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Successful Memory Aging

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Abstract

For more than 50 years, psychologists, gerontologists, and, more recently, neuroscientists have considered the possibility of successful aging. How to define successful aging remains debated, but well-preserved age-sensitive cognitive functions, like episodic memory, is an often-suggested criterion. Evidence for successful memory aging comes from cross-sectional and longitudinal studies showing that some older individuals display high and stable levels of performance. Successful memory aging may be accomplished via multiple paths. One path is through brain maintenance, or relative lack of age-related brain pathology. Through another path, successful memory aging can be accomplished despite brain pathology by means of efficient compensatory and strategic processes. Genetic, epigenetic, and lifestyle factors influence memory aging via both paths. Some of these factors can be promoted throughout the life course, which, at the individual as well as the societal level, can positively impact successful memory aging.

Contents

INTRODUCTION

The vast scientific literature on aging is heavily dominated by a concentration on losses and negative changes (e.g., Lupien & Wan 2004). However, although aging and successful might be conceived of as contradictory terms, a literature on successful aging has gradually emerged since the mid-1900s (e.g., Baltes & Baltes 1990, Havighurst & Albrecht 1953, Williams & Wirths 1965). Early work on successful aging had a strong focus on activities, attitudes, and life satisfaction. Havighurst (1961, p. 8) stated that "A theory of successful aging is a statement of the conditions of individual and social life under which the individual person gets a maximum of satisfaction and happiness." A quantitative analysis of citation networks (Kusumastuti et al. 2016) revealed that the Havighurst tradition, with its focus on an older person's qualitative perspectives on important aspects of life and to what extent these perspectives influence their experience of success, has continued to be a dominating line of work in the broad field of successful aging (see, e.g., Griffith et al. 2018). In this tradition, according to an influential early theory, the activity theory, successful aging could be defined as maintaining for as long as possible the activities and attitudes of younger and middle age (Havighurst 1961). Subsequent work broadened the perspective by highlighting qualitative differences in attitudes and preferences over the adult life span, thus challenging the use of younger-age activities and attitudes as normative for success in older age (e.g., Baltes & Carstensen 1996).

A second major tradition in publications (Kusumastuti et al. 2016) in the field of successful aging includes papers with a more quantitative orientation. The origin of this line of work may be traced back to the Katz et al. (1963) publication on the Activities of Daily Living (ADL) index as a tool in studies of illness in the aged. While Katz et al.'s paper was not on successful aging per se, measuring disability and physical functioning with the ADL or related indices remains the most frequently used method to define successful aging (Depp & Jeste 2006). In this more quantitative and researcher-oriented tradition, a landmark paper was published by Rowe & Kahn (1987). They argued that the traditional approach in research on aging was to distinguish between pathological and normal aging, and while avoiding pathology and disability on its own might constitute a definition of success, Rowe & Kahn instead stressed heterogeneity in the domain of normal by introducing the distinction between usual and successful aging. The Rowe & Kahn paper laid the foundation for a model (the MacArthur Foundation model) of successful aging with three principal components: (*a*) low risk of disease, (*b*) maintenance of high mental and physical function, and (*c*) continued engagement with life. Empirical studies indicate that few older adults meet all of these criteria of success (McLaughlin 2010, McLaughlin et al. 2012). It has also been argued that

different criteria may be of relevance for the younger old than for those in extreme old age (Carr & Weir 2017). Still, the model has continued to attract considerable interest and generated a wealth of discussion and debate (see, e.g., Hillgaard Bülow & Söderqvist 2014, Pruchno & Carr 2017). Some 20 years after their original publication, the model was updated to "Successful Aging 2.0" (Rowe & Kahn 2015).

We cannot, in this review, do justice to the "thousands of conceptual and empirical articles [that have] struggled to explain what successful aging is and how best to achieve it" (Pruchno & Carr 2017, p. 201)—in humans as well as in other species (see also Snigdha et al. 2013), such as Labrador retrievers (Adams et al. 2016). Instead, we focus on one key component that has frequently been used to define successful aging (Depp & Jeste 2006): maintenance of cognitive functioning. Specifically, we address successful memory aging in humans. We begin by providing an overview of pertinent patterns of memory decline in aging and discussing evidence for successful memory aging. Then, we turn to genetic and lifestyle characteristics of (*what*), and compensatory strategies for (*how*), successful memory aging. We end by introducing an integrative model in which what and how factors influence memory aging via brain integrity.

PATTERNS OF AVERAGE (USUAL) MEMORY DECLINE IN AGING

Largely, age-related memory decline is seen on measures of declarative but not nondeclarative (procedural) long-term memory (Brickman & Stern 2009). Within the declarative domain, age decline is markedly more apparent for episodic than for semantic memory (e.g., Rönnlund et al. 2005).

Episodic memory has been defined as "a recently evolved, late-developing, and early-deteriorating past-oriented memory system" (Tulving 2002, p. 5). In real life, it supports, for instance, remembering where one parked one's car and what to buy from the grocery store, as well as older events such as an episode from a vacation trip several years ago. In experimental settings, episodic memory can be measured with recall and recognition tasks using different kinds of stimuli (words, faces, pictures).

How to best describe usual (average) episodic memory decline in aging remains a debated topic. Rowe & Kahn (1987) argued for the usefulness of longitudinal data in defining normal aging, and the findings from some existing longitudinal studies with observations covering both younger and older segments of the adult life span (accelerated longitudinal designs) inform the issue of average episodic memory decline. In the Seattle longitudinal study (Schaie 1994), more than 5,000 individuals were tested in one or several (up to six) test waves from the 1950s to the 1990s. The longitudinal data for verbal memory (and most other markers except perceptual speed, which showed early-onset decline) revealed no significant age decrements prior to age 60.

In the Swedish Betula study, longitudinal analyses of data from 829 participants likewise revealed no decrements in episodic memory before age 60—even after practice effects were adjusted for (Rönnlund et al. 2005). Practice effects could be evaluated by including a previously untested sample at the second test wave, and the results revealed a practice effect despite 5 years having passed between test waves. Subsequent analyses, based on additional test waves over 15 years, confirmed accelerated change in memory decline from approximately age 65, along with early onset of decline in perceptual speed (Gorbach et al. 2016).

A third example comes from the UK Whitehall II study and its analyses of 10-year cognitive changes from more than 5,800 individuals divided into five age groups (Singh-Manoux et al. 2012). At baseline, the youngest group was 45–49 years old and were thus 55–59 years old at follow-up. At that time, evidence for memory decline was found even in this group, suggesting that memory decline may be detectable even prior to age 60.

These longitudinal studies indicate that the average onset of episodic memory decline is approximately age 60, although estimates may vary somewhat depending on factors such as the examined population; statistical approaches, including the treatment of practice and dropout effects; and cohort influences. The particular episodic memory task(s) may also influence the patterns of results from specific studies. The magnitude of age-related decline tends to be greater for tasks offering less (e.g., free recall) compared to more (e.g., forced-choice recognition) support at retrieval (e.g., Craik 1983, Nyberg et al. 2003), which may in part reflect a greater taxing of additional processes, such as working memory, by the more complex tasks. Indeed, measures of episodic memory can be combined with working memory and other cognitive measures into a fluid cognitive score. Correspondingly, some studies of successful aging that are discussed below were not limited to measures of episodic memory; instead, the findings more broadly reflected fluid (age-sensitive) cognition.

