

# Successful Cognitive Aging

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**Abstract** Given the rapid rate of population aging, basic science and public health efforts have increasingly focused on the determinants of successful cognitive aging. In this chapter, we review the definition and biological, psychological, and environmental determinants of cognitive health in later life. Successful cognitive aging is a multi-dimensional construct that lacks a consensus operationalized definition, and has been variously conceptualized in an ipsative, normative, or criterion-referenced manner. Nevertheless, there are a number of biomarkers, at the genetic and cellular level, that provide indicators of cognitive health in aging. Functional and structural neuroimaging suggest multiple pathways to successful cognitive aging, by way of brain reserve and cognitive reserve. A number of behavioral and environmental interventions, including dietary restriction, physical activity, and cognitive stimulation, are promising avenues for extending the cognitive healthspan associated with normal aging. Thus, there is a variety of recent findings providing optimism that successful cognitive aging, howsoever defined, will be attainable by more older adults in the future.

**Keywords** Aging • Older adults • Cognitive • Neuropsychology • Brain • Health behavior • Lifestyle

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1 Introduction

While the traditional focus of research on the aging brain has centered on delineating pathological from typical age-associated changes, a much smaller body of work has focused on successful cognitive aging. This literature includes research on the contributors to maintaining high cognitive performance into later life, as well as interventions that might enhance cognitive abilities beyond that typically associated with normal aging. As yet, successful cognitive aging lacks a consensus definition, and there are a number of long-standing challenges and controversies as to how to operationally define positive states of health in older age. There is no controversy, however, about the considerable public health need for better understanding how to lengthen the healthspan into older age. This imperative comes from the fact that there are now more people who are older than the age of 65 than at any time in recorded history. In fact, two-thirds of the people who have *ever* reached the age of 65 are alive right now (National Institute of Aging 2007).

Much of the work on successful aging has focused on the prevention of physical illnesses and disabilities that stem from age-associated conditions, and less has focused on defining and understanding the determinants of cognitive health, specifically. In a 2006 review of 28 quantitative studies that reported an operational definition of successful aging, only 13 of the studies included cognitive functioning as a component in their definitions (Depp and Jeste 2006). Nevertheless, there are a number of reasons for increased focus on successful *cognitive* aging as well as a number of exciting recent findings that suggest emerging avenues to maintaining brain health in older age. In this chapter, we describe research examining the constituents of successful aging, from traditional neuropsychological constructs to more esoteric ones like wisdom. We then review the evidence for the determinants of cognitive and brain reserve, including interventions aimed at

altering the trajectory of normal cognitive aging. Finally, we describe the utility of applying models of successful cognitive aging to selected clinical populations.

## 2 Rationale for a Focus on Cognitive Health

Tracing the demographic transition to an aging society, there are several reasons for the increasing relevance of cognitive health to overall health in older age. One hundred years ago, the leading causes of morbidity and mortality were infectious diseases—as many as 40% of people did not survive beyond childhood and the mean age at death was 40 years (Fogel 2005). Improvements in access to clean drinking water, along with other practices targeting the prevention and treatments of infectious diseases, dramatically reduced the leading causes of illness. With infectious diseases less likely to cause mortality, there was a subsequent shift to primary causes of mortality to those that were substantially age-associated (e.g., cancer, heart disease). Even so, more recent treatments have begun to delay the onset and reduce the incidence of heart disease, cancer, and stroke—in Robert Fogel’s classic comparison of the Civil War cohort to the baby boomers—the age at onset of heart disease was approximately 10 years later among baby boomers (Fogel 2005). Therefore, a variety of factors have lengthened both the human life span and healthspan in rapid fashion over the twentieth century.

In the past several decades, brain illnesses, particularly Alzheimer’s disease, have begun to increase as leading causes of mortality (Steenland et al. 2009). At the present time, there is a much larger armamentarium of treatments and prevention strategies for cardiovascular health than for preventing cognitive decline, and so it is reasonable to expect that cognitive health may become a more potent rate-limiting factor in avoiding age-associated morbidity as the present cohort of younger and middle-aged adults ages. Thus, research identifying strategies for maintenance of cognitive health in older age will be increasingly important.

