Connecting the Many Levels and Facets of Cognitive Aging

Shu-Chen Li[1]

Center for Lifespan Psychology, Max Planck Institute for Human Development, Berlin, Germany

Abstract

Basic cognitive mechanisms, such as the abilities to briefly maintain, focus, and process information, decline with age. Related fields of cognitive aging research have been advancing rapidly, but mostly independently, at the biological, information processing, and behavioral levels. To facilitate integration, this article reviews research on cognitive aging at the different levels, and describes a recent integrative theory postulating that aging-related deficiencies in neurotransmission cause increased noise in information processing and less distinctive cortical representation, which in turn lead to cognitive deficits. Aging-related attenuation of catecholaminergic modulation can be modeled by lowering a neural network parameter to reduce the signal-to-noise ratio of information processing. The performance of such models is consistent with benchmark phenomena observed in humans, ranging from age differences in learning rate, asymptotic performance, and interference susceptibility to intra- and interindividual variability and ability dedifferentiation. Although the details of the conjectured sequence of effects linking neuromodulation to cognitive aging deficits await further empirical validation, cross-level theorizing of the kind illustrated here could foster the coevolution of related fields through cross-level data synthesis and hypothesis testing.

Keywords

cognitive aging; catecholaminergic modulation; cortical representation; neural networks

Gradual declines in fundamental aspects of cognition pervade the aging process. Biologically, brain aging involves structural losses in neurons and the connections between them, along with deterioration in the neurochemical systems that support communication between neurons. Behaviorally, people's abilities to keep information in mind briefly (termed working memory), attend to relevant information, and process information promptly are compromised with age. Explanations for these cognitive aging deficits have been postulated at various levels. At the cognitive level, some researchers assume there is an aging-related reduction in processing resources, such as working memory, attention regulation, and processing speed. At the biological level, other researchers hypothesize there is an aging-related increase in neuronal noise (i.e., haphazard variations in neural information processing that reduce processing fidelity) or dysfunction of the prefrontal cortex, an area at the front of the cerebral cortex that is thought to be critical for working memory. Experimental designs used in neurobiological studies that involve animals are not always readily transferable to human cognitive studies, and vice versa. Therefore, until the recent advances with neuroimaging and related techniques that provide online measures of brain activity while people are performing cognitive tasks, data and theories of cognitive aging were mostly confined within their respective levels. The present article focuses on synthesizing what is known about cognitive aging in humans using a cross-level theory that postulates a sequence of events beginning at the mechanisms of neurotransmission and leading to the behavioral phenomena that have been documented.

AGING, CATECHOLAMINES, AND COGNITIVE PROCESSING RESOURCES

Although progressive neuroanatomical degeneration is characteristic of pathological aging such as Alzheimer's disease, there is now evidence suggesting that milder cognitive problems occurring during normal aging are mostly due to neurochemical shifts in still-intact neural circuitry (Morrison & Hof, 1997). In particular, the neurotransmitters referred to as catecholamines, including dopamine and norepinephrine, appear to play an important role in aging-related cognitive impairments.

There is consensus that catecholaminergic function in various regions of the brain, such as the prefrontal cortex and basal ganglia (a group of diverse structures, lying beneath the cortex, that regulate motor movements and category learning), declines with advancing age. Across the adult life span, in the various regions of frontal cortex and basal ganglia, the amount of dopamine and the number of protein molecules responding to the release of dopamine (i.e., dopamine receptors) decrease by 5 to 10% each decade (see Kaasinen et al., 2000, for review).

