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Editorial

Prospects for Improving Cognition Throughout the Life Course

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Life expectancy is at an all-time high and is likely to continue to improve rapidly in the future (Wang & Preston, 2009); this, coupled with a modest birth rate, means that the proportion of older adults will continue to grow in the United States, with the strongest growth occurring in the number of "oldest old"—those over the age of 85. Absent dramatically higher levels of immigration and higher rates of productivity growth, it is likely that all of us will either be consuming far less before and after retirement or working much longer than we might have expected. The current economic crisis has resulted in huge losses in financial assets including 401(k) retirement accounts; older workers close to retirement may choose to work much longer than they expected, while some of those already retired may try to return to the labor force. In this context, it has become imperative for us to preserve or enhance cognitive functioning among older adults and to compress the duration of any cognitive decline. But what can be done to prevent and remediate age-related declines in cognition? Given the central role that cognition plays in determining an individual's independence and well-being, this becomes a very serious question for research.

Hertzog, Kramer, Wilson, and Lindenberger (2008, this issue) present what we believe is the most comprehensive review to date of the science of cognitive improvement in aging and present a clear picture of the barriers to progress in this area. Although they take a clear stand on the question of whether it is possible to remediate age-related cognitive decline (for the impatient, their answer is: Yes we can!), those holding opposing points of view will also find much value in this monograph. The National Institute on Aging (NIA) considers this topic to be one of paramount importance. In 2007, the NIA and the McKnight Brain Research Foundation cosponsored a Cognitive Aging Summit that prominently featured animated discussion of cognitive enhancement in aging (see http://www.health.ufl.edu/brain/summit/index.htm for meeting materials). NIA's research focus on enhancement spans many levels, from genes to cells to neural circuits to systems and on up through social engagement and societies. Hertzog and colleagues cover many of these levels in some detail, so we will only point out some selected areas that received less attention here and that could have important implications for the public interest and future research.

DECLINE AND FALL: WHY DO PEOPLE DIFFER SO MUCH?

Hertzog et al. do an admirable job describing how cognitive trajectories can and do differ over the life span in response to various types of enrichment, good and poor choices in individual behavior, and random shocks. They also mention the potential contribution of genes to different patterns of decline. But, strikingly, they do not mention the kinds of natural experiments that we feel clearly demonstrate how powerful differences in environment truly are, and why study of gene–environment interplay might be an important tool for understanding what enrichment truly requires.

The study of monozygotic (identical) and dizygotic (fraternal) twins can help unravel to what extent complex phenotypic features (e.g., memory performance, personality, height) are the direct product of genes, shared environment (e.g., family and other shared experience), and unshared environmental influences. Working within this framework, behavioral geneticists have consistently shown that many complex traits show substantial heritability (e.g., on the order of 50% of the variation can be explained by genes) but also notable environmental effects. This is clearly true of aspects of cognition such as processing speed, as well as for developmental *changes* in processing speed (Finkel, Reynolds, McArdle, & Pedersen, 2005). These data support the claim that the (relative) enrichment of one twin's environment over that of the other can cause their trajectories of

[1]This material is presented from the perspective of the authors, and should not be taken as representing the viewpoint of the Department of Health and Human Services, the National Institutes of Health, or the National Institute of Aging.

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cognition to diverge. Then, to the extent we can show that such divergence continues to increase later in life, we might hypothesize that enrichment can affect cognition in older individuals as well. Of course, these observations alone leave unanswered the question of *what* aspects of the environment were responsible. This is an open research question that NIA-supported researchers are pursuing using many longitudinal twin studies of aging, as well as other modern behavioral genetics approaches.

WHY (AND WHEN) DOES EDUCATION MATTER?

Another important point raised in the following monograph is that most attempts at cognitive enrichment have smaller effects on average than one might hope to see. But the duration and intensity of the interventions studied are often exceedingly modest, almost infinitesimal. One of the more powerful protective factors against the onset of cognitive decline (although not the severity of the decline once it occurs) is pre-existing level of education. As Hertzog et al. detail, it is remarkably difficult to parse out whether some people are protected because they have acquired more skills and knowledge, or whether they are protected by some other factor that also, independently, predicts that they will acquire more skills and knowledge. Perhaps there are rural communities in less developed areas of the world where children received minimal education and where this could be tested. But because education and relative cognitive preservation are correlated in the United States, the question could be moot as a practical matter.