SUCCESSFUL MEMORY AGING

The existence of heterogeneity in episodic memory performance in normal aging has been acknowledged (e.g., Lindenberger 2014; see also **Figure 1*a***). However, how best to distinguish usual from successful aging remains a complex issue, and several different strategies have been adopted to identify individuals who may qualify as displaying successful memory aging. One approach has been to subdivide samples of older adults on the basis of their memory or cognitive performance or based on broader criteria. A study originating within the MacArthur Foundation Research Network on successful aging operationalized high functioning as performance in the top tertile on a series of screening instruments assessing both physical and cognitive functioning (Berkman et al. 1993). The parent sample consisted of 4,030 individuals between 70–79 years old, and of these, 1,192 (i.e., the predefined one-third) were assigned as high functioning. In separate follow-up comparisons, it was shown that significant differences were apparent for several measures of episodic memory when the high performers were compared with medium- and low-functioning groups. Interestingly, significant group differences were also observed on some parameters that were not part of the screening, such as pulmonary functioning and life satisfaction.

The applicability of the MacArthur model for studying successful aging in a geographical and cultural context other than the United States was examined within the Australian Longitudinal Study of Aging (Andrews et al. 2002). In a sample of 1,403 adults aged 70 years or older, the participants were classified as higher, intermediate, or lower functioning based on a similar set of broad criteria as in the study by Berkman and colleagues (1993). In the study by Andrews et al., a total of 503 individuals (36%) were classified as higher functioning. A more recent example of this approach comes from the Harvard Aging Brain Study (HABS; Dekhtyar et al. 2017). The top 20% of a sample of 125 individuals aged 75 or older was identified on the basis of the scores on challenging memory tests. In addition, the optimal memory performers were found to also outperform typical memory performers on both composites of executive functioning and processing speed.

Another approach to identifying individuals who display successful memory aging requires that both younger and older adults be examined. In their original paper on usual and successful aging, Rowe & Kahn (1987, pp. 143–44) stated,

> "In many data sets that show substantial average decline with age, one can find older persons with minimal physiological loss, or none at all, when compared to the average of their younger counterparts. These people might be viewed as having aged successfully with regard to the particular variable under study."

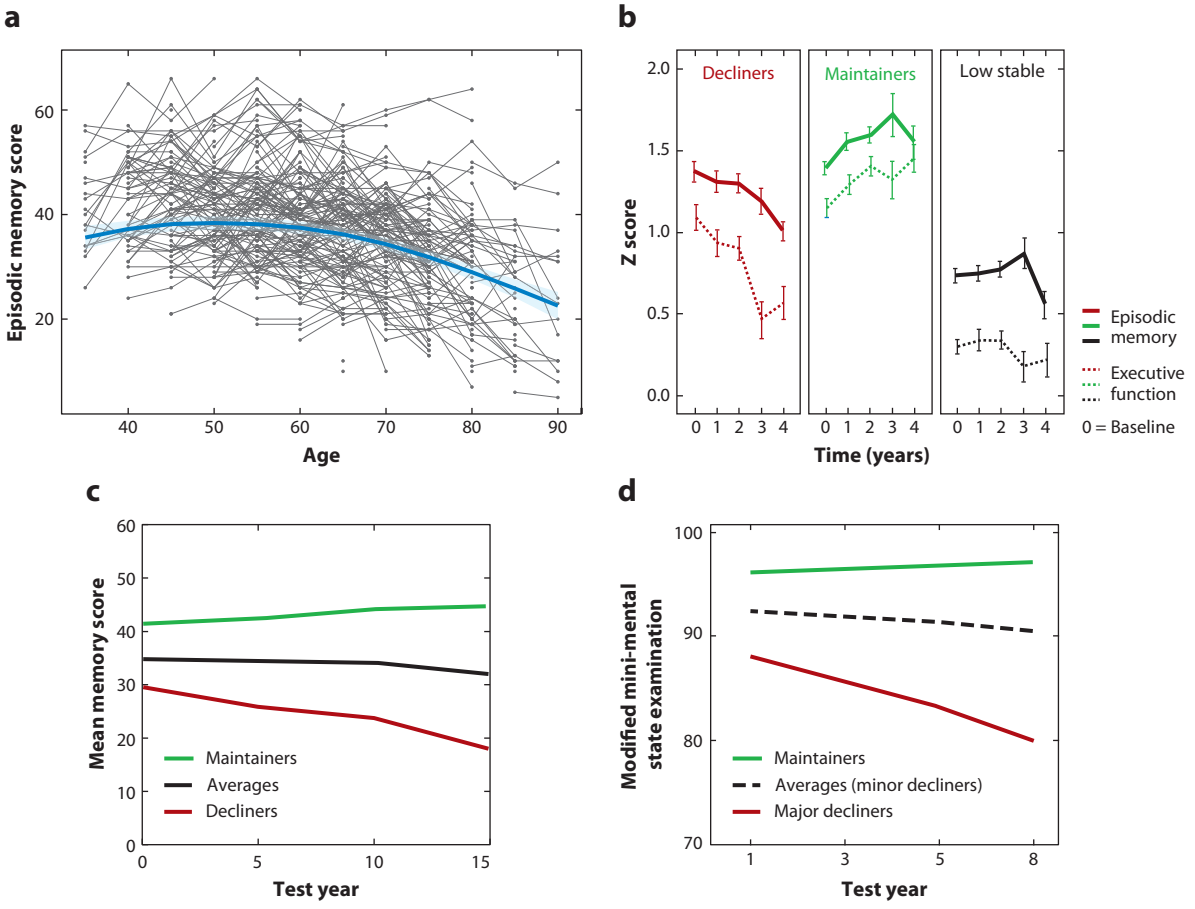

Figure 1

Successful memory aging. (*a*) Interindividual differences in episodic memory level and rate of change, based on a randomly selected subset of 300 participants from the Betula study, aged 35–90, who took part in between one and six measurement waves over up to 25 years (i.e., the same parent sample as in panel *c*). The blue curve illustrates the sample-average change. (*b*,*c*,*d*) Identification of successful memory and cognitive aging in longitudinal studies by (*b*) Lin et al. (2017b), (*c*) Josefsson et al. (2012), and (*d*) Yaffe et al. (2009), where green indicates the successful group. Panel *b* adapted from Lin et al. (2017b) with permission from IOS Press. Panel *c* adapted from Josefsson et al. (2012) with permission from Wiley. Panel *d* adapted from Yaffe et al. (2009) with permission from Wolter Kluwer Health Permission.

Thus, although many aging studies only include older age groups, this approach to identifying successfully aged older individuals requires the inclusion of a young reference sample that can provide normative data. One relevant example comes from the Swedish Betula study (Habib et al. 2007). Data from 1,463 individuals between 50–85 years old were analyzed, and the data set included both cognitive and noncognitive variables. The majority of the cognitive measures were episodic memory tasks. The noncognitive variables included responses to questions aimed at disclosing disease, lifestyle, and socioeconomic factors. Of 663 elderly individuals (70–85 years old), 55 (8.3%) scored above the mean for middle-aged individuals (50–65 years old). When the same type of analysis was repeated on data collected at a separate test wave 5 years later, 25 (6.2%) of the older individuals were classified as high functioning in relation to the performance level of the middle aged.

