Review

Cognitive reserve and the neurobiology of cognitive aging

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Abstract

A hypothetical construct of “cognitive reserve” is widely used to explain how, in the face of neurodegenerative changes that are similar in nature and extent, individuals vary considerably in the severity of cognitive aging and clinical dementia. Intelligence, education and occupational level are believed to be major active components of cognitive reserve. Here, we summarize the main features of cognitive aging and their neuropathological correlates. We describe the neurobiology of cognitive aging and conclude that perturbations of neural health attributable to oxidative stress and inflammatory processes alone are insufficient to distinguish cognitive aging from Alzheimer’s disease. We introduce the concept of cognitive reserve and illustrate its utility in explaining individual differences in cognitive aging. Structural and functional brain imaging studies suggest plausible neural substrates of cognitive reserve, probably involving processes that support neuroplasticity in the aging brain. The cognitive reserve hypothesis conforms with reported associations between early and mid life lifestyle choices, early education, lifelong dietary habit, leisure pursuits and the retention of late life mental ability.

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1. Introduction

The neurobiology of cognitive aging presents a complex set of problems familiar to those who work on the biology of human behavior. Individual differences in cognitive ability in late life are influenced by two sets of factors. Firstly, level of cognitive ability in old age is substantially (about 50%) determined by intelligence in childhood (Deary et al., 2000). In turn, childhood intelligence is influenced by diverse biological influences that include an important genetic component (Deary, 2000). This first factor represents the baseline of cognitive ability that is an enduring feature of mental life throughout adulthood. The second factor concerns the rate of cognitive aging and is much influenced by processes that impair neural health. The distinction between baseline of cognitive ability and rate of age-related cognitive change follows the recommendation of the NIA Aging and Genetic Epidemiology Working Group (2000). The study of molecular genetic influences on cognitive aging is for example, assisted by distinction between genetic influences on childhood intelligence and genetic influences on rate of age-related cognitive change.

Until recently, the prevalent model of cognitive aging was one of unavoidable decline attributed to impaired neuronal function leading to inevitable neuronal loss. The contemporary view is radically different. Neuronal loss is no longer considered to be as extensive within or among individuals as previously supposed (Morrison and Hof, 2003); the aging brain is capable of considerable adaptation to lessen the cognitive consequences of impaired neural health in old age when the brain continues to utilize its neuroprotective (Mattson et al., 2002) and neurorestorative (Gage, 2000; Limke and Rao, 2002) capacities. Further, social adaptive processes continue in old age and so alter the behavioral context (and expectations) within which old people are allowed time to adapt their altered cognitive functions through social opportunities, environmental choices with adjustments of priority given to specific life goals (Baltes et al., 1999). Seen in these terms, cognitive aging can be understood as the net outcome of multiple positive and negative determinants of retention of cognitive function in old age.

1.1. Cognitive aging

The term cognitive aging describes a pattern of mild age-related impairments in cognitive functions. From childhood onwards, different domains of cognitive function are substantially inter-correlated, resulting in a general cognitive factor. In later life there are mean age-related declines in cognitive domains such as fluid reasoning, mental speed, memory and spatial ability (Deary, 2000). Cross sectional and longitudinal studies indicate that much of the age-related change is attributable to a decline in the general cognitive factor, but there are domain-specific changes too (Salthouse and Ferrer-Caja, 2003; Wilson et al., 2002). It is probably not safe to assume simple linear relationships between cognitive decline and chronological age, and more complex relationships probably exist. There are debates about whether some domains of cognitive function are the focus of the primary age-related changes which mediate the effects of age on other abilities. Candidate domains include impaired executive function (Salthouse et al., 2003) and slowing of mental speed (Salthouse, 1996).
The aim of many cognitive aging studies is to study normal or “non-pathological” aging. Unfortunately, studies rarely define “non-pathological” or healthy aging or extend beyond the categorical exclusion of specific medical conditions known to impair cognition (e.g. dementia or stroke).

The distinction between “normal” and “pathological” aging seems arbitrary and is perhaps not helpful to understanding processes—especially biological—that underpin cognitive aging. It is not yet known whether, when all disease pathology is discounted, there is much age-related change in cognitive functions. A related and provocative finding in one recent study is that there might be little age-related cognitive decline in old people other than among those who will die within the years or so after a baseline assessment (Wilson et al., 2002). Historically, the distinction between “normative” and “non-normative” cognitive aging seems more helpful largely because this encourages study of performance on specific cognitive domains (Nesselroade and Baltes, 1979). When cognitive aging is “non-normative”, it is not necessarily linked closely with chronological age and may be better understood as an effect of a disease process, including subclinical conditions, that affects cognitive performance.