A second, more optimistic reason to focus on cognitive health is the shift in conceptualization of the aging brain, from static to malleable. Early in the twentieth century, Sigmund Freud captured the prevalent view of intractability of the aging brain in his quote that “...near or above the age of fifty the elasticity of the mental processes on which treatment depends is as a rule lacking—old people are no longer educable” (Freud 1924). Nevertheless, several decades of animal studies indicate that enriched environments are associated with evidence of greater neuroplasticity, even when experiments were conducted on animals that were already aged. Later research studies have evidenced the adaptability of the aging brain in humans. Thus, excitement has increased about the potential for altering aging trajectories, in contrast to previously entrenched beliefs.

A third reason for the importance of cognitive health comes from the broader context of successful aging, and many of the best studied interventions to prevent physical decline, reduce disability, or improve emotional and social functioning involve volitional behaviors. For example, physical activity appears to reduce the

risk for cognitive decline, yet cognitive impairment reduces the likelihood of engagement in physical activity (Geda et al. 2010). Thus, various cognitive abilities are involved in the daily decisions that individuals make in regard to engaging in physical activity or to adapt to chronic illness. Therefore, successful cognitive aging will be increasingly important, and we review attempts and challenges in defining this construct in the following section.

### 3 Defining Successful Cognitive Aging

There are several challenges in arriving at a consensus definition of successful cognitive aging. Perhaps the closest to consensus is that proposed by the 2006 National Institutes of Health's Cognitive and Emotional Health Project (Hendrie et al. 2006). This workgroup described cognitive health with the following definition as "Not just the absence of cognitive impairment, but the development and preservation of the multi-dimensional cognitive structure that allows the older adult to maintain social connectedness, and ongoing sense of purpose, and the abilities to function independently, to permit functional recovery from illness and injury, and to cope with residual cognitive deficits." Key elements of this definition are that successful cognitive aging combines multiple cognitive domains, extending beyond traditional neuropsychological abilities, such as memory and executive functions, to more esoteric constructs such as wisdom and resilience. In addition, this definition considers central the link between cognitive health with functional independence and engagement with life.

While the CEHP's definition provides a useful focal point, there are several issues in operationalizing this, or any other, successful aging construct. In particular, successful cognitive aging can be defined in terms of thresholds, normative comparisons, or in comparison with past performance. Examples of threshold criteria used in prior studies of successful aging include having a Mini-Mental Status Examination score greater than 24. The advantage of this approach is the ease of generalization and comparability with other samples, yet the performance of cutoffs varies by a number of factors, not the least of which is age. Moreover, not all cognitive abilities decline at the same rate, and some abilities, such as vocabulary and social cognition, may actually improve with age. Therefore, at the cognitive domain level, the cutoff for some domains may change little with age, whereas for processing speed the cutoff may change a great deal.

An example of a normative criterion that has been used in the definition of successful cognitive aging includes being above the median score on neurocognitive tests. This approach may be more robust to the increasing variance in cognitive abilities across individuals with age and may be more likely to maximize power to detect differences between successful and 'unsuccessful' groups. Nevertheless, using normative criteria is disadvantageous in regard to generalizability relative to the criterion approach, as sample characteristics have a strong impact on relative performance. An additional approach to operationalization

would be to define success in reference to preservation of past performance—i.e., maintaining levels of cognitive performance attained at mid-life. This approach dovetails with the portion of the CEHP definition that corresponds to maintenance of independence, yet would require longitudinal data on cognitive abilities from earlier ages. For example, Yaffe showed that individuals who maintained cognitive abilities into their 80s and 90s were less at risk for disability and death (Yaffe et al. 2010). Thus, overall, even if agreement is reached on the broad constituents of the successful cognitive aging construct, its operationalization presents many unresolved challenges.

## 4 Determinants of Successful Cognitive Aging

Given the caveats about attaining a precise and useful definition of successful cognitive aging, there are a number of putative biological, behavioral, and social mechanisms by which cognitive abilities can be maintained and perhaps even improved into older age. We review these determinants in the following section, beginning at the genetic and molecular level, then to the aging brain, and finally broadening into various lifestyle factors.

