

## Review Article

# Environmental Influences on Cognitive and Brain Plasticity During Aging

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**In the current article, we provide a critical review of the extant literature that has focused on environmental influences on cognitive and brain plasticity over the adult life span. The review includes both human epidemiological, and human and nonhuman cross-sectional and longitudinal research. We review a number of factors that have been suggested to reduce age-related cognitive decline including both formal and informal education, leisure pursuits, intellectual engagement, and expertise in different skill domains. We also examine the literature on cognitive and physical fitness training. We conclude with a discussion of the gaps in the literature and suggestions for future research.**

**T**HE goal of this review article is to examine the scientific evidence, both for and against, the old adage “use it or lose it.” This adage is widely promoted in the popular press and self-help literature, which is focused on maintaining and enhancing cognitive vitality in old age [e.g., (1)]. However, it is less clear from the scientific literature both whether and under what conditions this adage might hold. For example, does staying engaged in intellectually stimulating activities throughout the life span protect and maintain cognitive and brain function as we age? What is the role of education, lifestyle, and occupational choices, and socioeconomic status in maintaining and enhancing cognition during the aging processes? To what extent do high levels of experience and expertise in occupational and leisure pursuits serve to protect perceptual, cognitive, and motor processes? What is the role of formal intellectual training programs in the maintenance of high levels of cognitive function in the later years? Does physical fitness, and more specifically aerobic fitness, buffer cognition and brain function as we age? What can we learn from the animal literature on environmental, fitness, and training effects on brain function and structure that can be applied to our understanding of human cognitive aging and to the development of interventions to promote cognitive and brain vitality throughout the life span? These important questions will serve as the basis for our critical review of the literature on cognitive and brain aging. However, before beginning to address these questions, we will review the literature that has characterized the nature of cognitive and brain changes across the adult life span.

### CHANGES IN COGNITION AND BRAIN ACROSS THE ADULT LIFE SPAN

A relatively universal observation in both cross-sectional and longitudinal studies of cognitive aging is that performance on a multitude of tasks that require a variety

of different perceptual and cognitive processes declines across the adult life span. Indeed, this is the case regardless of whether performance is assessed in a relatively impoverished laboratory environment in which individuals push buttons in response to simple visual or auditory stimuli or in real-world tasks such as driving, interactions with medical or consumer products, or pursuing leisure activities (2–6). There is, however, an important distinction between two different types of processes that differ in their susceptibility to adult aging. It has generally been observed that knowledge-based or crystallized abilities (i.e., the extent to which a person has absorbed the content of culture) such as verbal knowledge and comprehension continue to be maintained or improve over the life span. This is in contrast to process-based or fluid abilities (i.e., reasoning, speed, and other basic abilities not dependent on experience) that display earlier age-related declines (7).

Similarly, many studies in animals have revealed declines in cognitive-behavioral abilities across the life span. Deficits are seen in both motor skill and conditioning tasks [e.g., (8,9)] and in cognitive tasks dependent upon forebrain structures [e.g., (10,11)]. While some evidence indicates that motor task deficits may reflect gross motor abilities more than functions such as procedural memory [e.g., (12)], the overall tendency, particularly in relatively inactive animals, is for declines with age.

In human aging research, there have been a variety of different theoretical explanations proffered to account for decreases in fluid or process-based abilities across the adult life span. These explanations fall into two broad classes of theories. General or common-cause explanations suggest that a common factor may be responsible for age-related declines (13). Common factor models have suggested that a number of different factors including speed of processing, working memory, inhibition, or sensory function may be responsible for cognitive decline observed across a variety

of different tasks. For example, Salthouse (6) argued that processing speed serves as a common factor in age-related cognitive decline. Assuming a model of information processing in which different processes (e.g., perception, decision making, response selection, and execution) are executed in a serial fashion, he suggested that the time to perform later operations is reduced when a large proportion of the available time is occupied by the execution of earlier operations. Thus, the slowed processing that occurs during the normal course of aging has a cascading effect on information processing. Furthermore, it is assumed that slowed processing can also result in the loss of the output of earlier processing, as a result of decay, before these outputs can be integrated with the output of later processing operations. Thus, in this way, slowed processing also leads to decrements in working memory. Similar arguments have been made for the primacy and centrality of other processes such as working memory (14), inhibition of extraneous and task-irrelevant information in the environment and in memory (15), and deficits in sensory and motor function (16,17). Indeed, a variety of studies have shown that such processes, especially processing speed, can often account for a large proportion of age-related variance across a wide assortment of tasks and environments.

Recent studies, however, have begun to suggest that multiple processes with different life span trajectories might be needed to provide a complete account of age-related changes in cognition. For example, Kramer and colleagues (18) examined the general inhibitory account of aging (15) and found, contrary to the predictions of the model, that age-related changes in a variety of different inhibitory processes were specific rather than general in nature. That is, not all types of inhibitory processes showed evidence of age-related decline [see (19–21) for reviews of this literature]. Similarly, Verhaeghen and colleagues (22) [see also (23)] found age equivalence in sequential numeric operations (i.e., adding one number to another followed by subtracting another number from the result of the initial addition operation) while observing substantial and disproportionate age differences in coordinative operations (i.e., holding some products in mind while carrying out additional computations). Such data are inconsistent with a common-cause account of cognitive aging and suggest instead that it is important to examine age-related trajectories in a variety of perceptual, cognitive, and motor processes as well as the relations among these processes across the adult life span.

Mirroring the cognitive literature, recent studies have also found regional differences in the time course and magnitude of age-related differences and changes in brain structure. Correlations between age and cortical volume have been reported to be largest for prefrontal regions, somewhat smaller for temporal and parietal areas, and small and often nonsignificant for sensory and motor cortices (24,25). In general, the disproportionate changes in brain structure across the adult life span parallel findings of age-specific changes in executive control and a subset of memory processes, which are supported in large part by prefrontal and temporal regions of the brain (26,27).

While theoretical accounts of aging declines based on animal studies have sometimes focused on specific aspects

of behavioral impairment such as spatial learning or eye-blink conditioning, the predominant tendency, perhaps because of the greater access for measurement, has been to assess differences in brain function that occur with advancing age. Two important themes have recently emerged from animal studies of aging and cognition. One theme is that cognitive impairment for specific tasks (e.g., spatial learning and memory) in some older animals is not necessarily associated with either neuronal loss or decrease in newly generated neurons at putative brain sites that underlie these specific behaviors (28,29). The other theme is that age-related cognitive impairment for a specific task can be correlated with changes in the functional properties of neurons associated with the task (11) and in transcriptional mechanisms and specific neurochemical signaling pathways that are critical for neurotransmission and synaptic plasticity in these neurons (30). Animal studies of age-related changes in cognition have been focused primarily on the hippocampal region at the behavioral, microscopic, and molecular levels, there is a gap in our knowledge with regard to identifying global changes in the brain and—at least at this point—that appears to be better understood by functional brain imaging in humans.

Changes in human brain function, as indexed by positron emission tomography (PET) and functional magnetic resonance (fMRI) studies, have also been recently examined and have resulted in a number of tentative general observations. For example, it has often been reported that older adults show lower levels of activation, in a wide variety of tasks and brain regions, than younger adults (31,32). Two different interpretations have been offered for such data. One is that aging is associated with an irreversible loss of neural resources. Another possibility is that resources are available but inadequately recruited. Although the reason(s) for under-recruitment remains to be determined, some evidence points towards the second possibility. Logan and colleagues (31) found that under-recruitment of prefrontal regions could be reduced when old adults were instructed to use semantic association strategies during word encoding.

Another frequent observation, in PET and fMRI studies, is that older adults show nonselective recruitment of brain regions. That is, relative to younger adults performing the same task, older adults often show the recruitment of different brain areas in addition to those activated in the younger adults. Indeed, one variety of nonselective recruitment, the bilateral activation of homologous brain regions, has been codified into a model of neurocognitive aging by Cabeza (33). The model referred to as Hemispheric Asymmetry Reduction in Older Adults (HAROLD) suggests that, under similar circumstances, cortical activity tends to be less lateralized in older than younger adults. An important question with regard to this asymmetry is whether the additional activity observed for the older adults is compensatory or a marker of cortical decline (i.e., a failure to recruit specialized neural processors). At present, this is an open question with some studies reporting that older adults who perform better on a task show bilateral recruitment of homologous areas, while older adults who perform more poorly show unilateral activation (34, 35) when other studies have either failed to find a relationship between laterality and performance (31) or have reported unilateral prefrontal

activation for better-performing old adults and bilateral activation for poorer-performing older adults (36). However, thus far, studies have examined performance–brain activation pattern differences across subjects. Clearly, future studies are needed to examine these relationships within subjects as a function of levels and types of cognitive challenges as well as a function of training and practice.