A complementary approach has been to use published norms data for younger adults as a benchmark for successful memory aging. In the Northwestern University SuperAging Study, individuals above age 80 who performed at or above the normative values of 50–65-year-olds for episodic memory were referred to as superagers (e.g., Harrison et al. 2012). Similarly, in a study by Sun and colleagues (2016) using normative performance for 18–32-year-olds on a free-recall memory test, older adults in the age range 60–80 were classified as superagers or typical older adults. In this study, 17 of 40 elderly participants (42%) were classified as superagers.

Arguably, the strongest evidence that some individuals actually fulfill the criterion of maintaining cognitive functioning will come from longitudinal studies that follow the same individuals over time. Strictly speaking, the assessment of maintenance of any function requires repeated assessment of the same individual over time, but relatively few studies of successful aging have involved a longitudinal design. One early exception is a Canadian study of 3,573 individuals aged 65–84 who were interviewed in 1971 and reinterviewed in 1983 (Roos & Havens 1991). The criteria of successful aging were living to advanced age, functioning well at home, and remaining mentally alert. Of the sample, 20% met these criteria. Another example of a study with a longitudinal design is a Japanese study of successful aging in relation to ADL measures of functional status (Liang et al. 2003). In that study, cognitive ability was used as a predictor rather than an outcome, and greater cognitive impairment at baseline was related to early onset of functional impairment.

In an investigation of successful longitudinal memory aging, 18 of the superagers from the Northwestern study (Harrison et al. 2012) were followed up longitudinally over 18 months (Gefen et al. 2014). For both measures of episodic memory and other cognitive measures, performance was well maintained across this time period. These findings indicate stable cognitive performance levels in some older adults. Relatedly, the study by Habib and colleagues (2007) assessed within-person changes. The longitudinal analysis revealed that 35% of the individuals classified as successful at the first time point remained successful at the second time point, 5 years later. Of those classified as usual at the first time point, 98% retained the same status, whereas only 2% (seven individuals) transitioned to the successful category. An additional relevant longitudinal observation was that 93% of those classified as successful at the first wave returned for testing at the second wave, whereas the corresponding number for the usual group was 58%. Thus, although not everyone in the successful group maintained a cognitive performance level above the mean level for middle-aged individuals, the striking difference in return rates over 5 years constitutes additional support for the validity of a distinction between successful and usual aging. In the HABS (Dekhtyar et al. 2017), a total of 16 of 23 (70%) initial optimal memory performers for whom follow-up data were available maintained their optimal memory status at a 3-year follow-up session. This subgroup also showed better maintenance of executive functioning than those who did not maintain optimal status.

Three additional studies with multiple longitudinal assessments over variable time intervals are of considerable relevance for successful memory aging. In a study within the Alzheimer's Disease NeuroImaging Initiative, Lin and colleagues (2017b) analyzed data from annual sessions repeated over 5 years in a sample of 354 adults with a mean age of 75 years (**Figure 1*b***). They identified one group of successful agers (41%; class 2) with high and stable episodic memory and executive function that were distinguished from declining agers (21%; class 1) and low stable agers (38%; class 3). In a longitudinal study from the Betula project, a statistical model was used that defined maintained memory based on both baseline level and change (slope) over two to four test waves covering up to 15 years (Josefsson et al. 2012). The model also considered nonignorable attrition, as study dropout in older age has been associated with accelerated memory decline. The data from 1,954 individuals on an episodic memory composite score based on five tasks were

analyzed. The results revealed that 18% of the participants could be classified as maintainers with high and stable performance, 13% as decliners, and the remaining two-thirds of the sample as average (**Figure 1*c***). Finally, in a study by Yaffe and colleagues (2009), 2,509 older adults (aged 70–79 at recruitment) were examined on the modified mini-mental state examination at a baseline session and at years 3, 5, and 8. Based on the performance slopes across sessions, participants were classified as maintainers or as minor or major decliners. It was found that 30% maintained cognitive function over the 8 years (**Figure 1*d***).

The above estimates of the proportion of individuals that were classified as displaying successful memory aging varied across studies, from some 6% to over 40%. Relatedly, for other kinds of definitions of successful aging, Depp & Jeste (2006) reported that the mean sample size–weighted proportion of successful agers across 27 studies was 35.8%, with a range from 0.4% to 95% (see also Bosnes et al. 2017, McLaughlin et al. 2012). Variation in how many participants are classified as successful will no doubt reflect the specific criteria used for defining success, but also factors such as geographical region (Mariolis et al. 2016), how developed the studied country is (see García-Lara et al. 2017), heterogeneity in study design, the specific means of probing memory, the statistical cut off, and the sampling procedure (see Lupien & Wan 2004). Still, this brief and nonexhaustive review of the literature supports the notion of successful memory aging by showing (*a*) marked heterogeneity within the domain of normal aging, (*b*) that the performance levels of some older adults can be on par with or greater than that of younger and middle-aged adults, and (*c*) that some older adults well above age 60 show a stable level of memory performance over years and even decades.

It can still be asked whether stability over, say, 15 years (see Josefsson et al. 2012) truly means maintenance of memory and cognition relative to one's peak performance. In this context, it is intriguing that several lines of work suggest long-term stability of interindividual differences in cognition. In one study, 132 veterans from World War II were followed over 45 years, from approximately 25 years of age at initial testing to a mean age of 69.4 at the final session (Arbuckle et al. 1998). They were measured on several intelligence and aptitude tests, and the results revealed moderate to high 45-year correlations for each intellectual subtest across three test waves. Thus, a high degree of stability of intellectual functioning was demonstrated from younger to older age. A similar conclusion was reached in a unique study, the Scottish Lothian Birth Cohorts of 1921 and 1936 (Gow et al. 2011). Stability coefficients for the performance on a cognitive task at age 11 and later at age 70 was high (0.67), and while the magnitude was reduced somewhat over an even longer time period (11–87 years), it still remained sizable (0.51). A similar pattern of long-term stability was observed in analyses of data from the Swedish Betula study (Rönnlund et al. 2015). Cognitive data from military conscription were used to relate general cognitive ability of a sample of 262 men measured at age 18 to their performance when participating in the Betula study at age 50–65. Again, very high stability coefficients were observed. Collectively, across individuals, these findings confirm a high degree of stability in memory and cognitive abilities over the life span. As such, although these studies addressed stability in individual differences rather than mean levels per se (and some tendencies toward mean decline could be seen), they leave open the possibility that stable longitudinal memory performance in older age may indeed reflect resistance to age-related decline from youth (see Gefen et al. 2014).

More generally, the long-term stability perspective is in line with the notion of considering successful aging as successful life-course development (e.g., Schulz & Heckhausen 1996), a perspective that continues to be emphasized in contemporary projects, as exemplified by the Lifebrain consortium (Walhovd et al. 2018). The observations of stability may also partly reflect lifelong hereditary influences on cognition, a topic that we address below.

