Cognitive Aging Research: An Exciting Time for a Maturing Field

A Postscript to the Special Issue of *Neuropsychology Review*

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Received: 8 November 2009 / Accepted: 9 November 2009 / Published online: 22 November 2009
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“... And I think to myself, what a wonderful world.”

From the song “What a Wonderful World” by Robert Thiele and George David Weiss

These are exciting times for the field of cognitive aging research. The reviews in this issue comprise a wonderfully illustrative set of the wide-ranging research endeavors and thoughtful approaches to the hurdles and questions in this field. Traditionally, cognitive aging research has served as the plain stepsister to the higher profile field of age-related disorders of cognition, Alzheimer’s disease being primary among them. Nonetheless, this plain stepsister has toiled at the task of bringing fundamental understanding to the phenomenon of age-related change in behavior and brain function. Today, these contributions are being recognized as landmark, informing us about the adaptive capacities of the brain and behavior, and directing us toward strategies and therapeutics for remediation of decline.

Distinguishing individuals who will maintain adequate, if not excellent, cognitive function into their later years from those on a trajectory to dementia is a central and

driving force in cognitive aging research. In this issue, Rodrigue, Kennedy, and Park explore the literature surrounding one of the newest “old” findings—that a significant proportion of cognitively intact older adults harbor a level of beta amyloid deposition in their brains to warrant a neuropathological diagnosis of Alzheimer’s disease. Using recently developed ligands to visualize beta amyloid deposition in living individuals, investigators have been quick to explain the phenomenon as a possible reflection of a cognitive reserve, enabling those with higher ‘reserve’ to function longer in the face of neural damage. The attendant inconsistencies in findings for support of this hypothesis have been predictable for such a fledgling field. Nonetheless, these provocative data have launched new theories about how the brain tolerates pathology, what constitutes a healthy aging brain, the predictive value of amyloid deposition for AD, and the informative nature of lifespan, or at least “adultspan,” studies.

Perhaps because research has indicated that age-related decrements in implicit learning are rather small or non-existent, this component of cognition has received relatively little attention compared to the more obvious domains of explicit learning and memory. Yet implicit learning is the cornerstone of our information about the world, reflecting our ability to understand relationships, detect continuity or divergence in situations, and navigate successfully both intellectually and socially. Rieckmann and Backman present fascinating findings from neuroimaging studies of implicit learning in older adults that help construct a clearer picture of the aspects of implicit learning that may diminish with age; importantly, their synthesis of the neuroimaging literature helps to enlight-

This editorial was written by the author in her capacity as an NIH employee, but the views expressed in the article do not necessarily represent those of the NIH.

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en our fundamental understanding of a popular concept in current cognitive aging research—compensation. Couching compensation in terms of “neural reorganization,” they simultaneously manage to circumvent the seemingly paradoxical findings of both increased and decreased regional brain activation that accompanies maintenance of or improvement in cognitive function with age and present a cogent hypothesis involving possible unidirectional compensation by medial temporal lobe regions for declining striatal function in order to maintain implicit learning with age.

Lustig et al. also address the compensation concept in their beautifully comprehensive review of cognitive and cardiovascular (aerobic exercise) training interventions in healthy older adults. Besides evaluating the promise and limitations of these interventions, they offer a thoughtful interpretation of how training may serve to both increase engagement (increased activation) and efficiency (decreased activation) of “task-relevant” brain regions. They argue that functional imaging studies may present more sensitive indices of cognitive and brain changes because of the multi-dimensionality of functional neuroimaging data—magnitude, extent, location and time—compared to more restricted dimensional measures for cognition. Based on the literature, the authors offer suggestions of how to broaden and improve transfer of training effects—or at least how to approach the research—and acknowledge the need to determine ways to increase the efficiency and durability of training effects.

Moffat elaborates on another relatively unexplored domain of aging cognition—spatial navigation. Particularly relevant to the issue of real-world cognitive function, declines in this domain restrict our world to smaller and smaller spaces. Plagued by difficulties in measuring this capacity effectively in humans, he offers the employment of virtual environment approaches to more effectively evaluate spatial learning and memory. By noting that vestibular function, proprioception, and vision are all employed in successful spatial navigation and that multiple cognitive processes, including spatial ability, explicit memory, working memory and executive function, are tapped, Moffat drives home his point that everyday function is the more relevant aspect to measure and currently may not be adequately assessed via one-dimensional laboratory-based tasks.