Given the relatively gloomy picture painted by the review of cognitive and brain changes across the adult life span, we now turn to the central topic of the article—whether it is possible to maintain or enhance cognition, brain function, and brain structure of older adults and, if so, how this might be accomplished.

#### **THE IMPACT OF EDUCATION, LIFESTYLE, AND ENGAGEMENT IN LEISURE AND PROFESSIONAL ACTIVITIES ON COGNITIVE VITALITY IN LATE ADULTHOOD**

It is well established that the impact of aging on cognitive function is complex, being influenced by both biological and environmental factors. Animal studies suggest that environmental factors such as learning directly impact cognitive function and can in some cases serve a protective function with regard to the deleterious effects of aging (37–42). These animal studies indicate that changes engendered by “enriched environments” and formal training in behavioral tasks include increased dendritic branching and synaptogenesis, changes in supportive glial cells, addition to the brain’s capillary network, and the development of new neurons presumably from adult stem cells, as well as a cascade of molecular and neurochemical changes. However, addressing this issue in humans requires an operational definition of environmental richness or cognitive stimulation. (Even in the animal studies, the use of the term “enriched” seems inappropriate when the challenge offered by a cage containing a variety of toys and other animals is contrasted with the stimulation provided by the animals’ natural environment, which is why we normally use the term “complex.”) Educational background is surely a critical experience that evolves over several decades, and its impact is likely to modulate later experiences of an individual’s life. Thus, many studies have investigated the potential impact of years of formal education on cognitive vitality. In the first part of the present section, studies that have assessed the effect of education on cognitive vitality (longitudinal designs) and age-related cognitive differences (cross-sectional designs) will be discussed in an attempt to evaluate the positive impact that a complex and stimulating environment might have on cognition.

Of course, education is not the only measure of environmental and experiential richness, nor is it a pure measure of this construct. A high level of education often leads to employment that involves high levels of intellectual challenge and cognitive stimulation, which, in turn, can often lead to large incomes, high levels of well-being, and others factors that are likely to shape lifestyle and engagement in activities over the adult life span. Given the multidimensional nature of environmental and experiential richness, other studies have controlled for educational level and examined the influence of the type of professional work pursued by individuals as well as self-reports of the

types and amounts of leisure activities as moderators of cognitive vitality in the latter part of the adult life span.

#### *Formal Education as a Predictor of Cognitive Vitality*

*Longitudinal studies.*—A substantial number of longitudinal studies that have examined the effects of education and other environmental factors on the cognitive vitality of older adults have been launched in the last 50 years, and many of them are still under way. Schaie and Hofer (43) enumerated and briefly reviewed 24 ongoing longitudinal projects worldwide that are concerned with psychological aging. In some cases, delay between initial testing (baseline performance) and follow-up testing extended to 42 years (e.g., the Seattle Longitudinal Study launched in 1956). In a recent review, Anstey and Christensen (44) reported 14 longitudinal studies that explicitly examined the effect of educational level on cognitive change (delay between time of education and time of testing ranging from 1 to 46 years). The authors observed that the relation between cognitive vitality and educational level is related to the type of cognitive measures obtained. Studies using measures of general mental status (e.g., Mini-Mental Status Examination [MMSE]), which are known to poorly distinguish among highly functioning individuals, generally showed a protective effect of education. For instance, Lyketsos and colleagues (45) tested a group of 1488 individuals aged 18 to 70 years at three occasions over 11.5 years and observed that having more than 8 years of education was associated with maintenance of cognitive function during aging.

Similarly, studies reporting change in memory measures and crystallized intelligence suggest that education has a protective effect. For instance, results from the MacArthur Studies of Successful Aging showed that low levels of education (apart from cognitive performance at baseline) was the strongest predictor of cognitive decline in measures of verbal and nonverbal memory, conceptualization, and nonverbal abilities over 2–2.5 years in a sample of 70–79 seniors (46). However, education seems to be a less powerful predictor of changes in fluid abilities and processing speed. Christensen and colleagues (47) reported that education predicted general mental status and verbal abilities (vocabulary, similarities), but not speed of processing, in a group of 70–79 seniors over a 3.6-year period, after controlling for age, health, and disability [see also (48) for a similar pattern of results with World War II veterans ranging from 62–79 years over a 45-year period].

More recent reports from longitudinal studies confirm the positive effect of education on cognitive vitality. Cullum and colleagues (49) examined cognitive changes in highly educated (>15 years) and less well-educated (<15 years) older adults aged 75–80 years. Examining results from a cognitive battery assessing perceptual, memory, and attention abilities, the authors observed greater decline in memory subscales in less well-educated individuals and decline in an attentional subscale related to work class, being greater in the manual work class. Although the authors suggest that the latter results are at odds with the observation in their study that highly correlated predictors

such as social class and education are not associated with decline in the same cognitive tests, their findings concerning education are consistent with other studies. For instance, a significant relation between education and decline in memory function was also observed in a recent report from the MacArthur Studies of Successful Aging (50). Also related to this issue, the influence of educational level on cognitive vitality appears to be at least somewhat independent of the influence of measures of socioeconomic status [income and wealth, see (51)]. Therefore, it would appear that while the relation between education and cognition can be modulated by socioeconomic status, a separate contribution of education to this relation is also observed.

Despite the apparently ubiquitous effect of education on cognitive vitality, some studies have not observed strong evidence for the education effect. A recent report of the PAQUID (Personnes [people] Agéed [aged] QUID [Latin: "about what"]) research program with a sample of 547 French seniors aged 65–94 years suggests that education is associated with better MMSE scores at baseline but does not predict decline over a 1 to 10 year period (52) [see also (53,54)]. However, the authors observed that level of formal education differed among phenotypes, being much higher in noncarriers compared to carriers of Apolipoprotein e4 (APOE e4). APOE has often been associated with greater risk of cognitive decline, and indeed APOE e4 was associated with the lowest MMSE scores in the PAQUID study. Interestingly, however, the influence of the e4 allele on cognitive performance disappeared when adjusting for education.

*Education as a modulator of age-related differences in cognitive vitality (cross-sectional studies).*—Longitudinal studies offer the advantage of providing an intraindividual assessment of the influence of education on cognitive vitality. This is especially important since the educational system has changed considerably in the last several decades, and therefore it is important to examine individuals who were educated at approximately the same time (better yet is the examination of several different-age cohorts in longitudinal studies to enable an assessment of the impact of different educational and other experiences on cognitive vitality). However, with rare exceptions, longitudinal studies have not been able to provide a fine-grained assessment of cognition given the temporal constraints of testing large populations. Given this potential limitation, cross-sectional studies can also be informative with regard to the relation of education to varieties of cognition.

Indeed, there is considerable support from cross-sectional studies for the beneficial effect of education on cognitive performance in the aged. Not surprisingly, and as observed in longitudinal studies, the influence of education was not uniform with respect to cognition. For instance, Arbuckle and colleagues (55) reported an age by social class interaction on an index score of memory performance based on free recall, memory for prose, inference, and digit span, but the interaction was not significant when controlling for education, intellectual activity, and health. An interaction between age and education was also reported by Mathy and Van der Linden (56) in story recall, low-educated elderly participants recalling fewer items than young participants and high-

educated elderly people. However, the authors observed that education did not affect recognition. Capitani and colleagues (57) also found that the effect of education differs across cognitive tasks, and reported that age-related cognitive decrements in verbal fluency and spatial memory tests were parallel in high- and low-educated people, but not in visual attention and verbal memory tests, which showed larger age-related decrements in the less well-educated group. Interestingly, there was no evidence of an interaction between age and educational level on short-term memory measures.