CHARACTERIZING SUCCESSFUL MEMORY AGING

In this section, we review characteristics and predictors of successful memory aging, focusing on genetic and lifestyle-related factors. We highlight studies that examined declarative memory or, at least, included memory measures as a part of a global cognitive score. However, as alluded to above, fluid cognitive abilities, including episodic memory, tend, to a large extent, to decline together in aging (Ghisletta et al. 2012, Tucker-Drob et al. 2014), and therefore, factors linked to successful memory aging overlap substantially with those linked to successful cognitive aging in general [as covered in several excellent reviews (e.g., Daffner 2010, Depp & Jeste 2006, Depp et al. 2012)]. Furthermore, in line with the preceding emphasis on the importance of longitudinal studies, we highlight, as far as possible, studies in which memory or cognitive functions were assessed longitudinally. This is crucial, since factors related to level of cognitive functioning can be different from those related to change in functioning. Given the demonstrated lifetime stability of individual differences in cognitive functions (see the above section; e.g., Gow et al. 2011), to a considerable extent, the level of cognition in older age appears to be determined by the cognitive level in youth. It is therefore unsatisfactory to only demonstrate that a variable predicts cognitive level in old age, since that association could be driven by an association between that variable and cognitive level in youth. With that said, we acknowledge that reliably estimating change over time can be challenging in the presence of few measurement points, imprecise and not perfectly reliable cognitive measures, and participant attrition. Furthermore, the statistical power for detecting significant predictors of change can often be lower than that for detecting significant predictors of level. This is because individual differences in levels tend to be larger than those in change, and thus, estimation of change is more affected by measurement error than estimation of levels. Factors like these may explain why some predictors discussed below have not consistently been found to be associated with longitudinal cognitive change.

In the tradition of Rowe & Kahn (1987), our aim is to focus on characteristics that distinguish successful from usual memory aging, but such characteristics are not always easy to disentangle from those acting as risk and protective factors for Alzheimer's disease (AD) and other pathological neurocognitive disorders. For instance, lower rates of genetic risk for AD and cerebrospinal markers of AD pathology differentiated successful agers, with high stable episodic memory and executive function trajectories over four years, from declining agers in a study of healthy controls from the Alzheimer's Disease NeuroImaging Initiative Study (Lin et al. 2017b). One reason behind this overlap could be that undiagnosed premorbid neurocognitive disorders may account for a sizable portion of cognitive decline in the normal aging population. It thus remains to be conclusively determined whether predictors of successful cognitive aging can be identified over and above the absence of common risk and protective factors for neurocognitive disorders.

One important determinant of successful cognitive aging that is not addressed in detail in this review is general physical health. Several medical conditions, such as hypertension, insulin resistance, and inflammation, are associated with worse cognitive outcomes in later late (Yaffe 2013). Likewise, mental health conditions such as depression also predict cognitive decline in aging (e.g., Chodosh et al. 2007). Therefore, while this is not the primary focus of this review, we acknowledge the importance of preserving physical and mental health for successful memory aging and note that it may be one out of several mechanisms through which some of the factors discussed below exert their influences on successful memory aging.

Genetic and Epigenetic Influences

Intellectual functioning, including memory function, is considered to be highly heritable and polygenic (Davies et al. 2011). In other words, a substantial portion of the variability in

cognitive abilities is genetically determined. Many genes contribute to this variability, although the effect of each gene is typically very small. Twin study–derived heritability estimates for different cognitive abilities vary, but they often range between 40% and 80% in adult populations (Deary 2012). It has been debated whether heritability remains stable in older adulthood (McGue & Christensen 2013), declines (Lee et al. 2010), or has increased influence in older age, possibly also varying across cognitive domains (Reynolds & Finkel 2015). Still, there is evidence that heritability can be sizeable even in old age, as demonstrated in a study of Swedish twins over the age of 80 (McClearn 1997). In that study, 52% of the variance in memory ability could be ascribed to genetic factors, with estimates for other cognitive domains varying between 32% and 62%.

In searching for genetic determinants of successful memory aging, as noted above, it is important to consider the fact that heritability estimates for levels of cognitive function can differ substantially from those for age-related changes in cognition. In longitudinal studies on aging, it has usually been found that genetic influences are larger for level than for change (for a review, see Lee et al. 2010). In an analysis of 857 individuals from the Swedish Adoption/Twin Study of Aging (SATSA), Tucker-Drob et al. (2014) found that genetic effects accounted for 92% of the variation in the level of a global cognitive factor composed of verbal and spatial abilities, memory, and processing speed, but only 53% of global cognitive change assessed over up to 16 years. When analyses were restricted to the older age range, 65–96 years ($n = 671$), genetic influences on cognitive change were reduced further to 29%, possibly reflecting larger environmental influences on older-age cognitive change than on cognitive level. In another study, Deary et al. (2012) found that 24% of the variation in cognitive change from childhood to old age (65, 70, or 79 years) could be attributable to genetic causes. This estimate reflected so-called single nucleotide polymorphism (SNP)-based heritability and was arrived at by studying the genetic similarity between 1,940 unrelated individuals from the Aberdeen and Lothian Birth Cohorts. Since SNP-based heritability estimates do not capture all genetic effects, the true genetic influence is likely larger. Collectively, these studies, although they did not explicitly study successful cognitive aging, are informative in firmly demonstrating a sizable genetic influence on cognitive aging in general.

The search for specific genetic variants, or candidate genes, associated with cognitive abilities is complicated by the polygenic nature of cognitive function, in which single genes have very little influence, and by the fact that different phenotypic effects can arise from gene–gene and gene–environment or gene–lifestyle interactions. In general, the identification of genes that contribute to the risk for major neurocognitive disorders, such as AD (e.g., Loy et al. 2014), has been more successful than the search for genes that explain performance variation in normal or successful cognitive aging. Still, several candidate genes have been associated with memory and cognitive functioning in normal aging, typically in cross-sectional studies [e.g., Kibra and brain-derived neurotropic factor genes (Almeida et al. 2008, Kennedy et al. 2015)], although replication has sometimes proven difficult (e.g., Boraxbekk et al. 2015). Crucially, few genes have been firmly associated with longitudinal changes in healthy older adults' cognitive functioning. One prominent exception is the apolipoprotein E gene (APOE). Although originally identified as a risk gene for late-onset AD (e.g., Corder et al. 1993), APOE has also been linked to nonpathological age-related cognitive decline in genome-wide association studies (Davies et al. 2014, Zhang & Pierce 2014). Even in studies specifically aimed at identifying successful cognitive aging, the absence of the APOE ε4 risk allele has been shown to differentiate between longitudinally defined successful and declining agers (Lin et al. 2017b). In another study in which successful memory aging across 15 years was identified, the APOE ε4 allele differentiated declining from average agers, but not successful from average agers (Josefsson et al. 2012). Instead, compared to the average group, the

successful memory group contained more Met allele carriers of the Val158Met polymorphism of the catechol O-methyltransferase (COMT) gene, which is associated with higher prefrontal dopamine levels. Josefsson et al. (2012) thus provide tentative evidence that genetic predictors for successful cognitive aging may be different from those predicting accelerated memory decline, while, for instance, the findings of Lin et al. (2017b) suggest that genetic predictors of decline and success are overlapping.

Another subsequent study (Persson et al. 2016) on the same cohort as that of the Josefsson et al. (2012) study used a different statistical approach and found that pulse pressure moderated the effect of the COMT polymorphism on 15-year episodic memory change, such that Val carriers showed accelerated decline at higher levels of pulse pressure. Similarly, in the Seattle Longitudinal Study, the presence of APOE ε4 in combination with hypertension was found to result in accelerated cognitive decline over up to 21 years (de Frias et al. 2014). These two studies, along with several others, illustrate that genetic effects can interact with other individual characteristics, such as physiological risk factors, to magnify the risk of decline. Conversely, beneficial lifestyle factors, such as physical activity, have been shown to counteract adverse genetic effects on memory performance (Ferencz et al. 2014).