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Research over the past two decades suggests that catecholamines modulate the prefrontal cortex's utilization of briefly activated cortical representations of external stimuli to circumvent constant reliance on environmental cues and to regulate attention to focus on relevant stimuli and appropriate responses (Arnsten, 1998). In addition, there are many findings indicating functional relationships between aging-related deficits in the dopaminergic system and reduced cognitive processing resources in terms of information processing speed and working memory. For instance, reduced density of dopamine receptors in old rats' basal ganglia decreases response speed and increases variability in reaction time (MacRae, Spirduso, & Wilcox, 1988). Drugs that facilitate dopaminergic modulation alleviate working memory deficits of aged monkeys who lose 50% of the dopamine in their prefrontal cortex because of aging (Arnsten & Goldman-Rakic, 1985). In humans, aging-related attenuation of one category of dopamine receptors (i.e., the D2 receptors) is associated with declines in processing speed and word and face recognition (Bäckman et al., 2000).

MODELING AGING-RELATED DECLINE OF CATECHOLAMINERGIC MODULATION

Although there is growing evidence for the catecholamines' involvement in various aging-related cognitive impairments, the details of these functional relationships await further explication. Theoretical inquiries into general computational principles aimed at capturing how neuronal signals are processed and integrated might help unravel mechanisms underlying the associations between deficient catecholaminergic modulation of neurons' responsivity and cognitive aging deficits.

The specifics of catecholamines' roles in modulating neuronal responsivity notwithstanding, in general terms, catecholamines' effects can be conceptualized as altering the balance between the intensity of the to-be-processed neuronal signals and other random background neuronal activity in the brain (i.e., the signal-to-noise ratio), thus regulating the neurons' sensitivity to incoming signals. This effect can be modeled with artificial neural networks, computational models that consist of multiple interconnected layers of simple processing units whose responsivity can be regulated by a network parameter (Servan-Schreiber, Printz, & Cohen, 1990). Neural signal transmission in such systems is simulated by forwarding the effect of an external stimulus signal, represented by the activity profile across units at the input layer, to output units via the intermediate layer. The activity level (activation) of each of the intermediate and output units is usually defined by a mathematical equation describing the function relating input signals to output (the most commonly used equation is the S-shaped logistic function). The activation function transforms the input signal into patterns of activation at the subsequent layers. The thus-transformed activation profile across units at the intermediate layer constitutes the network's internal representation for a given external stimulus. The gain (G) parameter is a component of the activation function that determines its slope. Conceptually, the G parameter captures catecholaminergic modulation by altering the slope of the activation function, thus regulating a processing unit's sensitivity to input signals (Fig. 1a). The randomness inherent in mechanisms of neurotransmitter release can be implemented by randomly choosing the values for the G parameters of the network's processing units at each processing step. Reducing the mean of these values can then simulate aging-related decline in catecholaminergic function (Li, Lindenberger, & Frensch, 2000).

FROM DEFICIENT NEUROMODULATION TO NEURONAL NOISE AND REPRESENTATION DEDIFFERENTIATION

A classical hypothesis regarding cognitive aging is that it is due to an aging-related increase in neuronal noise; however, mechanisms leading to such an increase and its immediate consequences have not been unveiled thus far. Simulating aging-related decline of neuromodulation by attenuating the average of the G parameter hints at a possible chain of mechanisms that may be involved.

Reducing mean G reduces a unit's average responsivity to input signals (Fig. 1a). For instance, a given amount of difference between two inputs—say, an excitatory input (e.g., +1) and an inhibitory input (e.g., −1)—produces a much greater difference in activation when G equals 1.00 than when G equals 0.1. At the extreme case when G equals 0, the unit's response always remains at its baseline activation regardless of differences in inputs (see Fig. 1). Furthermore, when the values of a unit's G are randomly chosen from a set of values, the lower the average of that set, the more variable is the unit's response to a given external signal. An increase in the variability of activation within the network, in turn, decreases the fidelity with which signals are transmitted. Put differently, a given amount of random variation in G, simulating random fluctuations in release of