### 4.1 Genetic Influences

Although most studies on the genetic influence on aging have focused on the phenotype of longevity, a number of studies have assessed the degree to which genes influence aging-related trajectories in cognitive health. Among twin studies, there does appear to be evidence that cognitive performance in later life is heritable. In the Swedish twin study (Finkel et al. 1998), 54% of the variance in a general cognitive factor was attributable to heritability. However, it was notable that the proportion of variance attributed to genetic factors in middle-aged adults was much higher (~80%), such that the relative influence of environmental factors on cognitive health is likely to increase with age (Finkel et al. 1998). In regard to functional performance, Gurland found that 20–25% of the variance in disability was accounted for by genetic factors in a sample of 1,384 monozygotic and 1,337 dizygotic septenagenians (Gurland et al. 2004). Therefore, cognitive health in older age likely has a moderate degree of heritability, providing confidence in the potential utility of the search for specific genes that influence this phenotype. Nevertheless, the influence of genes may lessen with age and certainly environmental factors play a large, if not larger, role than genes in late-life cognitive health.

Several studies have examined candidate single nucleotide polymorphisms (SNPs) in case-control studies comparing a successful aging group to older adults who do not meet the criteria for successful aging. Glatt et al. (2007) reviewed 29

studies that examined genetic influences, and while these studies were not restricted to cognitive health as a phenotype, it is notable that the genes clustered into three groups (Glatt et al. 2007): (a) genes involved in cardiovascular health and cholesterol, lipid, and lipoprotein transport or metabolism (e.g., PON1, APOE), (b) genes involved in inflammatory processes (e.g., IL6, IL10), and (c) genes involved in cell cycling, growth, and signaling (e.g., SIRT3). Although this body of literature is quite small, these fundamental physiological processes are linked, in the related literature, with indicators of cognitive decline. For example, a large body of literature indicates the associated links with the APOE SNP (Haan et al. 1999) and inflammation (McGeer and McGeer 2003) with Alzheimer's Disease.

More recent work has employed the rapidly growing armamentarium of genomic and molecular biology to address the genetic determinants of cognitive health in later life. Zubenko et al. (2007) used a genome-wide association approach in comparing 100 cognitively intact adults 90 years or older to 100 young adults. A total of 16 markers were identified that were associated with membership in the cognitively intact older adult group, yet these were not consistent across men and women, suggesting a need for future study to examine gene by sex interactions. Additional work has investigated mitochondrial DNA and epigenetic factors, such as DNA methylation.

The advantage of an epigenetic approach is that it enables capturing the impact of environmental stress on cellular functioning, thereby potentially permitting future interventions to act at the intersection between environment (e.g., nutrition, lifestyle) and genetic markers, so as to compensate for potential deleterious effects of genes. A particularly exciting area is the epigenetic regulation of the telomere, a portion of the chromosome that appears to provide an indication of cellular aging. Shorter telomeres appear to be associated with accelerated aging, and greater environmental stress appears to be associated with telomere shortening (Aviv et al. 2003). One recent study in Ashkenazi centenarians showed that older adults who had longer telomeres had significantly better scores on the Mini-Mental Status Examination, which is remarkable considering that the population of 100-year olds has already been subjected to substantial attrition due to mortality (Atzmon et al. 2010). Therefore, the telomere represents an objectively measurable phenotype intermediate between basic physiological processes and environmental factors, and is related to cognitive health even among the oldest old.

## ***4.2 Stress and Resilience***

In general, older adults have different stressors than younger adults, as the issues that older adults face tend to be more likely to be health-related, chronic, and uncontrollable stress (e.g., bereavement, caregiving) rather than acute stressors that involve decision making (e.g., losing a job, divorce—Karel 1997). There is remarkable diversity among older adults in their response to stressors, even when

the nature and type of stressor is similar across people. The impact of psychosocial stress on the aging brain has been examined for decades, and a more recent body of work has examined the characteristics of resilience to stress. It is clear that chronic unrelenting stress in older adults influences a network of physiological processes that often results in neuronal degradation. Specifically, the stress-associated stimulation of the Hypothalamic-Pituitary-Adrenal axis results in the secretion of glucocorticoids such as cortisol, which is associated with damage to various brain structures, and particularly the hippocampus. In addition, stress may induce inflammatory cytokines and decrease immune response, which also result in deleterious impacts on the brain (McEwen 2000). O'Hara and Hallmayer (2007) found greater reactivity to stress, as defined by increased levels of cortisol, among carriers of the 5HTT short allele (O'Hara and Hallmayer 2007). These factors related to reduced hippocampal volume, and thus genetic variation may produce greater vulnerability to stress and associated cognitive deficits—such links may explain the well-documented links between depression and anxiety with cognitive impairment in later life.