One means through which experiences and environmental or lifestyle factors can interact with our genes to influence cognitive aging is through epigenetics, a term denoting various mechanisms that alter gene expression without changing the genomic sequence itself (Mather et al. 2014). Most current knowledge about epigenetic influences on cognition and cognitive aging stems from animal research, but one major epigenetic mechanism, DNA methylation (DNAm), is increasingly being studied in human populations (for a review, see Jones et al. 2018). DNAm involves addition of methyl groups at specific sites of the DNA molecule, which can lead to subsequent alterations in gene expression. One application of DNAm has been to study DNAm profiles at particularly age-informative genomic positions to accurately predict chronological age across individuals in a population (Hannum et al. 2013, Horvath 2013). This approach can also be used to assess the epigenetic age of an individual, also referred to as the epigenetic clock. Discrepancies between an individual's chronological and epigenetic age have been taken to reflect acceleration or deceleration of the physiological aging process.

The epigenetic clock has been studied in relation to many outcomes, including longitudinal cognitive change in aging. For instance, Marioni et al. (2015) found that epigenetic age acceleration was correlated with physical and cognitive fitness in 920 individuals from the Lothian Birth Cohort 1936 at age 70. However, age acceleration at baseline did not predict cognitive change across the 6-year longitudinal follow-up. In another study, individuals characterized by having maintained a high memory performance over a 15-year follow-up period were found to have a significantly younger epigenetic age (by almost 3 years) compared to individuals with average or accelerated memory decline over the same period (Degerman et al. 2017). This result was evident both at study baseline and at a 15-year follow-up. Although these results are quite striking, a caveat in epigenetic studies of humans is that the analyses are typically based on DNAm profiles in peripheral tissue, such as blood or saliva, and may, due to the high tissue specificity of the DNAm process, not necessarily correspond to brain DNAm patterns (Horvath 2013). Still, even peripheral DNAm may reflect intraindividual variability in the biological aging process, driven by both genetic and environmental factors, and therefore serve as a valuable biomarker of preservation or loss of cognitive abilities in aging. In the next section, we consider evidence for lifestyle-related influences on cognitive aging. Although not explicitly considered in the following sections, epigenetic mechanisms could be among several pathways through which lifestyle factors can influence cognitive aging (Mather et al. 2014).

Lifestyle Factors

In this section, we consider evidence for the influence of lifestyle factors on cognitive aging in general and successful memory aging in particular. We begin by considering cognitive activity, then physical activity, and finally some additional characteristics and interactions among lifestyle factors.

Education, occupation, and cognitively stimulating activities. Among lifestyle factors, higher educational attainment is one of the most commonly identified variables associated with successful cognitive and memory aging (e.g., Albert et al. 1995, Habib et al. 2007, Josefsson et al. 2012). However, although higher education has invariably been found to be associated with a higher level of cognitive function in older adults, several longitudinal studies have failed to find robust associations between education and longitudinally assessed cognitive changes in older age (e.g., Wilson et al. 2009, Zahodne et al. 2011). Many factors may account for failures to observe significant associations with cognitive change, including the above-noted methodological factors (length of longitudinal follow-ups, statistical power). In addition, sample characteristics (e.g., age, sociodemographic diversity versus selectivity) and the societal context (such as educational and occupational opportunities or access to social welfare) may play a role. An association to cognitive level is likely partially driven by innate ability differences leading to both higher educational attainment and cognitive function in older adulthood and may therefore be more robust and commonly observed, whereas a true protective effect on cognitive change may only arise in certain contexts. The causal pathway through which education can contribute to preserving cognitive function in aging is currently not well understood, and causal mechanisms may actually differ between different subsamples of the population. For instance, a large-scale ($n = 3{,}435$) study on a sociodemographically diverse sample demonstrated protective effects of education on rate of change on a general cognitive factor composed of memory, language, visuospatial ability, and processing speed variables, measured for up to 18 years (Zahodne et al. 2015). Whereas a protective effect in a high-education subgroup (9–20 years of education) was largely mediated by income, the corresponding effect in the low-education group (<9 years) appeared to be independent of income. Since the effect in the latter group was also independent of illness burden and depressive symptoms, the authors speculated that early education (fewer than 9 years of schooling) may confer its protective effect by promoting neurodevelopment in childhood. This account is conceptually similar to the idea of cognitive reserve (Stern 2009), a hypothesized concept thought to offer resilience to functional impairment in the face of neuropathology and often linked to factors such as higher educational or occupational attainment. In contrast, the effect of later education in the Zahodne et al. (2015) study was mediated by income, which is a key determinant of socioeconomic status (SES) that likely also entails benefits such as better access to high-quality health care, better-quality neighborhoods, and fewer life stressors. Indeed, in other studies, SES on its own has emerged as a significant predictor of successful aging (Britton et al. 2008). Yet an alternative explanation for a protective effect of education could be that it promotes more favorable health- and lifestyle-related decisions, which in turn act to preserve cognition in aging.

Education is usually attained in youth, but other lifestyle factors, such as one's occupation and leisure activities in adulthood and older age, have also been linked to more successful cognitive aging. For instance, some longitudinal studies have reported more favorable cognitive change trajectories for older individuals with more intellectually challenging jobs, even after controlling for level of education (e.g., Potter et al. 2006). However, other studies mainly found effects on older individuals' levels of cognitive performance and no protective effect on change (Lane et al. 2017,

Vemuri et al. 2014). It may be that occupational complexity has beneficial effects on cognitive performance trajectories before retirement but not after (Finkel et al. 2009). This would be in line with the use it or lose it hypothesis of cognitive stimulation (Hultsch et al. 1999). Several longitudinal studies have also found that cognitively stimulating leisure activities are associated with less cognitive decline in later life (Andel et al. 2016, Hultsch et al. 1999, Vemuri et al. 2014), with some indications that leisure activities may compensate for negative influences of low occupational complexity even after retirement (Andel et al. 2016). The type of occupational complexity may also matter. In two studies from SATSA (Andel et al. 2016, Finkel et al. 2009), complexity in relation to people had beneficial effects on cognition, but not complexity in relation to data or things. The dimension of complexity in relation to people included aspects such as mentoring or managing, exemplified by professions such as social worker or counselor. It is likely that such professions involve high levels of social interaction, which in itself has been shown to protect against cognitive losses in older age (e.g., Lövdén et al. 2005). This is just one example of how different lifestyle influences may be intertwined, sometimes making causal pathways challenging to isolate.

The discussion above shows that, although cognitively stimulating factors such as education, occupation, or leisure activities have been found to be associated with preservation of old-age cognitive functions, the effects are more elusive when assessed in longitudinal studies. It is also important to acknowledge that, while education is most often construed as a lifestyle factor, it is also partially genetically determined (Branigan et al. 2013, Okbay et al. 2016), and its genetic determinants likely overlap with those for general cognitive function (Trampush et al. 2017). Gene–environment correlations also imply that individuals with higher innate ability tend to acquire more years of education and seek out more cognitively complex occupations and leisure activities, which may at least partially account for cross-sectional associations between these lifestyle factors and levels of cognitive functioning in older age. Therefore, longitudinal associations with cognitive change constitute stronger evidence, especially if initial ability levels are accounted for to mitigate some of the confounding effects of innate ability differences (see Potter et al. 2006).