In specific sub-populations of old people there will be a minority whose cognitive function declines more rapidly and progresses to clinical dementia. Their presence will have slight effects on mean cognitive differences between subjects with “normative” or “non-normative” cognitive aging but large effects on the individual trajectories of cognitive aging. The impact of sub-clinical dementia on the study of cognitive aging is also important because the two processes appear to have contrasting effects on the cognitive domains. Alzheimer’s disease is characterized by an initial amnesic stage after which cognitive deficits progress to include impaired divided and selective attention with preservation of sustained attention (Perry and Hodges, 1999). Later deficits include language and visuo-spatial ability. Evidence from neuropathological, neurophysiological and neuroimaging studies suggest that temporal progression along the pathway from memory to attentional deficits to disturbances of language and spatial ability can be explained by progressive worsening of connectivity between cerebral areas that sub-serves these functions. This view arises because cognitive test performance relies on the integrity of cerebral structures that support specific cognitive domains (“modules”) and on the efficiency of connections between them (Delbeuck et al., 2003). The memory loss so characteristic of Alzheimer’s disease differs from cognitive aging because it arises on the basis of two independent processes, one causing memory problems (“modular” degeneration) and the other causing a separate information processing deficit (Morris and Kopelman, 1986).

1.2. The aging brain: inflammation, oxidative stress and apoptosis

The exact biological basis of cognitive aging is unknown. Recent studies have not supported traditional teaching that brain aging involves widespread and severe loss of neurons and their synapses. Contemporary thinking is that there is restricted loss of neurons in relatively few cortical areas (Rasmussen et al., 1996) and overall numbers of neurons are relatively well-maintained with continuous remodeling of synaptic connections and, in specific structures like the hippocampus, there is some replacement of neurons (Gould
In the face of maintenance of neuronal numbers, the possibility arises that cognitive aging is attributable to reduced ability to remodel synaptic connections. Such age-related reductions in synaptic plasticity are detectable using current methods in animal studies (Trachtenberg et al., 2002). Cerebral metabolic measurements have provided general estimates of local neural function but as yet not achieved the degree of fine structural resolution to correlate changes in synaptic density or efficacy with specific cognitive domains.

The aging brain is vulnerable to the effects of oxidative stress, which is an important cause of age-related neurodegeneration (Coyle and Puttfarcken, 1993). Molecular components of the inflammatory response are found at increased concentrations in Alzheimer’s disease and in lower amounts in the aging brain without dementia (Duong et al., 1997; Grammas and Ovase, 2001). For example, C-reactive protein (CRP) is a circulating acute-phase reaction protein that is substantially increased during the inflammatory response. It is synthesized primarily in the liver and its release is stimulated by interleukin 6 (IL-6) and other pro-inflammatory cytokines. This inflammatory marker is associated with dementia (Schmidt et al., 2002) and cognitive aging (Weaver et al., 2002; Yaffe et al., 2003; van Exel et al., 2003) sometimes in association with increased IL-6. It is as yet unclear if increased inflammatory biomarkers are linked to neuro-inflammation or atherosclerosis associated with Alzheimer’s disease. Hackam and Anand (2003) have critically reviewed the role of inflammatory markers (including CRP) in atherosclerotic vascular disease and conclude that these are reliably increased in the presence of atherosclerosis. The density of peripheral benzodiazepine binding receptors is increased in activated microglia, which allows positron emission tomography (PET) to be used to measure increased microglial activation. Cagnin et al. (2001) showed that in Alzheimer’s disease, peripheral benzodiazepine binding was increased in those brain areas most affected by Alzheimer-type pathology. Importantly, serial magnetic resonance imaging (MRI) scans (12–24 months) in the same subjects showed that these highest areas of binding were associated with the highest rates of cortical atrophy. This preliminary study suggests that neuro-inflammation is an important component of the early pathogenesis of Alzheimer’s disease and may be causally associated with selective neuronal death. Evidence reviewed elsewhere (Wilson et al., 2002) points to likely involvement of cytokine and cognitive functions in health and disease.