With regard to short-term memory, a positive effect of educational level on forward and backward digit span tasks was reported but without an interaction with age (58,59). Thus, highly educated people appear to possess better short-term memory capabilities irrespective of age. This contrasts with the education by age interaction observed in the studies reported above. Bherer and colleagues (60) argued that education might modulate the age-related difference only in tasks necessitating the allocation of substantial cognitive resources. The authors tested this hypothesis by comparing low- and high-educated individuals with the Brown-Peterson task, in which participants must recall a series of items after variable delays during which they complete an interference task (e.g., mental addition). The results indicated that, although higher task demands impaired recall, and more so for less well-educated individuals, this effect did not interact with age. Education was also found to have a larger impact than age on short-term recall, a finding consistent with Ardila and Rosselli's (58) findings.

Although the pattern of results reported here seems to suggest that short-term memory, though sensitive to age and education, is not affected by an interaction between these two factors, education seems to modulate the age-related decrement often reported in long-term memory (often verbal memory). However, Ardila and colleagues (61) warned against oversimplification of the effect of education on age-related differences based on their recent findings. The authors divided 806 participants from different Mexican regions into four groups based on educational level and four groups based on age (from 16 to 85 years). Consistent with Capitani's (57) results, when comparing the two extreme groups (illiterate vs more than 10 years of education), they observed different patterns of education effects across different cognitive measures: 1) parallelism (equivalent decline in different education groups was observed for figure copying), 2) protection (higher education lead to reduced decline in words recalled), 3) confluence upwards (less well-educated people benefited from age, as in digit-backward, especially from early adulthood to mid adulthood), 4) confluence downwards (highly educated declined and approached low-educated performance, as in verbal fluency test).

Finally, it should be noted that brain data have been reported that support these cross-sectional behavioral data. Jacobs and colleagues (62) examined, in human autopsy material, the size of dendritic fields of neurons in Wernicke's area, a language-associated brain region. Participants were categorized as having less than high school, through high school or university education. Dendritic field size measures increased with increasing amounts of education. As in the other correlative work, whether brain complexity gave rise to

educational attainment or vice versa cannot be determined from this result.

To briefly summarize, the research reviewed above clearly suggests that education can serve as an effective moderator of cognitive vitality in late adulthood. However, the specificity of this relationship and its interaction with difficulty of cognitive processing, and with other factors such as lifestyle, socioeconomic status, and occupational complexity, remains to be established.

### *Influence of Engagement in Leisure and Professional Activities on Cognitive Vitality*

*Longitudinal studies.*—It has been suggested that a cognitively stimulating environment can lead to high levels of intellectual function in late adulthood. To assess the effects of environmental factors other than education, researchers have investigated the role of professional work, membership in academic or scientific societies, and cognitively challenging leisure activities. A recent study by Schooler and colleagues (63) provides an exemplar of how such studies are constructed and implemented. In this study, a nationally representative sample of men and women who had participated in previous studies, in 1964 and 1974, of work and intellectual functioning and who were still employed in 1994/1995, were interviewed as to their current employment status. These individuals also completed a battery of cognitive tasks. The complexity of work was defined on the basis of the extent to which the position entailed thought and independent judgment. Intellectual function was measured in two different ways. Intellectual flexibility was assessed through the completion of a portion of the Embedded Figures test and an interviewers assessment during a series of standardized interactions (e.g., a rating of the quality of the participants' answers to questions like "What are all the arguments you can think of for and against allowing cigarette commercials on TV?"). Cognitive function was assessed through the administration of a set of standardized memory, verbal ability, fluency, and visuospatial tests.

The main finding of this research was that the level of complexity of an occupation positively influences the level of intellectual functioning for both men and women. Furthermore, this relationship between occupational complexity and intellectual function increases with age. Similar effects have been reported in other studies of the relationship between occupational complexity and intellectual functioning in the United States, Poland, Japan, and the Ukraine (64–70). Schooler and Mulatu (71) reported additional evidence of a relationship between cognitively complex activities and cognitive functioning when leisure time activities are considered. Cognitively stimulating leisure activities were defined as activities such as the number of books and magazines read, numbers of hobbies and other interests, and so forth. Results indicated that participation in such activities was associated with high levels of cognitive function.

Hultsch and colleagues (72) examined the relationship between an engaged lifestyle, as defined by participation in a variety of intellectually challenging activities, and cognition. High levels of participation in activities associ-

ated with an engaged lifestyle, and particularly novel information-processing activities (e.g., learning a new language or a game such as Bridge), were associated with higher levels of cognitive function over a 6-year period. However, the directionality of the relation, over the 6-year period, between engagement in novel activities and cognitive vitality was ambiguous. As suggested by Pushkar and colleagues (73), the ambiguous and somewhat modest relationship between lifestyle engagement and cognitive function may be due, in part, to the high mean level of education of the participants in the Hultsch and colleagues study (44% had more than 14 years of education and 83% at least 11 years). It is conceivable that an engaged lifestyle may have a larger influence on the cognitive vitality of an educationally heterogeneous group of older adults [see (74)]. Indeed, this proposal is consistent with the results of a study conducted by Christensen and colleagues (75) in which the relationship between lifestyle engagement and cognitive change over a 5-year period was stronger for blue-collar workers than elite academics.

*Cross-sectional studies.*—One limitation of the longitudinal studies reported above was the relatively short time delay over which cognitive changes were measured [see (48,74) for an exception]. Indeed, it has been argued that the magnitude of cognitive decline is smaller in longitudinal studies compared to cross-sectional studies in which age groups differ by many decades (76). Thus, it might be useful to examine the influence of engaged lifestyle on cognition in cross-sectional studies. However, caution is in order in considering the results of these studies given the potential for cohort effects and self-selection biases.

Shimamura and colleagues (77) compared three age groups of university professors in aspects of cognition known to be highly sensitive to age including speed of processing (simple and choice RT [reaction time]), long-term memory (paired-associate learning and prose recall), and working memory (self-ordered pointing task). They observed slower decline in measures of proactive interference and prose recall for the university professors than for the control participants. However, similar patterns of decline were observed for both groups on measures of reaction time, paired-associates memory, and some aspects of working memory. Compton and colleagues (78) also assessed cognitive function in 102 highly active professionals (94 of who were college professors) divided into four age groups (mean educational level was 19–20 years in each group). This study also showed that cognitive measures influenced by speed of processing (Trail, Digit) and inhibition (Wisconsin Card Sorting Test) were sensitive to age, even after controlling for education. However, memory measures were not sensitive to age in this highly selected group.

In these two studies, it is assumed that professional commitment is associated with the level of cognitive stimulation. However, other authors have defined cognitive engagement more broadly. For example, Salthouse and colleagues (79) had 204 adults between the ages of 20 and 91 years complete a self-report checklist of the frequency with which they participated in a variety of different activities associated with different levels of cognitive

stimulation. These same individuals also completed a battery of cognitive tasks. Results failed to provide support for the cognitive engagement hypothesis. That is, individuals who rated themselves as having high levels of participation in cognitively stimulating activities fared no better in their assessments of cognition than participants who had lower ratings of cognitive engagement. Interestingly, individuals scoring below the median on selective components of the cognitive function composite did display a significant relationship between a need for cognition measure and cognitive performance.

*Summary and Hypotheses Concerning the Relationship Among Education, Engaged Lifestyle, and Cognitive Vitality in Late Adulthood*

*Summary of general findings.*—The studies reviewed in the present section differ in terms of their methodological approach (longitudinal vs cross-sectional), sample (some involved poorly educated individuals and others involved fellows of elite scientific societies), statistical methods, and measures of environmental complexity and cognitive stimulation. Despite this diversity, some generalities emerged from our review. First, environmental factors appear to have greater impact on general (e.g., MMSE, memory composites) than specific measures of cognitive decline. Second, many of the general cognitive ability and memory tests that were sensitive to environmental factors were heavily loaded on aspects of verbal ability and knowledge (i.e., crystallized abilities). A third observation that emerged from both longitudinal and cross-sectional studies is that environmental factors seem to have a rather weak effect in homogeneous samples of participants, such as highly educated individuals or members of elite groups. Fourth, environmental factors seem to have a larger moderating effect on cognitive aging in studies that assess age effects over several decades. Finally, the causal relation between environmental stimulation and cognition remains a matter of considerable debate. Whereas Schooler and colleagues (63) suggests that a rich and stimulating environment enhances cognition in old age, recent findings suggest a reciprocal or bidirectional relation between cognitive status and cognitive stimulation (71,72).