Intervention studies can offer an important complementary perspective. However, such studies, too, may have limitations, including participant self-selection into the intervention. There is a large literature on cognitive training interventions for older individuals, and while the evidence supports improvement on specific trained cognitive tasks, the evidence for long-term maintenance and generalizability of the trained skill is more scarce (e.g., Buitenweg et al. 2012, Lampit et al. 2014). For example, a recent study found that 12-month university attendance improved language capacity in 359 healthy seniors, but it did not influence 4-year trajectories of episodic memory or executive function changes relative to controls (Thow et al. 2018). However, even such relatively long-term and naturalistic interventions may not be comparable to the potential protective effects of a lifetime of mentally stimulating activities, and it is also conceivable that mental stimulation in certain life periods is more relevant for obtaining beneficial effects in older age (see Chan et al. 2018).

Physical activity. There is a wealth of research demonstrating that physical activity has beneficial effects on general and neurocognitive health across the life span. Importantly, a beneficial effect of exercise on the rate of cognitive aging has been reported in many studies. For instance, Albert et al. (1995) found that higher self-reported strenuous activity and peak pulmonary expiratory flow rate predicted less global cognitive change (including verbal and nonverbal memory measures) over 2–2.5 years in 1,192 older individuals. Also, in the study by Josefsson et al. (2012), self-reported physical activity at baseline predicted maintained memory functioning over 15 years. Furthermore,

a meta-analysis of 15 prospective studies in which participants were followed for up to 12 years revealed a 35–38% reduced risk for cognitive decline for older individuals who were regularly engaged in low-to-moderate or high levels of physical activity (Sofi et al. 2011).

It is also informative to consider the evidence from exercise intervention studies, as these allow stronger causal inferences than observational studies. Several intervention studies show promising results of exercise interventions on neurocognitive outcome measures in older adulthood (e.g., Erickson et al. 2011, Jonasson et al. 2017). However, meta-analyses and systematic reviews have arrived at variable conclusions regarding the effectiveness of interventions in older age, ranging from no beneficial effects (Young et al. 2015), to mixed and limited effects (Kelly et al. 2014), to consistent and positive effects for aerobic training across many cognitive domains and types of exercises (Colcombe & Kramer 2003, Northey et al. 2018). The specific reasons for the mixed findings in intervention studies remain unclear but likely include methodological factors such as the type, length, and intensity of exercise intervention and the baseline fitness level of the sample (Kelly et al. 2014). Large interindividual differences in exercise outcomes have also been highlighted, arising from, for instance, genetic factors (Duzel et al. 2016). In one cross-sectional study, older Val-Val carriers of the COMT Val158Met polymorphism, who are usually at cognitive disadvantage, showed the largest cognitive benefit from being physically fit (Voelcker-Rehage et al. 2015), suggesting that those individuals with less beneficial genetic predispositions may benefit the most from exercise and other interventions (see also Ferencz et al. 2014). Furthermore, as discussed above in relation to cognitive training interventions, it is possible that optimal effects on neurocognitive preservation in aging are obtained by being physically active throughout the life course.

Additional characteristics and their interactions. We review above some key characteristics and predictors of successful memory aging, focusing on genetic and lifestyle-related cognitive and physical factors. There is evidence for a marked genetic influence on how well individuals maintain memory and cognition in older age. It also seems clear that lifestyle factors account for a sizable portion of the variation in performance level and change in aging, although the result patterns are somewhat inconsistent for both cognitive and physical activities. Several additional environmental and lifestyle factors are likely also relevant for successful memory aging, including stress (Seeman et al. 1997), dietary considerations (e.g., Milte & McNaughton 2016), and perhaps also less emphasized factors such as oral health (Habib et al. 2007). Ongoing efforts focus on exploring gene–environment interplay in late-life functioning (Pedersen et al. 2013), and we also note above that there is tentative evidence for a role of epigenetic mechanisms in successful memory aging. Most likely, there are synergetic effects of different lifestyle factors, such as diet and physical activity (van Praag 2009), and some positive results from studies that have combined different kinds of lifestyle interventions have been reported. One of the most comprehensive examples is the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER; Ngandu et al. 2015), which included 631 individuals (aged 60–77 years) with elevated dementia risk in a 2-year intervention that comprised not only cognitive training and physical activity, but also dietary advice and vascular risk monitoring. After 2 years, the intervention group had a significantly higher performance improvement (Cohen's $d = 0.13$) on a global cognitive test than the control group, which only received health advice at 6-month intervals. Thus, although the memory test included in the global cognitive measure did not show differential improvement between control and intervention groups (both groups improved equally), the results indicated that cognitive performance in older age is indeed malleable and can be affected by multidomain lifestyle interventions.

THE HOW OF SUCCESSFUL MEMORY AGING

More than two decades ago, it was argued that research on successful aging should be broadened from asking what successful aging is to asking how people age successfully (Baltes & Carstensen 1996). Rowe & Kahn (2015) also considered the distinction between the what and the how of successful aging. They argued that the original MacArthur model emphasized what factors, the core issue being identification of what predicts avoiding negative change and maintaining functionality—be it activities and attitudes of younger and middle age (Havighurst 1961), memory and cognition (e.g., Josefsson et al. 2012), or functional and structural brain integrity (Nyberg et al. 2012). Although some factors, like physical activity, may fit into both what and how categories, the what factors broadly correspond to the predictors that are discussed in the previous section.

How factors are more emphasized in psychologically rooted theories, such as Margret and Paul Baltes' selection-optimization-compensation (SOC) model (e.g., Baltes & Baltes 1990, Baltes & Smith 2003; see also Baltes & Carstensen 1996). According to the SOC model, "by using strategies of selection, optimization, and compensation, individuals can contribute to their own successful aging" (Baltes & Baltes 1990, p. 27). In this model, successful aging is defined as minimizing losses and maximizing gains, with the SOC processes enabling individuals to master goals despite inevitable losses at some time point. In essence, the how perspective highlights a dynamic, process-oriented nature of successful aging, where some individuals will be better able than others to cope with a certain kind of age-related loss (e.g., hippocampal atrophy). Core aspects of resilience play a prominent role in the SOC model (see Pruchno & Carr 2017), and successful aging has, in some contexts, been defined as resilience to adversity over time (Pruchno et al. 2015).

Selection broadly refers to a form of restriction. It could, for example, mean that a person who experiences cognitive or motor deficiencies selects to only drive during times of good visibility and little traffic. Selection could also be expressed as avoiding situations that may tax new learning and instead choosing well-learned familiar activities. Optimization refers to enhancement of, say, memory functioning, for instance, through some form of cognitive or physical intervention, as discussed in the previous sections. The third SOC process, compensation, comes into play when a behavioral deficiency of some kind prevents a goal being realized in the same manner as it could have been prior to the deficiency (i.e., a gap has emerged between one's competence level and the environmental demands). In the context of memory aging, one apparent example of a compensatory behavior is increased reliance on mnemonics or external memory aids in a person who experiences memory problems (see, e.g., Bäckman & Dixon 1992).

More generally, compensation could mean the use of alternative strategies and processes as a way of combating emerging memory problems. This topic has been intensively examined with functional neuroimaging techniques, with the hope of being able to objectively identify alterations in the recruited functional brain circuits in elderly individuals with memory decline. By far, the most-discussed alteration concerns increased functional response in the prefrontal cortex, which often manifests as a more bilateral frontal response pattern in older adults than in younger adults (e.g., Cabeza 2002). The functional interpretation of increased responses in aging remains unclear, with demonstrations that increased activity in older adults may be associated with better as well as worse task performance (see Grady 2012). Still, a dominating view is that "pervasive increased frontal activation with age is a marker of an adaptive brain that engages in compensatory scaffolding in response to the challenges posed by declining neural structures and function" (Park & Reuter-Lorenz 2009, p. 173). A 4-year longitudinal imaging study provided empirical support for this view by demonstrating that decline in episodic memory was related to a smaller hippocampus volume, along with upregulation of frontal activity during memory encoding and retrieval (Pudas et al. 2018).