The healthy cell detoxifies free radicals via its antioxidant defense systems (these include the antioxidant enzymes superoxide dismutase, glutathione peroxidase, glutathione reactase and catalase). Free radicals are not the only factors involved in cell death but seem to make a major contribution to neuronal damage and to trigger the apoptotic cascade. Advances in the molecular genetics of aging and Alzheimer’s disease have done much to clarify the molecular neuropathology of the aging brain and the genetic determinants of its intrinsic antioxidant defenses. In autosomal dominant forms of AD, more than 100 mutations in the amyloid precursor protein (APP) or presenilin genes are known (for more information, see the AD mutation database at http://molgen-www.uia.ac.be/ADMutations/). No consensus exists on the likely mechanisms by which these genes cause age-related neurodegeneration, whether these mechanisms are shared between genes or why specific sub-populations of neurons are selectively affected. However, the prevailing hypothesis is that the presence of these mutations hastens the same
age-dependent pathological cascades that occur in sporadic forms of these disorders, making the brain more vulnerable to the effects of oxidative stress (Mattson et al., 2002).

1.3. The neuropathology of cognitive aging

Rapid advances in understanding the molecular genetics of Alzheimer’s disease have done much to clarify the molecular pathology of the aging brain and have, in turn, facilitated studies of other neurodegenerative disorders. The precise neuropathological relationship between the biological changes of cognitive aging and those of Alzheimer’s disease, however, remains uncertain. In non-pathological aging, cognitive impairment would seem easiest to attribute to the effects of oxidative stress, inflammatory reactions and changes in the cerebral microvasculature (Riddle et al., 2003). However, the aging brain in the absence of dementia is also affected to varying degrees by the neuropathological features typical of Alzheimer’s disease (mostly amyloid plaques, and to a lesser extent, neurofibrillary tangles). Their presence confounds the simple distinction between cognitive aging and Alzheimer’s disease, and this lack of a clear neuropathological boundary is noted in most neuropathological surveys of the aging brain.

Population-based neuropathological studies reveal a spectrum of neuropathological change in aging brains. Critically, the ante-mortem presence of clinical dementia is not invariably associated with the neuropathological changes of Alzheimer’s disease that are categorically different in location, severity and extent from cognitive aging.

Large scale neuropathological studies that record longitudinal, clinical and cognitive data are required to test adequately the relationship between cognitive aging and Alzheimer’s disease. This is especially true of issues concerning selective neuronal loss in specific brain structures, for example dorsoventral prefrontal cortex (MacPherson et al., 2002), subcortical cholinergic projections and changes in hippocampal volume. Clinico-neuropathological surveys suggest that different cortical circuits are affected in aging and dementia (Morrison and Hof, 2003). When memory is extensively impaired, hippocampal changes are invariably present (Giannakopoulos et al., 1997). In keeping with the work of Braak and Braak (1994), neurofibrillary tangle formation in neocortical association areas is required to progress through defined stages in order for the cognitive impairments to development that are typical of Alzheimer’s disease. When cerebrovascular disease co-exists with Alzheimer-type neuropathology, a diagnosis of clinical dementia is more likely (Esiri et al., 1999). In the Honolulu-Asia Aging Study of Japanese-Americans, cerebromicrovascular pathology was as frequent an explanation for clinical dementia as Alzheimer neuropathology (White et al., 2002). Silent cerebrovascular lesions substantially increase the risk of dementia (Vermeer et al., 2003) suggesting that in the absence of a clinical stroke, cerebrovascular pathology commonly arises without Alzheimer changes. Cognitive impairment without dementia was a common finding (20%) in a population based, rural Italian survey and typically associated with risk factors for vascular disease. These findings point to the importance of cerebrovascular pathology; acting alone or in conjunction with Alzheimer neuropathology in the development of age-related cognitive impairment. Support for co-existence of Alzheimer and vascular pathologies without overt dementia was reported by Knopman et al. (2003) with microvascular lesions making an independent contribution to cognitive aging (Kovari et al., 2004).
Senile plaque density does not contribute reliably to the likelihood of a clinical dementia diagnosis and age-related neurodegenerative changes are commonplace with or without a dementia diagnosis (Davis et al., 1999; Morris and Price, 2001). Longitudinal studies suggest that cognitive aging is associated with increasing burden of both Alzheimer and vascular pathologies (Green et al., 2000).