Madden, Bennett and Song provide a thorough review of the research implicating white matter change with aging as a significant contributor to declines in cognitive efficiency. Although phrenology has long been discounted as neither accurate nor useful for understanding brain function, some current functional and structural neuroimaging studies display uncomfortably similar characteristics to this defunct approach. As Madden and colleagues rightly note, “. . . cognition depends on the communication of widely distrib-

uted neural networks . . .” Their comprehensive description of diffusion tensor imaging of white matter—what it can tell us, what are the limitations, and what are the new methodological developments that may help overcome the limitations—provides invaluable insight into research methodology that most assuredly needs to be exploited in order to advance our understanding of the mechanisms underlying cognitive decline and where to target therapeutics.

Payton tackles the decidedly murky but incredibly important arena of cognitive genetic research. Individual variation has long been considered a hallmark of cognitive aging. Steps toward achieving personalized “medicine” or approaches likely will be stymied without generating and understanding individual genetic profiles. Payton’s assertion that a single gene “can perform multiple tasks at various stages of development, alter the function of other genes, act in a tissue specific manner and respond to changes in the environment” clearly demonstrates the complexity of this research and underscores the reason for his declaration that consensus in the literature of gene associations with age-related change in cognition is poor at best and more effective ways are needed to study the role of genetics in cognition. His thoughtful, specific evaluation of what constitutes shortcomings in this research field serves to shine light on how to better address these questions going forward.

So what are the next steps? What should be our collective vision for advancing cognitive aging research and delineating prescriptions for maintenance, or restoration, of cognitive health? More research opportunities, more resources, and more money head the top of most lists for what will carry us into the future. However, these suggestions lack the visionary depth and specificity necessary to move us to our goals.

In October 2007, the National Institute on Aging, in partnership with the McKnight Brain Research Foundation through the Foundation for the National Institutes of Health, held the Cognitive Aging Summit. The overwhelming response from the field just to attend the conference far outstripped the organizers’ own exuberant recognition of the excitement in the field and their understanding of the pressing need for a forum to present current findings. Although the field had long enjoyed exposure and support, albeit often in smaller and segregated (basic vs. clinical, molecular vs. organism, animal vs. human, neural vs. behavioral) venues, the Summit brought recognition at a national level and to all of the contributors and galvanized the field. Recommendations from the conference stimulated federal research solicitations that in 2009 have resulted in the award of approximately \$28 million in research funds over 5 years to research forward into neural and behavioral profiles of cognitive aging and to push translational research forward by providing for pilot intervention trials for remediation of age-related cognitive decline. To

continue the momentum, a second Cognitive Aging Summit is planned for October 2010.

Shortcomings in measurement of cognitive function were noted by several of the authors in this issue, including the oft-cited mistake, but nonetheless perpetuated use, of employing measures developed for assessing cognitive disorders to track normal age-related change in cognition. In an effort to address this problem, the NIH is developing a set of instruments to measure cognitive (and motor, emotional and sensory) function in humans that would allow assessment in individuals ranging from 3 years to 85 years of age. Designed to be a set of brief yet comprehensive measures that will allow evaluation of change over time while avoiding ceiling and floor effects, the NIH Toolbox for Assessment of Neurological and

Behavioral Function, supported through the NIH Blueprint for Neuroscience Research, is scheduled for roll-out in late 2011 and is intended to serve as a national and international resource for scientists and clinicians.

But more can, and will, be done. What a wonderful time for scientific investigators in the field of cognitive aging research and for their beneficiaries, the aging public. The opportunities, the resources, the recognition of the importance that advances in this field hold for humankind are great and are waiting to be exploited. What wonderful minds already are contributing to this field, as evidenced by the corpus of research presented in these reviews—and think of the many more wonderful minds we can recruit to this cause, bringing new perspectives and approaches to the table. What a wonder-filled world for cognitive aging research.