Park & Reuter-Lorenz (2009) proposed that one basis for well-preserved function in older age can be a slow rate of cognitive aging, which is in the spirit of what factors and brain maintenance (Nyberg et al. 2012). Another basis for well-preserved function in older age could be particularly effective scaffolding mechanisms, which are more in the spirit of how factors. Of particular relevance to successful memory aging, Park & Reuter-Lorenz (2009) predicted that older individuals with exceptionally good cognition have both low genetic susceptibility to biological aging and effective scaffolding, i.e., favorable what as well as how factors.

What determines if a person has effective scaffolding or efficient use of SOC processes and is thereby more resilient to adverse changes in aging? One suggestion (Park & Reuter-Lorenz 2009) is that individual differences in cognitive reserve (e.g., Stern 2009) determine the quality, quantity, and effectiveness of scaffolding. Perhaps somewhat relatedly, Baltes & Carstensen (1996, p. 415) suggested that all three SOC processes "are activated more easily and readily when there is a rich array of resources available from which to draw." It is at present unclear how cognitive reserve and a rich array of resources are formed. As noted above, education and occupation factors have been linked to cognitive reserve (see, e.g., Stern 2009), and other factors like mastering and regularly using two or several languages could also play a role (e.g., Bialystok et al. 2012). Furthermore, a recent study (Chan et al. 2018) demonstrated that lifestyle activities in mid-life contributed, over and above education, occupation, and current activities, to cognitive reserve in old age. The mid-life activities moderated the relationship between late-life cognition and brain structure such that the cognitive functions of older individuals with higher reserve were less dependent on structural brain integrity.

Taken together, in the spirit of the supply–demand framework for adult cognitive plasticity put forward by Lövdén and colleagues (2010), we submit that many lifetime encounters (e.g., in school, at work, during leisure activities) of a gap between one's current competence level and the environmental demands constitute a vital determinant of building effective scaffolding and cognitive reserve.

BRAIN CORRELATES OF SUCCESSFUL MEMORY AGING

What characterizes the brains of older individuals with exceptional memory abilities and those who maintain their memory functioning better over time than their peers? The hippocampus plays a central role, given its well-established key role in episodic memory (e.g., Eichenbaum 2017). There is converging evidence from several studies of different samples for hippocampal atrophy in normal aging (e.g., Raz et al. 2005, Walhovd et al. 2011), even over as short a time span as 1 year (Fjell et al. 2009). Critically, 1-year hippocampal atrophy has been demonstrated even in individuals who, according to biomarker, genetic, and cognitive criteria, had very low risk for being in a presymptomatic stage of AD (Fjell et al. 2013). Thus, in persons who should meet criteria for usual rather than pathological aging, annual hippocampus atrophy is normative, albeit progressing at a lower rate than in pathological aging (see Jack et al. 1998).

As for the distinction between usual and successful memory aging, some studies have identified 70–90-year-old individuals with no annual negative hippocampus volume change (Fjell et al. 2009). Moreover, Sun and colleagues (2016) reported that their group of superagers had a hippocampal volume comparable to younger adults, whereas smaller volume was seen in typical older adults compared to young adults (see also Dekhtyar et al. 2017). Furthermore, there is longitudinal evidence that structural integrity of the hippocampus region stands out as a particularly strong predictor of well-preserved episodic memory in aging (Gorbach et al. 2016).

Other aspects of hippocampus integrity are also of relevance in the context of successful memory aging. In a functional magnetic resonance imaging (fMRI) study of maintainers and average

participants from the Betula study, Pudas et al. (2013) found that the successful older adults had higher activity in the left hippocampus and prefrontal cortex during encoding of face–name pairs compared to average (usual) participants and as high of activity as a young reference group. The hippocampus activity correlated with memory task performance, and it was not driven by group differences in hippocampus volume. As such, these findings indicate that maintaining hippocampus functional integrity is an independent predictor of successful memory aging (see also Düzel et al. 2011). Additional support for this view comes from findings that individuals who maintained memory well over 20 years had better-preserved (i.e., less elevated) hippocampus resting state connectivity as compared to older individuals with typical memory decline (Salami et al. 2014). Yet other aspects of hippocampus integrity that might characterize successful memory aging relate to preserved dopamine system functioning (e.g., Nyberg et al. 2016), preserved neurovascular functions (Düzel et al. 2016), and minimal tau protein deposition (Schöll et al. 2016).

Brain characteristics of successful memory aging outside the hippocampal region can be found in cortical regions. Minimal cortical β-amyloid (Aβ) deposition is likely a key factor not only in pathological aging, but also in the domain of normal aging (e.g., Farrell et al. 2017), and the co-occurrence of Aβ and hippocampus atrophy has been found to be a major predictor of memory decline (Mormino et al. 2014). In the HABS (Dekhtyar et al. 2017), maintenance of excellent memory performance over 3 years was associated with lower amyloid burden. Efficient structural and functional brain connectivity may also characterize successful memory aging, as exemplified by findings of stronger functional connectivity between the right hippocampus and the anterior cingulate cortex in older adults with excellent memory capacity (Lin et al. 2017a). Relatedly, in a study by Gefen and colleagues (2015), the cingulate cortex was found to be thicker in superagers than in usual elderly controls, and in some (anterior) segments, the cingulate cortex was even thicker compared to middle-aged controls. Postmortem investigations further suggested that the superagers had a higher density of von Economo neurons and the least neurofibrillary degeneration in the cingulate cortex (compared with cognitively average elderly individuals and individuals with amnestic mild cognitive impairment). Another study also reported a higher cortical thickness of superagers in the cingulate cortex as well as in several additional medial and lateral cortical regions, indicating that "older adults with youthful memory abilities have youthful brain regions" (Sun et al. 2016, p. 9659). A similar argument has been made in fMRI studies of working memory (Nagel et al. 2009) and processing speed (Waiter et al. 2008).

Taken together, while we caution that cross-sectional estimates of brain structure and function may markedly deviate from longitudinal assessment of true change (Nyberg et al. 2010), the available data on brain characteristics of successful memory aging are largely consistent with the brain-maintenance account of preserved memory in aging (Nyberg et al. 2012). According to this account, relative lack of structural and functional brain changes and pathology are the primary determinants of successful memory aging. In other words, while some brain changes may typically also characterize older individuals who meet criteria for successful memory aging, these changes are expected to be of a considerably smaller magnitude than in usual and pathological memory aging. Crucially, as we discuss in the following section, there may be more than one path to successful memory aging such that success may be also possible to achieve in the presence of more usual age-related brain changes.