*Some hypotheses concerning the relationship between cognitive stimulation and cognition during aging.*—Two general classes of nonmutually exclusive hypotheses have been proposed to account for the potential beneficial effects of education on cognitive aging. Given the close relationship between education and cognitive stimulation over the life span, these hypotheses may also be relevant for other environmental and lifestyle factors. One account, proposed at the level of cognitive psychology, posits a compensatory effect of education that occurs as a result of accumulated knowledge and verbal abilities (47). According to this view, the positive effect of education on age-related cognitive decrements is task specific. Specifically, positive effects would be more evident on tasks that involve crystallized intellectual skills, such as verbal and reasoning abilities, but

less evident for fluid abilities such as processing speed and working memory. This position is consistent with much of the research presented above.

The second account, proposed at the level of neuronal structure and function, suggests that complex and stimulating experiences provide reserve capacity and thus the preventive effect of education on cognitive decline may be explained by protective neurological effects. This may be accomplished through enhanced neuronal structure and brain function as a result of the additional environmental stimulation associated with high levels of education (62,80,81). Thus, education may protect against neurodegeneration. Alternately, enhanced neuronal networks engendered via education might delay cognitive decline even in the face of morphological and functional deterioration in the aging brain. Indeed, these two possible accounts are not mutually exclusive and may both support the beneficial effects of education and engaged lifestyle effects on cognition in the later adult years.

In addition to the direct measurements by Jacobs and colleagues discussed above, there is increasing support in the literature for education-based brain reserve effects, although the direction of the effects must generally be inferred. (To what degree does educational level achieved reflect initial brain capacity, and to what degree does brain capacity reflect the effects of education?) For example, a prospective analysis of the Canadian Study of Health and Aging (82) [see also (83)] based on more than 4000 persons aged 65 years and older showed that low levels of education are associated with a greater risk of Alzheimer's disease. Cognitive stimulation as achieved through intellectual activities (reading books and newspapers, playing games, and so forth) has also been associated with lower risk of Alzheimer's disease in a recent longitudinal study (mean follow-up, 4.5 years) with 801 older Catholic clergy members (84). A second type of evidence supporting the brain reserve hypothesis comes from quantitative MRI studies that have compared brain structure among seniors of different educational backgrounds. Koga and colleagues (85) recently reported a significant relation between white matter lesions, cerebral atrophy, and low levels of education in a sample of nondemented older adults living in the community (but with a MMSE lower than 24). In another study, Coffey and colleagues (86) reported that, among cognitively intact seniors (MMSE greater than 24), each year of education was associated with an increase in peripheral (sulcal) cerebrospinal fluid, an indirect marker of cerebral atrophy. This result was obtained after controlling for age, sex, and a number of other potentially confounding factors. Such a pattern of results may be interpreted to suggest that high levels of education can delay cognitive decline even in the face of increasing cerebral atrophy. However, such data must be cautiously interpreted given the cross-sectional nature of the study, high proportion of healthy individuals in the sample, indirect measure of cortical atrophy, and potential for other variables that covary with education, such as socioeconomic status, to account for age-related brain and cognitive decline.

*Animal brain aging and environmental factors.*—Whether environmental factors and sociodemographic variables

such as educational background have a compensatory or protective influence on cognitive vitality in later adulthood does not solve the directionality problem, or causal link. It might be the case that initially gifted individuals pursue formal education for a longer period of time or become more easily engaged in cognitively complex activities. Moreover, socioeconomic status should also be considered as a partial determinant of formal education and other complex and intellectually challenging experiences. These possibilities make it difficult to determine the directionality of the relationship between education (or other significant cognitive experiences) and cognitive functioning in old age. One arena that addresses these issues are animal studies in which random assignment equates intrinsic strengths and allows more specific assessment of the contribution of experience to, for example, brain structure. Studies in which experience is manipulated during development provide a model, for example, for the effects of education. The conclusions from these studies are generally quite clear and consistent. Exposure of comparatively young rodents or nonhuman primates to challenging experiences such as complex, or "enriched," environments and learning opportunities alters brain structure and function in dramatic ways. Not only are neurons and the synapses through which they communicate altered by such treatment, but other components of the brain, such as the glial cells that permit and enhance neuronal function, are dramatically altered [e.g., (39,42,87–89)]. Most of these effects also occur—although often more slowly—in the mature and even in the "middle-aged" brain [e.g., (37,38,90)], becoming more restricted at more advanced ages (91,92). While changes in some elements of the brain, such as astrocytes, tend to be transient, those in neurons tend to persist (93,94) and hence could underlie a neural reserve that appeared at advanced ages. Of course, truly elderly rodents and primates are rarely if ever seen in their natural environments. In any case, studies of experience and learning effects on the brain in animals argue strongly for the possibility of an experience-induced reserve capacity in brain structure and function. It is important to restate that these experience effects are widespread, affecting glial cells (by far the most common cell type in the brain) and blood vessels as well as neurons and their synaptic connections.

One of the most remarkable and highly reproducible findings in the last 5 years is neurogenesis observed in brains of adult animals and its modulation by their engagement in physical exercise and learning-memory tasks (40). Neurogenesis in adult brains is also affected by stress and related hormones, estrogen, and by neurotrophic factors associated with exercise [see review (95–97)]. Neurogenesis in the hippocampus and olfactory bulb of rodents, primates, and humans is sustained from early postnatal life to old age (98–101). Recent studies have suggested that neurogenesis can also be found in neocortical association areas such as the prefrontal and posterior parietal cortices (102,103) and olfactory-related cortical areas such as the piriform and inferior temporal cortices (104) of adult primates and anterior neocortex of rats (103). However, other investigators using similar methodological approaches with appropriate experimental controls have not been able to substantiate cortical

neurogenesis in the frontal and prefrontal cortices of adult nonhuman primates (105,106) and neocortex of mice (107,108). This issue of cerebral cortical neurogenesis in adults remains hotly debated (109–114) and has immense clinical implications for potential treatment of brain injury and for maintenance of cognitive vitality.

A voluminous body of literature is available regarding hippocampal neurogenesis and its modulation by environmental and experiential factors. Because of the importance of the hippocampal region to memory and learning, it is important to point out that a number of studies have documented, in both rodents and monkeys, an aged-related decline in neurogenesis in the dentate gyrus (98,100,115,116). More specifically, a decrease in mitotic activity of neuronal precursor or progenitor cells in the subgranular zone and in subsequent proliferation of their progeny into the granule cell layer has been consistently demonstrated and may contribute to a functional decline of the hippocampus. Numerous studies have demonstrated up-regulation of adult hippocampal neurogenesis in adult animals exposed to "enriched" or complex environment such as those discussed earlier (40,117–120). The experience-induced neurogenesis was positively correlated with general improvements in performing tasks that tested spatial learning and memory. Further studies have shown that the opportunity for physical activity increases cell proliferation, cell survival, and net neurogenesis in the adult hippocampal dentate gyrus (121) and improves hippocampus-dependent spatial learning and enhances long-term potentiation (synaptic plasticity) in the dentate gyrus (122). Other studies have suggested that the learning component of exposure to a complex environment increases neurogenesis and new cell survival (123). The evidence showed that training on associative-learning tasks requiring hippocampal participation increased neurogenesis in the adult dentate gyrus, whereas, training on associative-learning tasks that were hippocampus independent did not increase neurogenesis. The impact of results from all these studies is tempered by the fact that few new neurons were generated in the senescent dentate gyrus and little is known about their long-term survival, functionality, and contribution to behavioral performance. One issue that has not been addressed is whether experience at an earlier age can affect the potential for neurogenesis at subsequent ages, which might render this a unique basis for reserve capacity. A number of laboratories have attempted to establish a causal relationship between newly generated neurons in the adult and learning. Shors and coworkers (124) showed that reducing the number of newly generated neurons in the dentate gyrus by using a systemic toxin for proliferating cells impaired hippocampal-dependent but not hippocampal-independent forms of associative memory formation. Appropriate controls were used to reduce neurogenesis but not induce death of mature hippocampal neurons, permanently alter the function of CA1 hippocampal neurons (long-term potentiation (LTP) responses), or alter levels of motor activity. Moreover, they found that recovery of neurogenesis was concomitant with associative memory formation. Their studies suggest that formation of hippocampal-dependent memory not only increases neurogenesis

