-related cerebral changes not captured by conventional MRI techniques. For example, diffusion tensor imaging (DTI) methods now provide a window into white matter damage at microstructural levels [2]. A relatively new and highly promising technique is positron emission tomography (PET) with protein-specific radiolabeled ligands [3]. Such techniques can image fibrillar beta-amyloid cortical accumulations, representing an in-vivo window into brain pathology. Finally, various applications of PET or functional MRI (fMRI), allow for the assessment of age-related changes in metabolic or synaptic function.

In this special issue, cerebral atrophy patterns associated with presymptomatic stages of AD are reviewed by Smith, while atrophy patterns associated with early FTD are reviewed by Roher et al. An original contribution by Burns et al. shows that insulin resistance differentially affects brain structure in normal aging and AD. The role of vascular factors and white matter hyperintensities (WMH) in AD is reviewed by de Leeuw et al., and the use of specialized iron sensitive MRI sequences to detect neurodegenerative conditions associated with brain iron accumulation is reviewed by Schipper. The original contribution of Raz et al. presents new evidence that certain genetic factors that promote inflammation contribute to WMHs in healthy seniors. The importance of amyloid imaging in the diagnoses of presymptomatic AD is covered by John Morris's group (Vlassenko et al.). An original contribution by Agneta Norberg's group (Forsberg et al.) provides evidence that a single dynamic amyloid label PIB-PET scan can provide a time-sensitive biomarker of early AD.

A total of five articles are devoted to the exploration of WM microstructural changes in aging and/or dementia. Madden et al. provide a comprehensive review of the literature on patterns of WM integrity changes associated with normal aging. An original contribution of van Norden et al. from a large prospectively followed cohort of healthy seniors ($N = 503$) demonstrates significant relationships between WM integrity and both memory functioning and psychomotor speed. An original contribution from Lars Nyberg's group (Salami et al.) suggests that age-related WM integrity declines may have stronger effects on psychomotor processing speed than cognition. Gold et al. review findings suggesting that WM integrity changes are present in normal individuals at high risk for future AD. Interestingly, an original contribution from Andrew Saykin's group (Wang et al.) shows that WM integrity declines are evident in normal seniors with cognitive complaints, providing further evidence of DTI's utility in the detection of prodromal AD-states.

Functional brain imaging articles include reviews of default mode brain imaging changes in aging and dementia by Serge Rombouts's group (Hafkemeijer et al.). Alterations in default mode are promising as potential functional biomarkers because they capture dementia-related changes when subjects are at rest, and thus do not reflect overt difficulties in task performance frequently encountered in dementia. An interesting alterative, or complementary, functional paradigm may be one showing robust activation changes on a task performed near ceiling in early dementia states. In this vein, Woodard et al. review evidence suggesting that functional activation alterations during semantic tasks may represent a useful biomarker of presymptomatic AD because performance on this task remains intact in early

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AD states. Concerning other functional imaging modalities, an original contribution by Steven Potkin's group (Rasmussen et al.), describes a method for empirical derivation of the denominator region for computing degeneration sensitive FDG-PET ratios in AD.

It is important to note that the potential of neuroimaging goes far beyond identification of early dementia states. For example, one of the remarkable insights that neuroimaging research has provided over the last 20 years is to show that the brain does not merely respond passively to age- and dementia-related declines. Neuroimaging studies have demonstrated that individuals with higher cognitive reserve (e.g., higher education) can tolerate more AD pathology than those with lower reserve and still appear clinically normal [4]. In this special issue, Stern's group (Steffener et al.) review neuroimaging findings suggesting that cognitive reserve may operate through two brain mechanisms: structural variables termed neural reserve and functional variables termed neural compensation. An open question concerns how positive lifestyle variables may bolster cerebral reserve. In this special issue, Lautenschlager et al. review the literature on physical activity as a protective factor in aging, and the review of Wang et al. summarizes the potential benefits of stimulating leisure activities in delaying age-related declines.

We hope that these articles provide a stimulating and thought-provoking collection of works on cutting edge research in the field of neuroimaging of aging and dementia. We would like to thank everyone who has contributed to this special issue. Firstly, thanks to the authors for their excellent contributions. Secondly, thanks to the reviewers: their time and effort improved the quality of the final articles. Last, but not least, thanks to the editorial staff of BBA for their help in the compiling and production of this special issue.

References

[1] A. Kertesz, S.E. Black, G. Tokar, T. Benke, T. Carr, L. Nicholson, Periventricular and subcortical hyperintensities on magnetic resonance imaging. 'Rims, caps, and unidentified bright objects', Arch. Neurol. 45 (4) (1988) 404–408.
[2] P.J. Basser, J. Mattiello, D. LeBihan, MR diffusion tensor spectroscopy and imaging, Biophys. J. 66 (1) (1994) 259–267.
[3] S.K. Ziolko, L.A. Weissfeld, W.E. Klunk, C.A. Mathis, J.A. Hoge, B.J. Lopresti, S.T. DeKosky, J.C. Price, Evaluation of voxel-based methods for the statistical analysis of PIB PET amyloid imaging studies in Alzheimer's disease, NeuroImage 33 (1) (2006) 94–102.
[4] Y. Stern, G.E. Alexander, I. Prohovnik, R. Mayeux, Inverse relationship between education and parietotemporal perfusion deficit in Alzheimer's disease, Ann. Neurol. 32 (3) (1992) 371–375.

Brian Gold is an Associate Professor in the Department of Anatomy and Neurobiology at the University of Kentucky (UK). Dr. Gold obtained his Ph.D. in psychology (cognitive neuroscience focus) from York University in 1999. He then did his postdoctoral training at Washington University. Dr. Gold's research focuses on characterizing cognitive and brain changes associated with normal aging and early Alzheimer's disease. In addition, he is investigating how certain lifestyle variables (e.g., exercise, education) may slow cognitive decline and brain aging. Both functional and structural magnetic resonance imaging techniques are used to address these questions. For example, Dr. Gold's lab has shown that functional response in ventral temporal cortex can distinguish between normal aging and amnestic mild cognitive impairment. Work from his lab has also identified age-related reductions in white matter (WM) microstructure as a contributor to age-related slowing of task switching and demonstrated that aerobic fitness is positively correlated with WM microstructure in healthy seniors. In addition, Dr. Gold's lab has identified some gray matter volumetric and WM microstructural changes present in cognitively normal seniors at high risk for future AD. Dr. Gold's research is funded through grants from the National Institutes of Health (NIH) and the National Science Foundation (NSF). He has served on multiple study sections at the NIH and NSF, as an ad-hoc reviewer for over 35 journals, and is on the editorial board of the Journal of Alzheimer's Disease.

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