Clearly, however, there are some individuals who do not experience the deleterious effects of stress. For some, this may be because of genetic advantages, such as the research on 5HTT SNP indicates. However, for others, behavioral coping strategies may reduce the impact of stress on the brain. Resilience has been the focus of a small body of literature, yet Lamond et al. found in a sample of 1,395 community dwelling older women that the predictors of resilience (lower levels of depression, greater optimism, social engagement) tend to be relatively stable across the life span (Lamond et al. 2008). However, the structure of resilience was slightly different from that found in younger adults, with greater positive associations between emotion-focused coping (e.g., tolerating negative affect) and freedom from depression than problem-focused coping. In regard to cognitive health, resilience represents a trait that may buffer the effects of stress on the brain, with future research necessary to understand its biological mechanisms.

### ***4.3 Brain Reserve and Cognitive Reserve***

Moving from molecular biology to the aging brain, two organizing concepts that are relevant to successful cognitive aging are brain reserve and cognitive reserve. Brain reserve is defined as the ability to withstand damage and yet continue to function, metaphorically the “hardware” of the brain. Normal aging is associated with global volumetric shrinkage in brain structures such as the caudate, cerebellum, hippocampus, and prefrontal areas (Raz et al. 2005) as well as decreased organization and integrity of white matter tracts leading to potential consequences on cognitive functioning. Additional studies have demonstrated a relationship between increasing age and reduced glucose metabolism and blood flow at rest, specifically in the frontal regions and anterior cingulate. Brain reserve theory is

considered passive in that it presupposes that there is some threshold of damage required that will result in cognitive deficits when met.

Brain reserve has been most commonly used to provide an explanation describing a subset of individuals (approximately 25%) who, at autopsy, have the hallmarks of Alzheimer's disease (AD) including amyloid plaques and neurofibrillary tangles and yet who during their life do not show clinical manifestations of the disease (Snowdon 2003). This discrepancy between having extensive brain neuropathology without cognitive impairment led to the theory that perhaps having a larger brain volume, larger neurons, and more synaptic connections can act as a buffer, or protective factor in preventing or slowing down cognitive decline. Several studies provide compelling evidence in support of the brain reserve theory including a recent study by Pernecky et al. (2010) showing that larger head circumference attenuated the relationship between cerebral atrophy and cognitive functioning in 270 patients diagnosed with AD patients.

Cognitive reserve, on the other hand, is more akin to the "software" of the brain and involves active compensation rather than the passive model of brain reserve.

One potential compensatory strategy that has been noted in functional imaging studies comparing younger adults to older adults is that prefrontal activity during cognitive performance tends to be less lateralized (localized specifically to the right or left side of the brain) in older adults compared to younger adults. One theory of this qualitative difference in brain response between the two groups (referred to as Hemispheric Asymmetry Reduction in older adults, HAROLD—Cabeza et al. 2002) is that the aging brain, compared to the younger brain, uses more of its resources in an attempt to compensate for structural and functional decline. This theory has been further supported by the Scaffolding Theory of Aging and Cognition (STAC) which states that the brain utilizes complementary, alternative neural circuits with increasing age (scaffolding) in an effort to maintain or strengthen particular cognitive objectives (Park and Reuter-Lorenz 2009). It is important to note that brain reserve and cognitive reserve are not competing or mutually exclusive models, rather these are two parallel processes that help to explain that there is more than one pathway to maintaining cognitive health in older age.

#### **4.4 Wisdom**

In considering the phenotypes related to successful cognitive aging, memory and processing speed are prototypical cognitive domains that are associated with age-related declines. However, some cognitive abilities may increase with age, and such increases may contribute just as much, if not more, to the maintenance of independence. Wisdom is one cognitive ability that is commonly associated with older adults. Wisdom remains a fledgling area for neurobiological research, and it suffers from the same definitional issues as successful cognitive aging. Nevertheless, newer measures such as the three-dimensional wisdom scale (3D-WS) have resulted in both a clearer understanding of wisdom (Ardelt 1997), as well as



the start of biological research in this area. A recent study employing the Delphi method—a widely used and accepted method for seeking consensus among experts within a certain topic area—to defining wisdom surveyed experts on wisdom research from around the world and concluded that wisdom is uniquely human; a form of advanced cognitive and emotional development that is experience driven; and a personal quality, albeit a rare one, that can be learned, increases with age, can be measured, and is not likely to be enhanced by taking medication (Jeste et al. 2010).