and new cell survival (123) but these newly generated neurons may contribute to the formation of hippocampal-dependent memory. A subsequent study reported that neurogenesis may not be associated with all types of hippocampal-dependent memories (125). Using a different experimental approach to establish a causal link between neurogenesis and learning, Kemperman and Gage (126,127) showed in strains of recombinant inbred mice a significant correlation between the level of new neurons generated in the dentate gyrus and level of performance in hippocampal-dependent tasks that involved the acquisition of new information. These elegant sets of studies are supported by the physiological findings of Snyder and colleagues (128) who showed a causal relationship between neurogenesis and dentate gyrus LTP. They reported that reducing new cell proliferation in the dentate gyrus by gamma radiation treatment selectively blocked LTP in the dentate gyrus and thus the participation of new neurons in functional plasticity. A recent study by van Praag and colleagues (129) convincingly showed that such newly generated cells in the adult dentate gyrus have a neuronal morphology and mature into functional neurons with characteristic electrophysiological response properties.

From these exciting findings, there are a number of intriguing but important questions that can be posed to guide future studies. How long do newly generated, hippocampal neurons in adults survive, and what factors affect their longevity? Is their longevity dependent on continued exposure to the environmental conditions (i.e., physical activity, associative learning) that induced their generation, or dependent on exposure to nonspecific environmental and task demands? Do these new neurons remain functionally specialized, or do they become functionally generalized? Are there enough newly generated neurons at a given time that would contribute significantly to improved behavioral performance? How are these new neurons integrated morphologically and functionally with the existing neurophil and neural networks?

A number of recent studies have been seeking answers to some of these questions, and we expect that more studies along these lines will be forthcoming. Gould and colleagues (103) have found that newly generated cells in the adult neocortex of nonhuman primates have a transient existence; their numbers declined between 2 and 9 weeks. In contrast, Kempermann and colleagues (130) showed that new neurons generated in the hippocampus of adult mice were not transient, and their numbers remain stable in the granule cell layer for at least 11 months (maximum observation period). These investigators have proposed a cogent functional scenario in which new neurons are morphologically and functionally integrated into the neuronal network of the dentate gyrus over a lengthy period. Because functional integration of new neurons within a short time period is unlikely for processing complex environmental information that initiated the neurogenesis, these new neurons that become integrated with older neurons will more likely process novel and challenging environmental information in the future.

*Potential interactions between genetic and environmental factors.*—A different way to address the issue of di-

rectionality of effect between predispositions and intrinsic strengths and environmental and experience variables with regard to performance is to examine interactions of experience with genetic differences. For example, recent studies have assessed the relation between education and genetics with regard to cognitive aging. The e4 allele of the APOE gene has often been associated with greater risk of memory impairment and dementia in late adulthood. Thus, one could ask whether the potential role of this genetic factor comes into play early in life. Indeed, the relationship between polymorphism of the APOE gene and predisposition to higher education has been studied. Unfortunately, inconclusive results have been obtained. For instance, Hubacek and colleagues (131) reported that, in a sample of 366 participants aged 25–64 years, e4 carriers attained a higher level of school education. This contrasts with the prediction that e4 is associated with lower cognitive performance. It also contrasts with results from the PAQUID study, which showed that e4 carriers are those who completed less formal education than non-e4 individuals. Further studies with larger samples will be needed to clarify the potential relationship between cognitive function and APOE gene polymorphism and potentially with other genetic factors (131). Ultimately, this will provide better understanding of the relationship between environmental and genetic factors that potentially influence the course of cognitive aging.

#### EXPERTISE AND EXPERIENCE AS POTENTIAL MEDIATORS OF COGNITIVE VITALITY

The question of whether expertise or experience, often acquired over a substantial portion of the adult life span, can (a) reduce age-related decline in basic perceptual, cognitive, and motor processes or (b) aid in the development of domain general or specific strategies that can compensate for the impact of aging on complex skills or their component processes, has been addressed in a variety of studies over the past couple of decades.

In many ways, these studies are similar to other research, reviewed above, in which the influence of an “engaged lifestyle” or intellectually challenging activities have been examined as possible moderators of cognitive decline. However, in the present case, the studies focus on specific types of work and attempt to relate high levels of expertise in selective professional domains to specific aspects of cognition.

Research has focused on the development of high levels of expertise in content areas, such as driving, flying, music, medical technology, graphic art, architectural design, typing, and complex game-playing, and the role that high levels of expertise play in the moderation of age-related declines in intellectual function. These studies have often been conducted within the context of a specific research strategy referred to as the molar-equivalence molecular decomposition strategy (132,133). This research strategy entails three main steps. First, individuals are selected who differ widely on both age and skill but for whom the correlation between these two factors is near zero. Second, the influence of age, skill, and their interaction on a series of component processes of the task/skill of interest is

examined. Third, the influence of age and skill effects on basic perceptual, memory, and motor processes not considered to be relevant to the skill of interest is examined. Within such a research framework, expertise might be said to moderate age-related decline in performance to the extent that older highly skilled individuals showed a smaller performance decrement than older less-skilled individuals on the skill-based component tasks. In other words, older and younger highly skilled individuals should perform more similarly than less-skilled old and young individuals. The extent to which such effects were also found for the non-skill-related tasks would provide an assessment of the degree of generality of the expertise effects on age-related differences in cognition.

The molar-equivalence molecular decomposition research strategy has been applied in a number of domains of expertise. For example, Salthouse (134) examined the performance of young and old adult typists on both domain-specific (i.e., typing tasks) and less domain-specific tasks (i.e., tapping, choice reaction time). He found a significant age-related decline in the performance of the general psychomotor tasks but no age-related deficit in measures of typing proficiency. Furthermore, the older typists demonstrated an interesting compensatory strategy, which likely minimized the general decline in processing speed on typing speed. That is, the older typists displayed a greater ability than the young typists to use preview of the text to decrease their interkeystroke times, thereby enhancing their typing span. Thus, the older typists were able to employ their accrued knowledge of the task domain to implement a strategy that compensated for declines in processing speed.

Bosman (135,136) replicated and extended Salthouse's typing studies. In addition to finding preview benefits for older typists, Bosman also found evidence for other experience-based benefits for older typists. In a series of component tasks that entailed making rapid responses to multiple sequentially presented letters, Bosman found significant age  $\times$  expertise interactions for the time it took to type the second of two responses to a stimulus pair. That is, while large age-related response time differences were found for the initial response, age-related differences were substantially reduced for the second response. A significant age  $\times$  expertise effect was also found for a multiple finger-tapping task. Bosman interpreted these results as suggesting that expertise moderates execution but not stimulus-response translation processes. Thus, it would appear that both compensatory strategies (i.e., preview effects) as well as selective sparing of task-relevant component processes (i.e., execution processes) can be obtained, at least with a well-practiced psychomotor task such as typing.

Similar age-related expertise-based effects have been observed for complex game-playing, such as Chess and Go (132,137,138), as well as in professions such as piloting (133,139–142), medical laboratory technical work (143,144), and for musical professions (145). However, age-related expertise effects have not always been observed (133,146–148). While the reasons for the discrepancy among the studies that show age-related expertise benefits on either component task processes or the development of compensatory strategies and the studies that do not observe

such effects remain an open question, there are several reasonable hypotheses that bear further study.

First, given the high degree of specificity of most skills, it is perhaps not surprising that there have been failures to observe expertise effects on a wide variety of cognitive processes. The breadth of transfer effects, from expertise developed in the arts, leisure pursuits, and occupations, to basic cognitive processes and compensatory strategies, is an important topic for future research. Second, Krampe and Ericsson (145) [see also (149)] have observed, in their study of pianists and other artists and athletes, that it is not the performance of the skill per se but deliberate practice (i.e., repeated practice on important skill components and their integration) on the skill that predicts maintenance of skill-related performance for older experts. These results suggest that the nature and measurement of expertise and the manner in which it is enhanced and retained across the adult life span is an important issue for further study. Third, some of the studies that have failed to observe that expertise can reduce age-related decline on domain-relevant tasks have done so in situations in which either relations between age and performance or expertise and performance on component tasks were weak [e.g., (146,150)]. In such situations, considerable power will be necessary to detect expertise effects on age-related differences in component task performance. Finally, studies of expertise and aging have not, for the most part, examined the influence of lifestyle, socioeconomic status, education, and other potentially important factors (e.g., personality factors, acute and chronic medical conditions) on expertise–age relations.