Remarkably, the dose-response curve for education predicting most outcomes is very poorly known, and just what the active ingredient is remains unclear. It is therefore even less clear whether this ingredient could be distilled, purified, and administered when needed. The ACTIVE study (e.g., Willis et al., 2006), for example, included one arm in which *reasoning* was systematically taught, and it is this manipulation that led to a modest and delayed (5 years post-training) effect on self-reported instrumental activities of daily living. But the ACTIVE reasoning intervention included at most 10 brief sessions of training, and although this led to significant and surprisingly lasting improvement in that domain (but no transfer to other cognitive domains), it is clear that the ACTIVE intervention was a vaccination treatment with an almost homeopathic level of active ingredient. Time on task was (most likely) less than that spent by undergraduates on a single college course and orders of magnitude less than the approximately 15,000 hours of conventional K–12 education most of us receive. The ACTIVE intervention domains were chosen carefully, but cognitive theory rather than real-world applicability was the guide. Thus, given the importance of numeracy in many daily activities, not the least being financial decision making, one wonders whether something as simple as a refresher course in mental arithmetic could have positive effects on cognition and greater application to daily life than training in solving letter-sequence tasks. There is, however, also the sobering prospect that although education may be wasted on the young, this is the best developmental period on which to waste it. There is evidence that it is primarily early exposure to education and enriched environments, rather than late exposure, that might have the most pronounced effects on both cognitive and noncognitive skills in old age. Interestingly, Cunha and Heckman (2008) have recently treated this as a formal economic question about where to expend public resources.

TALKING ABOUT MY GENERATION

Decades of research also give us some confidence in the proposition that at least some aspects of cognition are steadily improving with succeeding generations. A particularly prominent and well-controlled example of the "Flynn Effect" can be seen in a comparison of the cognitive scores attained by the initial Framingham Heart Study cohort with that of their children, the Framingham Offspring (Au et al., 2004). The Framingham offspring perform approximately 1 standard deviation better than their parents on most memory tests administered at comparable ages, despite (on average) sharing the same genes. These differences must be due to either improved environments or, possibly, the effects of gene–environment interplay. Education does appear to play some role, but a substantial difference remains in the Framingham data even after adjusting for education, occupation, and gender. A full explanation of the Flynn Effect could eventually prove vital for our efforts to improve cognitive in older adults.

WHAT WE MEAN WHEN WE TALK ABOUT "COGNITION"?

One other important aspect of the Hertzog et al. contribution (and work it responds to, including Salthouse, 2006), is that it is very sensitive to the fact that cognition is a multifaceted construct and that changes in cognition with age or under remediation are hardly unitary. Essentially all real-life activities tap a wide variety of underlying cognitive abilities, but there are many very important activities that have substantial overlearned or automatic components, acquired by learning, that may well be more important than "cognitive" activities for functioning in the real world. In the words of MIT robotics expert Rodney Brooks, elephants don't play chess (although older elephants certainly do live long enough to be wise). Perhaps the most notable activity that requires the coordination of complex but largely automated processes is *driving*, which in much of the United States can define functional independence of the elderly. Interestingly, driving success (as defined by differences in crash rates) can be predicted in part by performance on the Useful Field of View (UFOV) test (Ball, Edwards, & Ross, 2007). UFOV is particularly interesting because it turns out to be trainable, and training

appears to increase older driver safety. Hertzog et al. are careful to point out that many enrichment effects are small, but even a very small effect on a very important activity (like driving) can have a major functional impact on the individual and a positive financial impact on society.

TIME FOR CHANGE

Overall, the picture painted by Hertzog et al. is fairly optimistic; it could well be possible to design interventions that, when combined with appropriate lifestyle changes, could possibly at least slow the rate of cognitive decline. This same optimism led the NIA to plan and release a request for applications (with the support of the McKnight Brain Research Foundation through the Foundation for NIH) last year. More details are given online (i.e., http://grants.nih.gov/grants/guide/rfa-files/RFA-AG-09-009.html), and we would stress that the NIA has a long-term interest in this problem. Both the following monograph and this call for applications may well owe much to the increasing public interest in remediating cognitive decline. This interest has led to an increased demand for products that are sometimes marketed as cognitive elixirs. These elixirs include purported nutraceuticals, but more recently we have seen numerous computer training programs and games offering the promise of reversing cognitive decline or preventing dementia. Unfortunately, we have very little evidence concerning the short- or long-term efficacy of any of these products; neither the Food and Drug Administration nor any other U.S. government agency is charged with approving these programs or any behavioral intervention. In the absence of such a regulatory body, it might be possible for expert and unbiased researchers to conduct comparative effectiveness and cost-effectiveness studies of the burgeoning array of products now on the market.

Given the context of seemingly high if not formidable barriers to preventing cognitive decline (or achieving transfer from one cognitive domain to another), coupled with the significant need and high public demand for effective cognitive interventions, there might be need for greater immediate incentives, perhaps a prize. Although neither the NIA nor the National Institutes of Health can offer this kind of incentive, history teaches us that such a strategy can work. For example, the Longitude Prize, funded and adjudicated by the British government in the 18th century, improved navigation by leading to the invention of extremely accurate chronometers. In the 21st century, at a time when many scientists have been working on the basic science of life extension for many years, perhaps it is time to make an even more concerted effort for cognitive extension. Beyond public funding for research on several of the challenges involved in remediating cognitive declines, perhaps there is room for a different kind of Longitude Prize to stimulate new ideas and encourage scientists to change the field of cognitive aging. Perhaps then we will finally answer the field's most pressing question: What can be done to prevent or remediate age-related cognitive decline?

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