There is also the separate issue concerning brain aging in the oldest old. The relationship between Braak staging of neurofibrillary tangle formation and dementia severity weakens after the age of 90 years (Gold et al., 2000). These observations raise the possibility that “old-old” brains differ from “young-old” brains in their capacity to withstand structural damage (Schmitt et al., 2000). The same point was made by the writing group for the Cognitive Function and Aging Study (Neuropathology Group of Medical Research Council Cognitive Function and Aging Study, 2001), who could not establish thresholds of neuropathological change between cognitive aging without dementia and clinical dementia. Like earlier authors, the group suggested that the aging brain possesses some sort of “cognitive reserve”, with which to reduce the cognitive effects of neuropathological burden on aging brain. Their statistical models suggested that this burden was best estimated from a combination of quantified Alzheimer neuropathology and cerebrovascular lesions. The highly influential Nun Study (Snowdon et al., 1997; Riley et al., 2002) reported longitudinal data relevant to understanding the point of conversion from normal cognitive aging to dementia. Classification of 130 members of religious orders into cognitive states (including dementia) could be related to the extent and location of neurofibrillary tangles (Braak stage) whilst at the same time acknowledging considerable cognitive variability within Braak stages. These authors concluded that conversion to dementia was likely mediated by other factors including very advanced age, cerebrovascular lesions, cortical atrophy and “brain reserve”.

1.4. Cognitive reserve

Cognitive reserve is the hypothesized capacity of the mature adult brain to sustain the effects of disease or injury sufficient to cause clinical dementia in an individual possessing less cognitive reserve. The hypothesis predicts that older adults with higher cognitive ability will have a lower risk of dementia than individuals with less cognitive ability. Further, the hypothesis also predicts that factors associated with higher cognitive ability will also appear to lower the risk of dementia. These latter factors include optimal influences on adult cognitive ability (for example a balanced diet, high quality educational provision and occupational complexity).

In a thoughtful review, Stern (2003) made tractable many of the problems that arise in the study of cognitive reserve. He considered what might comprise cognitive reserve and proposed that active and passive components were at work. Among active components, experiences would be included such as high level of education, complex occupations requiring continuing education and sustained intellectual engagement requiring mental effort. Passive components would comprise brain structures that added capacity to efficient processing of information, enhanced retrieval of memories and problem solving. The efficiency of cortical circuits sub-serving specific cognitive tasks is well known to be
enhanced by repeated use and though anatomical in nature are classified as *active* rather than *passive* components of cognitive reserve.

Epidemiological studies have established low educational attainment and low occupational status as important risk factors for Alzheimer’s disease (Zhang et al., 1990; Launer et al., 1999; Cullum et al., 2000). In a longitudinal study of memory decline in Alzheimer’s disease, more rapid decline was detected in Alzheimer patients with higher educational attainments and occupational status. This association suggested that a greater burden of Alzheimer neuropathology was required if highly educated individuals were to develop dementia, but once their hypothesized “cognitive reserve” was overcome, the dementia progressed at a rate in keeping with their more extensive pathology (Stern et al., 1999). A careful clinico-pathological study of older members of religious orders was reported by Bennett et al. (2003). In this study, education was found to modify the deleterious effect of senile plaque density on cognitive performance. Because education and social economic status are highly correlated, large-scale studies are required to detect sufficient individuals who are highly educated but of low socioeconomic status, and vice versa. In one such study, Karp et al. (2004) showed that the association between the incidence of Alzheimer’s disease and low educational attainment remains significant when socioeconomic status was controlled for. A significant effect of education on cognitive aging was also reported by Le Carret et al. (2003) who found that education protected psychological performance in late life and related this to occupational complexity and acquisition of lifelong abilities to sustain attention and conceptionalize problems.

Lower childhood intelligence is a risk factor for late onset but not early onset dementia (Whalley et al., 2000). This association became stronger at later ages of onset suggesting that if childhood intelligence is a reliable proxy for cognitive reserve, this reserve becomes more important with later age of onset. In the British 1946 Birth Cohort Study, Richards et al. (2004) showed that cognitive decline between age 43 and 53 was partly explained by childhood intelligence and that this was independent of educational attainment, level of occupation and certain health parameters. An earlier study (Rabbitt et al., 2003) had suggested no association between childhood ability and rate of cognitive decline in mid to late life but this lack of association is probably accounted for by estimation of childhood mental ability from adult verbal ability scores. Lifestyle differences between individuals by level of occupation and education might also explain differences in dementia risk, especially when lifestyle factors include exposures that might increase the risk of vascular disease.