Despite these concerns, the literature that has examined the moderating effects of expertise and experience on the cognitive vitality of older adults does permit some tentative conclusions. First, cognitive sparing appears to be domain specific, rather than general. That is, expertise effects on the cognitive processes of older adults tend to be both more consistent and more substantial with component tasks that are similar to the complex skills on which expertise is expressed than for more general cognitive tasks. Second, in many cases the expertise  $\times$  age interactions appear to be compensatory in nature rather than directly influencing the component processes. For example, well-developed and elaborate conceptual models of relevant domain knowledge appear to enable the older expert to bypass perceptual, cognitive, and motor processes that decline with age (137,140,143,151). Third, expertise benefits in the form of age  $\times$  expertise interactions appear to depend on the maintenance of deliberate practice rather than just the performance of the complex skills and tasks (145,149).

#### **PRACTICE AND TRAINING AS MEANS TO MAINTAIN THE COGNITIVE VITALITY OF OLDER ADULTS**

Over the past several decades, a substantial literature has been devoted to address the question of whether and to what extent older adults can benefit from laboratory-based training on specific perceptual cognitive and motor skills. The results of this literature clearly suggest that older adults, like younger adults, can benefit from such training programs. However, it is also clear from the literature that the magnitude of the training effects observed for older

adults as compared to training benefits observed for younger adults have differed as a function of the processes examined and training methods employed.

In general, old and young adults have been found to learn new tasks and skills at approximately the same rate or to show the same magnitude of training gain (152–154). This finding has been observed across a wide variety of tasks including perceptual discrimination, visual search, recognition, recall, and spatial perception. Such data clearly suggest that older adults can learn new skills. However, given that older adults' baseline performance on most tasks is lower than that observed for younger adults, these data also suggest that age-related differences in level of performance will be maintained at posttest.

For example, Scialfa and colleagues (155–157) conducted a number of studies in which they examined improvements in performance of young and old adults on a variety of consistently mapped feature and conjunction visual search tasks. In general, they found that young and older adults improved at similar rates. Interestingly, when the role of the targets and distractors were reversed, they also found large and age-equivalent disruptions of performance, particularly for targets that appeared close to fixation. This is an important observation since disruption effects, when the role of consistently mapped targets and distractors are reversed, suggest that subjects have automatized their search processes (158).

Fisk, Rogers, and their colleagues (159–163) also examined age differences in the development of automaticity in a variety of search (visual, memory, and semantic search) tasks. Given the results of the research discussed above, one might expect similar patterns of learning and disruption effects upon reversal of the role of targets and distractors for young and old adults. However, instead, it was observed that, in consistently mapped tasks, younger adults showed faster rates of learning and larger disruption effects with the reversal of targets and distractors than did older adults. Such a pattern of results was interpreted as evidence of a failure for the older adults to automatize search performance.

An important question concerns the reason for the discrepancy in aging effects in the search tasks employed by the two different research groups. Although an unequivocal answer must await further research, one reasonable hypothesis concerns the nature of the tasks that participants performed. Scialfa and colleagues had the participants perform what are traditional visual search tasks, that is, search for a single target among distractors. On the other hand, Fisk, Rogers, and colleagues often had participants search for multiple targets (in essence, a memory search task) among multiple distractors (a visual search task).

Given the observation that older adults often have difficulty with large working memory loads as well as in switching between heterogeneous tasks (164,165), it is perhaps not surprising that the evidence for age-related equivalence in learning to perform the search tasks was not obtained when the tasks included both memory and attentional components. Thus, contextual constraints and additional processing requirements may limit the training benefits on visual search found for older adults.

The research described above concerning age differences in the learning of visual and memory search tasks illustrates

an important point, that is, that the extent to which old and young adults show similar practice benefits depends on the nature of the processes and skills being examined [see also (166–169)]. However, there have been, in recent years, some interesting exceptions to the general observations of age-equivalent and age-deficient training outcomes. For example, Baron and Mattila (170) examined the influence of training on the speed and accuracy with which young and older adults performed a memory search task, that is, a task in which they compared probe items to items stored in memory. Participants were trained for 44 hours with a deadline procedure in which they were required to constantly increase the speed with which they performed the task. Prior to training, young and older adults performed the memory search task with comparable accuracy but the older adults were substantially slower than the younger adults. During training with the deadline procedure, both young and older adults performed more quickly but with a substantially elevated error rate. Most interestingly, when the deadline procedure was relaxed, both young and old adults performed with equivalent accuracies, and the response time differences between the groups were substantially reduced. Thus, these data suggest a more substantial improvement in performance related to speed of responding for the old adults than for the younger adults [see also (171) for an age-related decrease in the effects of complexity on performance with practice].

A similar pattern of results was obtained in the study of training effects on the dual-task performance of young and old adults (172) [see also (173)]. Young and old adults were trained to concurrently perform two tasks, a pattern learning task and a tracking task, with either of two training strategies. In the Fixed Priority training strategy, participants were asked to treat each of the tasks as equal in importance. In the Variable Priority Training procedure, participants were required to constantly vary their priorities between the two tasks. On-line performance feedback was presented in both training conditions.

Several interesting results were obtained. First, consistent with previous studies, young and old adults improved their dual-task performance at the same rate with the fixed priority training strategy. Second, variable priority training led to faster acquisition and a higher level of mastery in performing the tasks together than did fixed priority training. Furthermore, individuals trained in the variable priority condition also displayed superior transfer to untrained tasks and better retention of timesharing skills, over a 2-month period, than did those individuals trained in the fixed priority condition. Finally, and most importantly, age-related differences in the efficiency of dual-task performance were substantially reduced for individuals trained in the Variable Priority condition [see also (174) for another example of diminished age effects with practice in task switching].

An obvious question concerning the Baron and Mattila (170) and Kramer and colleagues (172) studies is why these projects and several others have observed decreased age-related performance differences with training while many other studies have observed age-equivalent training effects. Although there is quite likely not a single answer to this

question, one possibility centers on the nature of the training procedures. Both the Baron and Mattila and the Kramer and coworkers training strategies (i.e., the Variable Priority strategy) explicitly focused on aspects of performance on which young and older adults showed large differences. For example, one may conceptualize the Baron and Mattila deadline strategy as encouraging individuals to shift their response criterion from emphasizing accurate to emphasizing speeded performance. Given that older adults typically emphasize accuracy rather than speed (175), the deadline strategy may be well suited to older adults. Similarly, older adults have been observed to have difficulty in flexibly setting and modifying processing priorities. The Variable Priority training strategy explicitly targets this skill. Indeed, while Sit and Fisk (176) found a decrease of age-related dual-task performance decrements with training, they also observed an increase in age-related performance differences when task emphasis instructions were changed. Interestingly, they did not formally train their subjects to shift priorities among multiple tasks. Thus, although additional research is clearly needed to further examine the techniques and situations in which the age gap in performance can be reduced, one potentially fruitful area of inquiry concerns targeting training strategies to specific difficulties encountered by older adults.

The research described thus far in this section has focused on cross-sectional differences between young and older adults in practice and training effects. There have also been a small number of studies that have examined training effects in longitudinal designs. Such studies have the clear advantage of asking whether individual patterns of cognitive change, which occur over substantial periods of time, can be influenced by formal training. An exemplar of this type of research is provided by a study conducted by Schaie and Willis (177) [see also (178)]. Study participants were recruited from among individuals in the Seattle Longitudinal Study, a long-term examination of cognitive change across the adult life span. Participants were classified as to whether they showed small or large deficits in either inductive reasoning or spatial cognition over a 14-year period. Individuals in both categories received either 5 hours of inductive reasoning or spatial orientation training. Forty percent of the individuals who showed substantial decline on spatial cognition or inductive reasoning showed training improvements that resulted in performance on the trained ability equivalent to what the individuals demonstrated 14 years in the past. Individuals who showed smaller performance declines, across the 14-year period, also benefited from training. Importantly, training benefits were specific to the nature of training. That is, individuals improved only on the trained ability—either spatial orientation or inductive reasoning. In a follow-up assessment, Saczynski and Willis (179) found that training benefits were retained for at least another 7 years.