Based on this definition and a review of multiple other related sources in the literature (Jeste and Vahia 2008), Meeks and Jeste (2009) have proposed a putative neurobiological basis for wisdom. According to their proposed model, wisdom comprises six distinct domains: prosocial attitudes and behavior; social decision making/pragmatic knowledge of life; emotional homeostasis; reflection/self-understanding; value relativism/tolerance and acknowledgment of and effective dealing with uncertainty and ambiguity. Based on a comprehensive review of the literature related to these domains, the authors suggest that multiple neurotransmitters have a role in acquiring and maintaining wisdom, including dopamine (in regulating impulsivity and selflessness), serotonin (in maintaining social cooperation), norepinephrine (regulation and dampening of stress-related performance and decision making), vasopressin (for affiliative behavior in animal models) and oxytocin (for social cognition and social decision making). The authors also identify several brain regions that may be part of a circuitry involved in the process of being ‘wise’. These regions were identified through multiple neuroimaging studies. The neurobiological model proposed by the authors suggests that lateral prefrontal cortex (PFC) in concert with dorsal Anterior Cingulate Cortex (ACC), Orbito-frontal Cortex (OFC) and Medial Prefrontal Cortex (MPFC), appears to have an important inhibitory effect on several brain areas associated with emotionality and immediate reward dependence (e.g., amygdala, ventral striatum). They also note that there is a complementary emotion-based subcomponent, including prosocial attitudes and behaviors that involve MPFC, PCC, OFC, superior temporal sulcus, and reward neurocircuitry. Finally, Meeks and Jeste suggest that the interplay and balance between phylogenetically older brain regions (e.g., limbic cortex) and the more recently evolved PFC is the key to maintaining wisdom. Research on wisdom shows how more esoteric concepts associated with successful aging can be deconstructed, studied using laboratory experiments, and related to brain structure and function.

## ***4.5 Lifestyle Behaviors***

### **4.5.1 Physical Activity**

Physical activity is associated with a variety of health benefits, including reduced risk of mortality, physical disability, cardiovascular disease, and osteoporosis.

Although fewer in number, the results of studies examining the impact of physical activity on cognitive health are equally impressive. Experimental animal studies employing a variety of protocols and species have indicated that physical activity is associated with reduced neurodegeneration (Cotman and Berchtold 2002). In humans, observational studies indicated that greater exercise participation is associated with a reduced risk for dementia (Larson and Wang 2004). A meta-analysis of 18 studies examining physical activity interventions that enrolled samples of older adults found that physical activity was associated with increases in performance on several cognitive domains, in particular executive functioning (Kramer et al. 2006). One recent study that randomized older adults who were sedentary to aerobic exercise or a control condition found evidence for increases in brain volume in gray and white-matter regions after one year of participation (Colcombe et al. 2006). This latter study was particularly notable in that the sample consisted of older adults who were not engaged in exercise at the time of enrollment, and thus initiating exercise participation in older age may still provide benefits to cognitive health.

The mechanisms of physical activity on brain health remain unclear, as there are a number of potential pathways that are indirect (e.g., improvement in cardiovascular health, increased social engagement). However, there do appear to be more direct influences of physical activity on the brain, in particular by reducing oxidative stress and inflammation (Kramer et al. 2006). Anterior brain regions appear to be more altered by cardiovascular fitness than posterior regions (Prakash et al. 2011). Finally, it is worth noting that only a minority of older adults in the United States meet at the Center for Disease Control recommendations for daily exercise participation, and older women are the segment of the population with the single lowest rate of engagement in physical activity. Therefore, there is much potential impact of increasing physical activity at the population level.