A more active lifestyle was found to be protective of late life cognitive function in several studies (Elwood et al., 1999; Dik et al., 2003) consistent with a report that cognitive function in mid life is associated with greater physical activity in childhood (Richards et al., 2003). Leisure pursuits are often chosen because they are mentally effortful and cognitively stimulating and may protect against AD. In a religious order study (Wilson et al., 2002), longitudinal data were collected from 801 older Catholic nuns, priests, and brothers without dementia. On recruitment, cognitive activities were rated and subsequently shown to be associated with retention of cognitive function and reduced risk of dementia after controlling for age, sex and education. The effect sizes in the sub-analysis of cognitive aging were sufficient to suggest that continuing effortful cognitive activity in later life might reduce decline in global cognition.
Leisure activities, irrespective of the extent of cognitive effort involved, surveyed in a non-demented general population sample were also found to have a cumulative effect on the risk of incident dementia (Scarmeas et al., 2001). Generally, it is assumed that cognitive aging is not easily detected before age 60. In the British 1946 cohort study (Richards et al., 2003), leisure activities were associated with better cognitive performance at age 43, and physical exercise at age 36 was linked to a significantly slower rate of memory decline from age 43 to 53 years. Although physical activity is associated both as a cause and consequence of better general health, the study does not identify biological pathways mediating the protective effects of leisure on mid life cognition. In the Swedish Twin Studies, Crowe et al. (2003) compared leisure activities between same sex twin pairs discordant for dementia. Factor analyses of activity reports obtained 20 years earlier identified three activity factors: intellectual/cultural, self-improvement and domestic activity. The authors concluded that greater participation in intellectual-cultural leisure activities was associated with a lower risk of Alzheimer’s disease in women, but not men.

Cognitive reserve was approximated to crystallized verbal ability in mid life in a study by Richards and Sacker (2003). This was related to concurrent verbal memory and psychomotor performance in the belief that these cognitive functions would be sensitive to aging effects. Childhood cognition provided the strongest contribution to this estimate of cognitive reserve, whereas adult occupation was the weakest. Studies of physical activity (Gomez-Pinilla et al., 1998) in juvenile rodent models of corticogenesis suggests that greater physical activity is associated with greater induction of neurotrophic growth factors and this may explain better cognitive function in old people who exercise (Kramer et al., 1999). Nutritional factors in early life may extend their influence from cognitive function in childhood to mid life and thus contribute to cognitive reserve (Richards et al., 2002).

1.5. Brain imaging in cognitive aging: the neural basis of cognitive reserve

Brain imaging studies have established that the human brain shrinks with age. In the absence of clinically significant neurodegenerative disease, there are consistent reductions in whole brain volume with concomitant increases in cerebrospinal volume (Raz et al., 2004; Fox and Schott, 2004). In normal aging without dementia, most studies find that gray matter rather than white matter shrinkage is the principal cause of total brain volume reduction. In the presence of cognitive impairment which is not sufficiently severe to meet criteria for a dementia diagnosis, hippocampal atrophy emerges as the most consistent observation (Du et al., 2001; Wolf et al., 2001; Xu et al., 2000). Wolf et al. (2003) suggest that the point of transition from normal cognitive aging to incipient Alzheimer’s disease may be detected by hippocampal atrophy which is consistent with the finding of Fox et al. (2001).

Positron emission tomography (PET) provides a measure of brain metabolic activity that can be coupled with cognitive performance at the time of examination. This allows regional brain metabolic activity to be measured during cognitive stimulation. The relationship between an estimate of premorbid intelligence and cerebral glucose metabolism was investigated by Alexander et al. (1997) in Alzheimer patients of similar severity disease. Higher premorbid intellectual ability was inversely correlated with cerebral glucose metabolism in specific brain regions. This finding suggests that more
cerebral pathology is required in those of higher original intelligence to produce the clinical features of dementia.

The first direct test of the relationship between hypothesized “cognitive reserve” and the extent of metabolic activation following the same cognitive test in healthy controls or Alzheimer patients was reported by Scarmeas et al. (2004). Their study devised a cognitive reserve variable from a combination of the National Adult Reading Test, Vocabulary subtest of the Wechsler Adult Intelligence Scale and years of education. This study showed that the relationship between their estimate of cognitive reserve and brain activation differed between normal aging and Alzheimer’s disease. Inherent mental ability may, therefore, be associated with reorganization of brain responses to the presence of Alzheimer-type neuropathology. In a study of patients following a traumatic brain injury, Kesler et al. (2003) found that larger brain size before injury, and greater educational attainments decreased the extent of cognitive deficits following traumatic brain damage in keeping with the importance of cognitive reserve. A structural MRI study tested the association between three hypothesized proxies of cognitive reserve (education, head size and occupational attainment). Lifelong cognitive change was estimated by adjustment of cognitive test results at age 79 for intelligence test results at age 11 years (Staff et al., 2004). Cognitive reserve was best estimated from a combination of education and occupation, each contributing about 5% to the total variance in cognitive reserve. This study differed from earlier studies which had used prior ability as a measure of cognitive reserve.