In a study conducted by Willis and Nesselraode (180), participants in their late sixties were followed over a 7-year period, with a subset of the participants receiving training on figural relations (i.e., the identification and use of rules and patterns to classify figural material). Participants in the training group showed significantly larger pre-post test

gains on tests of figural relations (which were independent of the problems used for training). Indeed, 64% of the participants in the training group scored at or above their baseline performance obtained 7 years in the past, while only 33% percent of the control participants achieved this level of performance. Thus, these data, like those obtained in the Schaie and Willis (177) study, suggest that older adults can show substantial but narrowly defined training benefits and that such benefits can be retained over substantial periods of time.

In spite of the impressive results obtained in the studies discussed above, the sample sizes were quite small, a small number of different cognitive abilities were assessed and trained, and transfer of the trained abilities outside the laboratory was not assessed. These concerns were recently addressed in a relatively large-scale randomized clinical trial of three different cognitive training interventions. Ball and colleagues (181) randomly assigned 2832 older individuals (aged 65 to 94 years) to three different cognitive training interventions or a control group. Individuals assigned to the training groups received 10 sessions of group training for verbal episodic memory, inductive reasoning, or speeded processing in a divided attention task. Sixty percent of the participants received four sessions of booster training 11 months after initial training. Each of the training programs produced an immediate improvement in the trained ability. Furthermore, these improvements were maintained for the 2-year period of the study. Booster training also had positive effects for the reasoning and speed groups, with the speed group also showing small benefits for proximal outcome measures including activities of daily living (ADLs), instrumental ADLs (IADLs), and an everyday speed measure. However, no significant effects on measures of everyday functioning were observed at the 2-year follow-up assessment.

The results of the Ball and colleagues (181) study are important in that they provide, for the first time in a randomized clinical trial, evidence for relatively stable benefits of cognitive training over a 2-year period. The failure to find stronger transfer effects to everyday tests of cognition is perhaps not surprising, given previous findings in the expertise and aging literature of narrow training benefits (140,141,143,145). Future studies of cognitive training as a means to reduce age-related decrements in complex skills might consider designing training programs that incorporate components of the skills of interest in the training protocol. Since complex real-world skills and tasks often require a multitude of cognitive processes, it may also be important to design cognitive training interventions that are not limited to a single process (such as reasoning, processing speed, or verbal episodic memory) but instead to incorporate a number of processes in the training program. Given the demonstration that participation in novel and varied activities is associated with spared cognition in later life (72), such activities might also be incorporated into future studies of formal training. It is also important to note that the participants in the Ball and colleagues (181) study were very high-functioning older adults and therefore potential training benefits may have been masked by ceiling effects in task performance. Evidence in support of this hypothesis was provided by the minimal decline in the

control group over the 2-year study period. Thus, future studies might include participants across a wider range of functional abilities to determine if larger training benefits are observed for lower-functioning older adults, as appears to be the case for engaged lifestyles (75,79).

#### **HEALTHY BODY, HEALTHY MIND?: THE INFLUENCE OF FITNESS TRAINING ON COGNITIVE AND BRAIN FUNCTION**

The study of the relationship between fitness, aging, and cognition dates back several decades to the pioneering research of Spirduso and colleagues (182,183). These researchers found that older athletes were significantly faster on a variety of different reaction time and movement time tasks than older nonathletes. Indeed, in many cases, the older athletes' performance was similar to that exhibited by younger low-fit adults. These initial observations were confirmed in numerous subsequent studies on cross-sectional fitness differences on the performance and cognition of older adults [see (184) for a review of this literature].

However, longitudinal studies in which older adults were randomly assigned to either aerobic fitness or control groups produced a more varied pattern of results with some studies reporting improvements in aspects of cognition with fitness training [e.g. (185–188)] while other investigators failed to observe a relationship between improvements in fitness and cognition [e.g., (189–191)]. Interpretation of these data is complicated by the variety of differences among the studies in the length, intensity, and type of fitness training regimens, the age, health, and beginning and ending fitness levels of the study participants, the methods used for the assessment of cardiorespiratory fitness, and the tasks used to index perceptual, cognitive, and motor function improvements.

Recently, Colcombe and Kramer (192) conducted a meta-analysis to ask whether (a) fitness effects on cognition could be discerned when aggregating data across longitudinal studies, and (b) whether these effects, if observed, are moderated by other variables such as age, length and intensity of fitness training, the nature of the tasks used to assess cognition, and so forth. Fitness intervention studies conducted from 1966 through 2001 were included in the analysis. Several interesting and potentially important results were obtained in the meta-analysis. First, a clear and significant effect of aerobic fitness training was found. Thus, when aggregating across studies, fitness training does indeed have positive effects on the cognitive function of older humans. Second, fitness training had selective effects on cognitive function. Although fitness effects were observed across a wide variety of tasks and cognitive processes, the effects were largest for those tasks that involved executive control (i.e., planning, scheduling, working memory, interference control, task coordination) processes. Executive control processes have been found to decline substantially as a function of aging (18,193) as have the brain regions that support them (25). Therefore, the results of the meta-analysis suggest that even processes that are quite susceptible to age-related changes appear to be amenable to intervention.

The meta-analysis also revealed that a number of other moderator variables influenced the relationship between

fitness training and cognition. For example, fitness training programs that were combined with strength and flexibility training regimens had a greater positive effect on cognition than fitness training programs that included only aerobic components. This effect may be the result of increases in the production of insulin-like growth factor-1 (IGF-1), which has been shown to accompany improvements in strength. IGF-1 is a neuroprotective factor that is involved in neuronal growth and differentiation (194,195). Fitness training programs also had a larger impact on cognition if the study samples included more than 50% females. Although highly speculative, this effect may be due, in part, to the positive influence of estrogen (in the present case estrogen replacement therapy) on both brain-derived neurotrophin factor (BDNF) and increased exercise participation (195). Estrogen has been found to up-regulate BDNF, a neurotrophic molecule that is also increased by exercise. Apparently, a normal estrogen level in exercising animals is necessary for maintaining voluntary activity levels (196). Both estrogen and BDNF are important for synaptogenesis and neurogenesis, especially in the hippocampal region (197,198). Finally, exercise effects on cognition were found to be largest for exercise training interventions that exceeded 30 minutes per session.

Physical exercise also has been shown to have direct effects upon brain structure in animals. Initial studies showed that rats in a complex, or "enriched," environment had a greater capillary volume in the visual cerebral cortical areas in which neurons had previously been found to be most extensively affected by experience (199). Subsequent studies demonstrated that the extent of the capillary effects were substantially less in older rats, possibly because they exercised less in the complex environment (200). To sort out the effects of exercise from the effects of learning in the complex environment, Black and colleagues (38,201) compared animals given 1) forced treadmill exercise or 2) access to voluntary exercise in activity wheels connected to their home cages with 3) animals that learned a nonaerobic motor skill task and 4) inactive controls that were handled daily to control for this effect on other groups. Both exercise groups had a higher density of capillaries than control and motor skill rats in the paramedian lobule of the cerebellum, a region involved in motor skill learning that is also activated by running. Motor skill rats did not differ from controls. In contrast, the number of synapses was elevated in the skill learning groups compared with the other three groups. The clear conclusion is that exercise at aerobic levels can affect brain vasculature but not synaptic connectivity to any very great extent, while learning drives the formation of synapses. Both types of change could affect performance of tasks using the affected brain regions. Subsequent work has shown that treadmill exercise in middle-aged monkeys similarly increases vasculature in motor areas of the brain (202). Finally, this added vasculature has been demonstrated to be functional: Activity wheel-exercised rats have both a greater resting blood flow and a greater "reserve capacity" in response to increased oxygen demand compared with those not allowed to exercise (203). It should be noted that the wheel exercise in the studies described above was voluntary on the part of

the animals—maybe they know something that we are still trying to demonstrate experimentally!