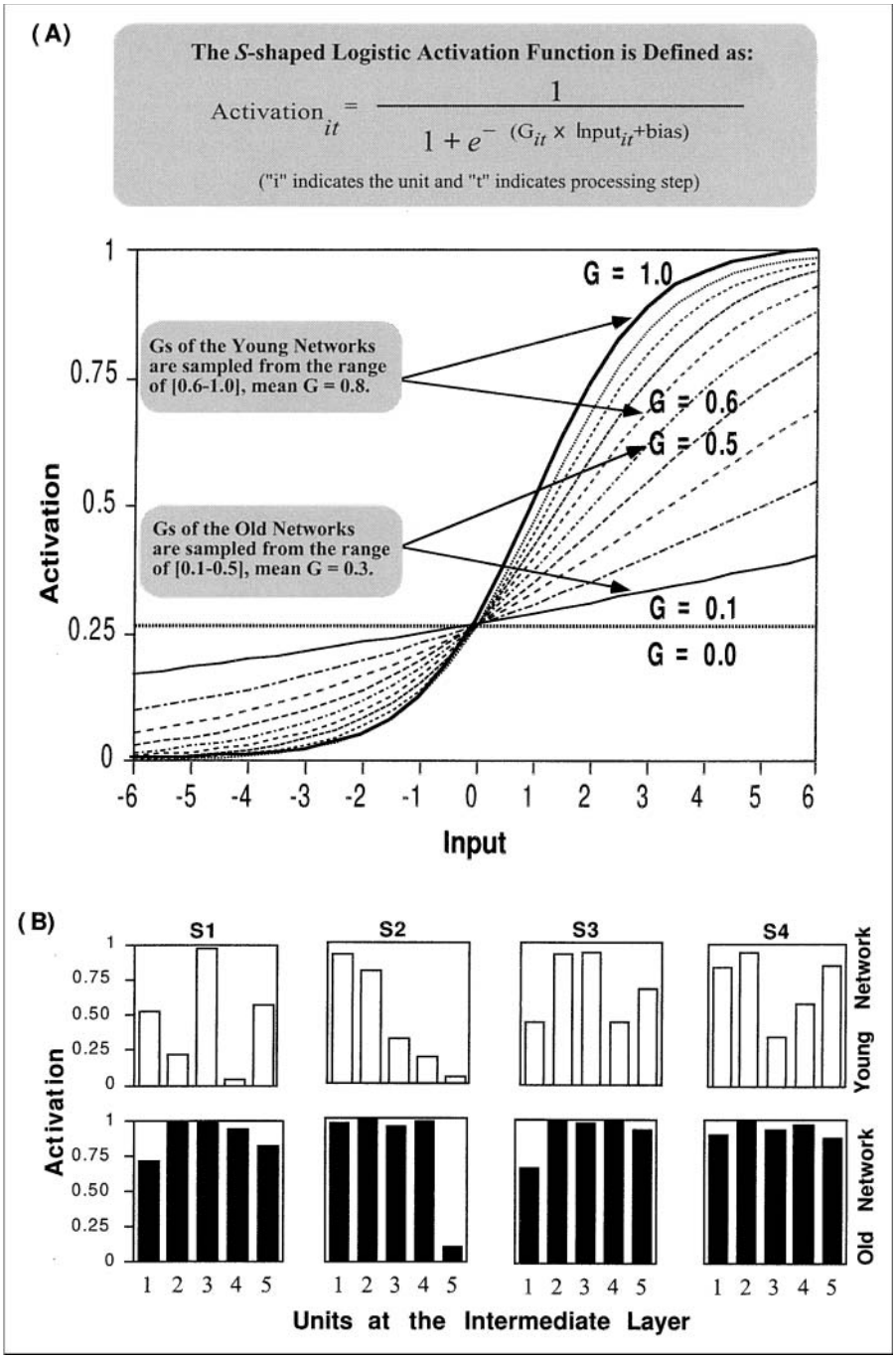

Fig. 1. The gain parameter: its impact on the slope of the activation function and the distinctiveness of activation patterns at the intermediate layer. The S-shaped logistic activation function is defined in (a), and graphed for different values of *G*. Values of *G* ranging from 0.6 to 1.0 were used in networks simulating young adults' performance, and values of *G* ranging from 0.1 to 0.5 were used in networks simulating older adults' performance. Internal activation patterns across five intermediate units of one "young" and one "old" network in response to four different stimuli (S1–S4) are shown in (b). From "Unifying Cognitive Aging: From Neuromodulation to Representation to Cognition," by S.-C. Li, U. Lindenberger, and P.A. Frensch, 2000, *Neurocomputing*, *32–33*, p. 881. Copyright 2000 by Elsevier Science. Adapted with permission.

neurotransmitters, generates more haphazard activation variability during signal processing if the average of the processing units' *G*s is reduced. This sequence of effects computationally depicts a potential neurochemical mechanism for aging-related increase of neuronal noise: As aging attenuates neuromodulation, the impact of transmitter fluctuations on the overall level of neuronal noise is amplified in the aging brain.

Moreover, reduced responsivity and increased random variability in the activation within a network subsequently decrease the distinctiveness of the network's internal representations of external stimuli. Low representational distinctiveness means that the activation profiles for different external stimuli are less readily differentiable from each other at the network's intermediate layer. To illustrate, Figure 1b shows the activation levels across units at the intermediate layer of one "young" (higher average *G*) and one "old" (lower average *G*) network in response to four input signals. Clearly, the internal stimulus representations are much less distinctive in the old than in the young network. Thus, according to this simulation, as people age, at the cognitive level their mental representations of different events, such as various scenes viewed at an art exhibition, become less distinct, and therefore more confusable with each other.

A potential biological implication of this theoretical property is that as declining catecholaminergic modulation drives down cortical neurons' responsivity and increases neuronal noise in the aging brain, cortical representations (the presumed biological substrates of mental representations) elicited by different stimuli become less distinct (i.e., become dedifferentiated). Cognitive processing depends on the cortical representations created