#### **4.5.2 Nutrition/Dietary Restriction**

Among the potential interventions to extend longevity, none have generated more enthusiasm than dietary restriction. In rodents, restriction of *ad libitum* diets in mice by approximately 1/3 is associated with 30–40% increase in life span (Fontana et al. 2010). Smaller but still significant effects have been seen among primates, and human trials have been completed. Importantly, other age-related phenotypes, including cognitive ability, also appear to be improved by dietary restriction. A recent randomized controlled trial in humans enrolled 50 overweight adults in a three-month trial of dietary restriction. Compared to the control group and a second group that received an increase of unsaturated fatty acids, memory performance was 30% better in the dietary restriction group at post-study (Witte et al. 2009). Further sensitivity analyses within the dietary restriction group found that improvement in insulin sensitivity and inflammatory markers correlated with improvement in memory functioning. The exact mechanisms by which dietary restriction could extend the life span or improve neurocognitive ability are

unknown and actively debated. However, it does appear that dietary restriction slows the metabolic rate and, as such, may reduce the oxidative stress associated with metabolic processes.

Dietary restriction and physical activity (as well as cognitive stimulation, described next) may share similar mechanisms of action in reducing neuronal vulnerability. According to Mattson and Magnus (Mattson and Magnus 2006), these three activities introduce a mild stressor, which causes the brain to release neurotrophic factors (e.g., BDNF), which, in turn, promote synaptogenesis. This process is called “hormesis” and is analogous to a vaccine, in which degraded pathogens are introduced to stimulate the immune response to develop antibodies. Thus, quite different behaviors (e.g., reduction in calories, engaging in cognitively stimulating activity) could produce similar positive effects on the brain.

There are a host of nutritional products marketed toward healthy brain aging. The current state of the evidence ranges from negative (e.g., Ginko Biloba) to inconclusive (e.g., Fish oil, resveratrol—Daffner 2010). However, there is evidence that vitamin deficiencies and dehydration are remediable risk factors for cognitive impairment. The list of conditions that result from vitamin deficiencies is expansive, but a growing body of research has recently emerged showing possible links between deficiencies in vitamins such as vitamin D, K, and B<sub>12</sub> in older adults and adverse cognitive outcomes. Also strongly encouraged by nutritionists is the intake of foods rich in antioxidants.

#### 4.5.3 Cognitive Stimulation

There have been a number of observational studies that have linked participation in cognitively stimulating activities, such as recreational activities (e.g., engagement in puzzles, games) and cognitively demanding vocations, with reduced risk of dementia. Conversely, a number of studies have found that greater engagement in less cognitively stimulating activities, particularly television watching, is associated with greater risk of dementia. This collection of studies has fed into the so-called “use it or lose it” hypothesis in regard to the influence of activity participation on the prevention of cognitive decline. There is some controversy as to whether such claims are overstated, as Salthouse (2006) has argued that no patterns of cognitive activities to date have proven to change the *rate* of cognitive decline (Salthouse 2006). It is also difficult to quantify the amount of cognitive stimulation associated with activities, which may differ across people within the same activity class. Moreover, it is difficult to parcel out the effect of selection, as people who gravitate toward and subsequently participate in cognitively stimulating tasks may have greater cognitive resources to begin with. Nevertheless, even if the true effect of cognitive stimulation is marginal, there may be additional benefits of engaging in cognitively stimulating activities (e.g., associated physical or social activity) that may occur.

Although cognitive training to alter the course of normal age-related decline has been a field of study for many years, there have been several recent developments.

For one, the ACTIVE trial, completed in 2006, was the largest trial of cognitive training to date, enrolling 2,802 older adults (Willis et al. 2006). Participants were older adults without evidence of cognitive impairments, and they were randomized to one of four types of cognitive training, each targeting a different cognitive ability: reasoning and problem-solving, memory, attention, and processing speed. The primary outcomes of the trial were performance on cognitive tests, and secondary or distal outcomes were functional measures. The results suggested that cognitive training was associated with statistically significant improvements in cognitive ability, although restricted to the domain that was trained. Improvements in functional measures were far more subtle, yet in the case of reasoning and problem solving, persisted for up to 5 years after randomization (Willis et al. 2006).

A second recent study shows the emergence of computerized approaches in the delivery of cognitive training (Mahncke et al. 2006). Finally, a number of non-traditional approaches to enhancing cognitive abilities have been evaluated—these do not engage individuals in specific cognitive training exercises, rather they provide standardized cognitively stimulating activities. Examples include narrative writing, acting, volunteering, and group problem solving (Park et al. 2007). Increases in cognitive stimulation may also be attainable from reducing cognitively sedentary behavior. For example, television use is higher among older adults than younger and middle-aged adults despite the observation that older adults enjoy television less than younger people (Depp et al. 2010).