1.6. Neuroplasticity and cognitive reserve

Neuroplasticity refers to changes detected in neural structure and function found in normal brain development, learning and memory, and in certain pathological states such as epilepsy. The biology of neuroplasticity includes: (1) transcriptional, translational and post-translational changes in gene expression; (2) long term alterations of synaptic efficiency attributable to changes in transmitter release, the density and/or affinity of transmitter receptors; (3) modifications in the functions of intracellular signaling pathways; (4) long term modifications of receptor affinity attributable to hormones or growth factors; (5) reorganization of neural circuits. New synaptic formation in the adult cortex occurs in an experience-dependent manner. In life, new synapse formation is continuous with elimination of synapses that possibly underpin adaptive remodeling of neural circuits in response to environmental change (Trachtenberg et al., 2002).

Neuroplasticity provides the means by which the developing brain “self-organizes” and remolds to meet environmental demands. Higher mental functions are presumed to require more complex neural circuitry with a richer and more rapidly responsive contribution of dense and complex synaptic contacts. In cognitive aging and Alzheimer’s disease there is greater vulnerability of neurons sub-serving higher cognitive functions (Arendt et al., 1998). The molecular mechanisms that allow neuroplasticity are difficult to study and poorly understood. The tools of molecular genetics provide useful insights which so far do not suggest that it is helpful to divide neuroplasticity into developmental, adaptive or neurorestorative components. Neurotrophic growth factors, growth associated proteins, cell adhesion molecules, synaptic proteins, lipids and their carrier proteins and microtubule-associated proteins reflect the complexity of the biochemical pathways
involved (Arendt, 2001). In Alzheimer’s disease, but not so far in cognitive aging, there are alterations in neuroplasticity (Selkoe, 2002).

2. Conclusion

There is a continuum from normal cognitive aging to overt clinical dementia. The frequent detection of subjects who were demented in life and for whom there is insufficient pathological explanation for the extent of their cognitive impairment challenges a simple threshold model of pathological burden impairing cognitive function. Additional factors seem likely to be either diminishing or amplifying the impact on cognition of pathological change. There is a potential role for factors such as sensory impairment, undetected medical illness or environmental influences. It is also reasonable to speculate that contemporary methods to detect brain pathology of relevance to cognitive function may be insufficiently sensitive. Future progress may reveal neuropathological change which when summated with current estimates for vascular and Alzheimer pathology more fully explains the extent of cognitive impairment (Silver et al., 2002).

Data from epidemiological, neuropsychological, functional and structural brain imaging support the cognitive reserve hypothesis that is relevant to cognitive aging and Alzheimer’s disease. Despite the heterogeneity of identified components of cognitive reserve, several common themes emerge. Firstly, childhood intelligence provides a premorbid baseline measure of cognitive function that remains relatively stable across the life course. There are many biological influences on childhood intelligence and these same influences remain important to cognitive function even in late life. Childhood intelligence is strongly associated with educational attainments and level of occupation in contemporary developed societies, but may have been less important in earlier generations. Higher mental ability leading to better scholastic achievements and more complex occupations has likely health consequences. These include better personal management of stressful experiences, assortative mating with a more able spouse, entry to safer work environments, choice of cognitively stimulating leisure pursuits, better use of health services and, perhaps critically, better implementation of health education into healthier lifestyles.

These factors, seemingly diverse and unrelated may have important consequences for the aging brain. Microvascular cerebral pathology, for example, is certainly lessened by treatment of hypertension, consumption of fresh fruit and vegetables and more exercise. Reduced oxidative stress promotes neural health and survival and represents, in present circumstances, the single most modifiable risk factor for cognitive aging. A proper understanding of the neurobiology of cognitive aging and cognitive reserve awaits a detailed explanation of the sources of individual variation in neuroplasticity. Current studies on recovery of cognitive function after stroke is likely to inform what the major influences on neuroplasticity might be and which are open to modification. Successful research on these complex topics will help design and implement interventions to improve retention of cognitive function in late life. Potentially, the permissive environment of the aging brain will be changed sufficiently to prevent cognitive aging. In such circumstances, progress to Alzheimer’s disease may be slowed or even halted.
References