CONCLUSIONS

Successful memory aging is an empirical reality, in that some older individuals have a very high level of performance in domains characterized by average age-related memory decline, and there is converging evidence from several longitudinal studies for stable memory functions well into

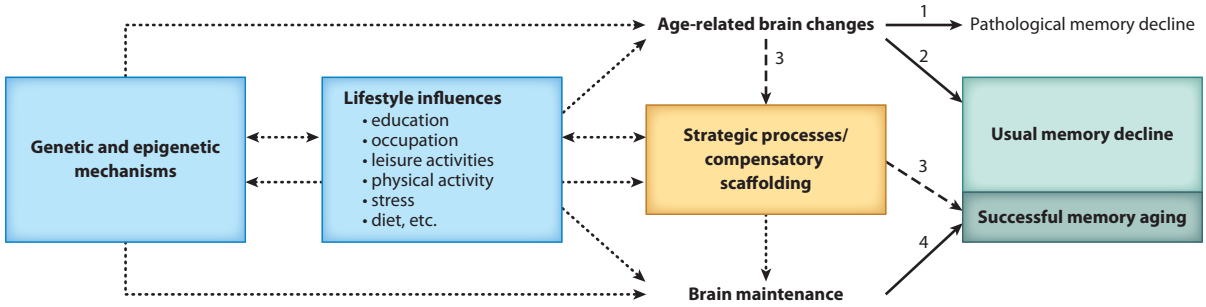

Figure 2

Model of life course paths to pathological, usual, and successful memory aging. Path 1 (not the focus of this review) represents conditions characterized by pathological memory decline (e.g., dementia). Paths 2, 3, and 4 lead to normal memory aging (*green box*). Path 2 represents usual memory decline in response to age-related brain changes (e.g., hippocampus atrophy). Path 3 (*dashed line*) is an indirect path to successful memory aging via compensation for age-related brain changes. Path 4 leads directly to successful memory aging via brain maintenance. The dotted lines reflect the influences of what factors (*blue boxes*) and how factors (*orange box*) on brain integrity (maintenance or change) and memory outcomes.

older age (**Figure 1**). We have reviewed some of the many factors that may contribute to successful memory aging. Although there is likely marked heterogeneity at the individual level with regard to which specific factors play a decisive role, a tentative integrative model is presented in **Figure 2**. A key feature of this model is the suggestion that there may be more than one life-course path toward successful memory aging. One path is via brain maintenance, i.e., relative lack of brain pathology (Nyberg et al. 2012), and we have highlighted integrity of the cingulate cortex and the hippocampus. The other, indirect, path builds on the idea that some individuals, despite age-related brain changes, can accomplish successful memory aging by means of efficient scaffolding (Park & Reuter-Lorenz 2009) and high cognitive reserve (see Chan et al. 2018). There is also compelling evidence for genetic contributions to successful memory aging. These contributions can impact brain integrity in a direct sense, such as via genetic predisposition for minimal hippocampus atrophy in aging (e.g., individual variation in APOE genotype). The genetic contribution could also be expressed indirectly by influencing what and how factors in memory aging and via epigenetic mechanisms through which environmental and lifestyle factors can alter gene expression. Although this is methodologically challenging to show, lifestyle factors likely also have influences on successful memory aging that are independent from the core genetic influence.

A potential lifestyle contribution is important in that it opens up the possibility of influencing the proportion of older individuals that go on to show pathological or normal memory aging, as well as the proportion classified as usual versus successful. For pathological memory aging, there is evidence that the dementia incidence is going down. One empirical example comes from the Framingham Heart Study, showing a decline in dementia incidence over the past three decades (Satizabal et al. 2016; see also Skoog et al. 2017). A lowering of the dementia incidence could translate into a redistribution of individuals who progress along path 1 to path 2 in **Figure 2**. With regard to alterations in the relative proportion of usual versus successful memory aging (i.e., path 2 versus paths 3–4 in **Figure 2**), there is a relative scarcity of longitudinal data on cohort differences in the rate (i.e., slope) of age-related cognitive decline. Furthermore, the existing data are not conclusive, with contradictory findings of no cohort differences in rates of decline, less steep rates of decline for later-born cohorts, and steeper rates of decline for later-born than for earlier-born cohorts (see Ganguli 2017). Such a complex pattern of results might, in part, reflect complex interactions between onset and rate of change, such that rate could be faster for later

onset of change. For memory level, 10-year cohort gains in immediate 10-item word recall were observed in a very large-scale study of a sample consisting of 92,739 individuals between 50–84 years old from 10 European countries (Hessel et al. 2018). The performance increased between 2004 and 2013 for all of the examined countries. Consistent with the arguments and model in this section (**Figure 2**), further analyses revealed that decreases in the prevalence of cardiovascular diseases and physical inactivity, as well as increases in educational attainment, were positively associated with the amount of gain.

Hessel and colleagues (2018) related their findings of secular cohort gains in memory level to past demonstrations that later-born cohorts have been found to show higher cognitive performance levels than their predecessors. This so-called Flynn effect (Flynn 1984, 2012) has repeatedly been demonstrated for younger individuals, but it has also been shown for older individuals [i.e., earlier-born cohorts (e.g., Rönnlund & Nilsson 2008)]. How this demographic trend might impact memory and cognitive aging at the population level was considered in a report based on the English Longitudinal Study of Ageing (Skirbekk et al. 2013). Projection findings, based on the assumption that the future Flynn effect would be on par with effects seen from 2002 to 2008, indicated a net improvement in cognition. According to this projection, at the population level, cognition will actually improve until 2042, which, at the individual level, should mean that a higher percentage of individuals will meet currently established criteria of successful memory aging. Obviously, the key assumption in this future projection is that trends like that described by Flynn will continue. While this remains to be seen, some current observations indicate that the Flynn effect has leveled off (Sundet et al. 2004) or even gone into reverse (Flynn & Shayer 2018; but see Trahan et al. 2014). Relatedly, Hessel et al. (2018) found that the secular cohort gains in memory level were markedly more pronounced in countries with initially lower performance levels. Based on the suggestion that educational expansion contributes to the Flynn effect, they suggested that the country effect could be due to these countries having had the largest reduction in the proportion of individuals with lower levels of education.

In view of global population aging, it is important to stress the interrelation between the individual and societal levels of successful aging (see Rowe & Kahn 2015). Thus, even a modest success at impacting successful memory aging at the individual level could translate into a substantial public health effect. We therefore end by emphasizing the importance of primary prevention in the context of reducing pathological aging (see Livingston et al. 2017, Satizabal et al. 2016), as well as for promoting successful memory aging.

FUTURE ISSUES

1. How many older adults in a given population meet the criteria of successful memory aging? Can a consensus on defining criteria be reached? Does the proportion of successful memory agers change over time within and between countries? What societal factors promote or hinder successful aging in different countries and among successive generations?
2. How do genetic and lifestyle factors interact in promoting successful memory aging? What are the critical epigenetic mechanisms?
3. Can trajectories toward normal, pathological, or successful memory aging be influenced by targeted intervention programs? Can personalized assessments be used to determine who will benefit the most from interventions and to tailor interventions according to individual needs?

4. To what extent can cognitive reserve and efficient scaffolding compensate for age-related brain changes and thereby promote successful memory aging? What lifespan factors and activities contribute to establishing efficient compensatory strategies?
5. What is the relationship between successful memory aging and successful cognitive aging in other domains? For instance, will individuals who meet criteria for successful episodic memory aging also display well-preserved working memory and executive functions?
6. What neural and non-neural mechanisms contribute to brain maintenance in general and to hippocampal maintenance in particular? What are the neural underpinnings of cognitive reserve? Do some mechanisms (e.g., neuronal morphology, vascular integrity) underlie both maintenance and efficient compensation?

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