## 5 Successful Cognitive Aging in Selected Clinical Populations

*Depression:* A number of studies have linked depression with risk for cognitive impairment in older adults. While the prevalence rates for major depression in older adults are lower than in younger adults, subsyndromal depressive (SSD) symptoms may in fact be three times more prevalent (Meeks et al. 2011). In one study, SSD was found to significantly increase the prospective likelihood of cognitive impairment and dementia at one-year follow-up (Han et al. 2006). There are direct and indirect pathways by which depression may impair cognitive abilities. Direct effects of depression on the aging brain may be through increasing cellular stress as described above. Indirect effects may be in interfering with activities that foster successful cognitive aging, as depressed older adults are less likely to engage in physical activity, and more likely to engage in sedentary solitary behavior. Thus, treatment for depression, if successful, may influence the likelihood of attaining successful cognitive aging through multiple pathways.

*HIV Infection:* Due to the advent of more advanced anti-retroviral treatments, the life expectancy of people living with HIV infection has increased dramatically over the past decade. The first surviving generation to be exposed to the HIV virus is currently entering older adulthood. Malaspina et al. (2011) examined the predictors of successful cognitive aging, using an operational definition which

included freedom from impairment on neurocognitive testing and lack of endorsement of subjective confusion (Malaspina et al. 2011). Patients who met these criteria were less likely to exhibit depressive symptoms, and they were also more likely to endorse greater engagement with treatment and adherence to anti-retroviral medications. Indicators of viral load did not differ between successful and unsuccessful groups. This study provides an exemplar for examining the characteristics of “survivors” of the HIV epidemic and the future work may delineate how these individuals have managed to avoid accumulating cognitive impairment over the course of their illness.

*Schizophrenia:* One of the core features of the illness is pervasive cognitive impairment, with average cognitive deficits at approximately one standard deviation below the mean of healthy comparison subjects (Dickinson et al. 2007). Although this general trend in differential cognitive functioning is found between patients and healthy individuals, there is enormous heterogeneity in both the level and pattern of cognitive deficits within patient populations. This substantial intragroup variability in cognitive functioning is further evidenced by the interesting discovery that an estimated 20–25% of schizophrenia patients have “neuropsychologically normal” profiles (Palmer et al. 2009). It does not appear as though patients without cognitive impairment have less severe psychopathologic symptoms, and thus preservation of brain function is not simply a function of lower disease severity. Rather, the evidence of greater educational attainment among non-impaired patients suggests that a number of hypotheses about brain reserve described above may also apply to schizophrenia.

## 6 Conclusions

In this chapter, we sought to describe a diverse body of literature on the determinants of successful cognitive aging. Due to the aging of the population and the relative paucity of effective means of slowing the rate of cognitive aging, cognitive health will likely have an increasing impact on the health and independence of older adults. There is no consensus definition of successful cognitive aging, let alone successful aging. Nevertheless, it is generally agreed upon that successful cognitive aging is multi-dimensional and extends beyond performance in traditional cognitive domains to more socioemotional constructs such as wisdom. It is unclear whether the operationalization of this construct should be based upon normative, ipsative, or threshold criteria—or some combination. The NIH CEHP project and the NIH Toolbox project represent attempts to create a common language in defining cognitive health and a core set of instruments to measure this construct, respectively.

Despite the lack of consensus, there is marked convergence among basic physiological markers such as genes, and environmental factors such as stress, that implicate fundamental aging processes in the effect of potentially modifiable aspects of aging. Moreover, the concepts of brain and cognitive reserve show how

early and late-life experiences can influence cognitive aging trajectories and indicate that multiple pathways are available to successful cognitive aging. Several lifestyle factors, including physical activity, cognitive stimulation, and dietary restriction appear to relate to improvement in cognitive functioning, even among older adults who initiate these activities in later life. Although involving unique behaviors, these lifestyle factors may share common pathways to stimulating neurotrophic factors to reduce neuronal vulnerability. Finally, there is some potential utility in examining the successful cognitive aging construct in illnesses that typically accompany cognitive impairments. It is clear that much needs to be learned in regard to defining and enhancing cognitive health, yet it is equally clear that the next several decades will generate a host of new hypotheses and potential strategies for maintaining cognitive abilities further into later life.

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