To summarize thus far, while many questions concerning the relationship between fitness and cognition remain to be examined, the results of the Colcombe and Kramer (192) meta-analysis when viewed in the context of animal research suggest that this intervention can indeed enhance performance and cognition, even for older organisms.

The research on the effects of cardiovascular fitness training on brain health and fitness markers using adult animal models suggests low-level biological bases for the improvements in human cognition with cardiovascular training. Colcombe and colleagues (204) recently explored the implied relationship between cardiovascular fitness and brain health in aging humans using a Voxel-Based Morphometric (VBM) approach. In VBM analyses, high-resolution brain scans are segmented into gray and white matter maps, spatially warped into a common coordinate system, and examined for systematic changes in tissue density as a function of some other variable (e.g., age, cardiovascular fitness). This technique allows examination of the entire brain in a point-by-point fashion, revealing spatially precise estimates of systematic variation in brain tissues. VBM provides a substantial advantage over other techniques, such as global estimates of gray and white matter volume, in that it allows researchers to localize the effects of a given variable to a specific region of the brain.

In a cross-sectional examination of 55 older adults, Colcombe and colleagues (204) found that, consistent with previous findings, age-related losses in gray and white matter tended to be greatest in the frontal, prefrontal, and temporal regions [e.g. (25,205)]. Moreover, consistent with predictions derived from the human and animal literatures, there was a significant reduction of declines in these areas as a function of cardiovascular fitness. That is, older adults who had better cardiovascular fitness also tended to lose much less tissue in the frontal, parietal, and temporal cortices as a function of age. Subsequent analyses, factoring out other potential moderating factors such as hypertension, hormone replacement therapy, caffeine, tobacco, and alcohol consumption, confirmed that none of these other variables moderated the effect of cardiovascular fitness.

A preliminary cross-sectional analysis of the relationship between cardiovascular fitness and brain function in older adults has shown promising results (36), and is consistent with the notion that cardiovascular fitness tends to spare the brain from the aging process. Participants in this study performed a modified version of the Ericksen flanker task, in which they were asked to identify the orientation of a central arrow presented among an array of distracting stimuli, while brain function was recorded using fMRI. In 50% of the trials, the orientation of the distracting stimuli was consistent with the central cue (e.g., “<<<<<<”), while in the other 50%, the distracting stimuli were oriented inconsistently with the central cue (e.g., “>>>>>>”). In inconsistent trials, participants were required to suppress the information provided by the flanking stimuli in order to make a correct response. On these trials, highly fit older adults, much like young adults, tended to show less activity in the prefrontal regions of cortex (e.g., dorsolateral prefrontal cortex, anterior

cingulate) than did their low-fit older counterparts. Furthermore, the high-fit older adults showed more substantial activation than low-fit adults in extrastriate and parietal regions of the cortex on the inconsistent trials. One potential interpretation of this pattern of results is that higher levels of fitness lead to more efficient prefrontal control of extrastriate and parietal regions of cortex that are responsible for the selective processing of stimulus attributes (206,207). These results, although preliminary, suggest that cardiovascular fitness may provide a prophylactic effect to the functional integrity of the older adult brain.

## CONCLUSIONS AND FUTURE DIRECTIONS

The research discussed above provides a cautiously optimistic picture with regard to the modifiability of age-related changes in cognition and underlying brain function. Factors such as lifestyle, education, occupation, expertise, and fitness have been found to influence the trajectory of cognition from young to old adulthood. Clearly, however, the relationship between these factors and cognition in late adulthood is, in many cases, still open to question. As discussed above, there are, for most of these moderating factors, just as many studies failing to observe a positive effect on cognition as studies that observe positive relationships. There are likely a multitude of reasons for these ambiguities including, but not limited to, (a) consistency and agreement (or lack thereof) in the definition of constructs that have been used as predictors of cognition (e.g., engaged lifestyle, fitness, activity level, expertise), (b) the definition and coverage, in different studies, of the outcome variables (e.g., from measures of specific perceptual, cognitive, and action processes to global measures of intellectual function), (c) the populations of study participants that range from homogenous, and often high functioning with respect to education and health, to more representative samples, (d) the methodologies that have brought to bear, from retrospective subjective reports to paper and pencil and computer-based measures to neuroimaging, in the measurement of outcomes, and (e) the infrequent examination of multiple factors purported to impact cognitive function and plasticity later in life and, perhaps more importantly, the interaction among these factors.

Despite these obvious inadequacies in our science, there is, in many situations, ample information available to both improve and guide future studies. For example, as suggested by the literature on education effects on cognitive maintenance, it would be prudent to include representative samples in future studies, given the relatively frequent report that the educational level achieved early in life (49,61), as well as socioeconomic status, are potentially important determinants of changes in cognition and brain variables in late adulthood (62). Furthermore, given changes in the educational system and more frequent shifts in occupations in our current-day society, it also would be prudent to assess the impact of the nature and frequency of formal educational experiences, as well as the success experienced in formal educational settings (208) throughout the adult life on cognitive maintenance later in life. Furthermore, studies of interventions such as Experience Corps (209,210), which train older adults to provide behavioral and educational support in primary schools, have shown great promise in

enhancing the cognitive function of the older adult participants as well as providing much-needed classroom support in inner city schools. Indeed, such interventions may be particularly effective as cognitive moderators because they fulfill the participants' desire to make a difference (211) while also engaging older adults in challenging cognitive, physical, and social support tasks and functions. Clearly, such interventions bear further study.

The research on lifestyle choices also provides some guidance for future research. The observation that participation in novel and intellectually challenging activities (72) appears to be a better predictor of cognition in later life than other components of this complex and multifaceted construct suggests that the development of a taxonomy of such activities may be worthwhile. Indeed, the relatively narrow transfer effects that have been observed in formal training studies [e.g., (181)] may also be the result, in part, of the lack of complexity and novelty in the material employed during training as well as the specificity of the skills that have been trained. Thus, an important question for future studies is whether the nature of training materials and the breadth of skills trained are important determinants of cognitive maintenance (and perhaps also cognitive enhancement) in late adulthood.

More attention should also be paid in future studies to the literature on practice effects in motor control and verbal learning. This literature suggests that manipulations that maximize performance during training can often be detrimental in the long run, while factors that slow acquisition of new skills can be more effective in retention and transfer of training to new tasks (212). An important question concerns whether principles such as spaced practice, infrequent feedback, and induced variability of practice can be used throughout the adult life span to enhance long-term learning and transfer.

Another important question for future studies concerns the potential benefit of multiple interventions on cognitive maintenance. Thus far, there has been a dearth of studies that have combined interventions such as formal intellectual training, fitness training, nutritional interventions (213), and so forth, as a means to influence the trajectory of cognitive changes in later life [but see (214,215) for small studies that do examine the influence of multiple interventions on cognition]. Given the promise shown in individual interventions, and other moderating factors such as education and lifestyle, it is important to systematically examine the joint influences of multiple interventions on cognitive change in late adulthood. Of course, such an endeavor will require a substantial commitment in terms of time and resources to systematically investigate the relationship between the nature and extent of different interventions (and combinations thereof) and different components of perception, cognition, and action. In parallel, in animal models, a wider range of experiential manipulations and more comprehensive test batteries might reveal similarly broader effects than heretofore reported.

Finally, the recent development of human neuroimaging techniques and knowledge of neuroanatomical and neurophysiological changes across the adult life span provides exciting new possibilities concerning the characterization of

intervention effects on the cognition of older adults. Indeed, proposals such as the Hemispheric Asymmetry Reduction in Older Adults (HAROLD) model (34) provide a framework in which to relate age-related differences and changes in cognition, as a function of moderating factors such as education, lifestyle, intellectual training, and fitness training, to changes and differences in brain structure and function. Additionally, it is important to include the assessment of biomarkers such as, for example, measures of inflammation such as C-reactive protein and interleukin-6 (216,217) and genotypes such as APOE, pre-sen, and catechol-o-methyl transferase in intervention studies (218). Clearly, the increasing collaboration between neuroscientists, psychologists, geneticists, and other scientists will substantially enhance our understanding of the nature and limits of cognitive plasticity across the adult life span.

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