by perception and accessed by memory. Therefore, by causing less distinctive cortical representations of different events, deficient neuromodulation could have an influential impact on various aspects of cognitive functioning.

SIMULATIONS LINKING NEUROMODULATION WITH BEHAVIORAL DATA

The theoretical path from aging-related impairment of neuromodulation to increased neuronal noise in the aging brain to dedifferentiated cortical representation and on to cognitive aging deficits has been tested and supported by a series of neural network simulations.

Aging, Learning Rate, Asymptotic Performance, and Susceptibility to Interference

Behavioral memory research shows that as people get older, they take longer to learn paired associates (arbitrary word pairs, such as "computer-violin"). In agreement with these empirical findings, neural network simulations have shown that old networks also require more trials than young networks to learn paired associates (Fig. 2a). If old and young people differ only in how fast they can learn, one would expect that, given enough training, old people would eventually reach young people's performance level. Alas, ample data show that maximum (asymptotic) performance often exhibits an aging deficit as well. The lower asymptotic performance observed in people in their 60s and onward can also be accounted for by reducing average *G*, as old neural networks display poorer asymptotic performance than young neural networks (Fig. 2b).

Another prominent cognitive aging deficit is older people's increasing susceptibility to distraction by irrelevant or no-longer-relevant information (i.e., increased susceptibility to interference). In the context of paired associate learning, 60-year-olds are more susceptible than 40-year-olds to interference of previously learned word pairs with subsequent learning of new pairs, and they need more trials to learn new word pairs if this interference is strong. In line with this empirical evidence, the simulations have shown that the degree of interference affects the rate at which new word pairs are learned more in old than in young networks (Fig. 2c).

Aging, Performance Variability, and Covariation

The behavioral data demonstrate not only decreases in performance levels, but also aging-related increases in performance variation within a person across time (or different tasks) and aging-related increases in differences between individuals. Furthermore, aging also seems to affect the relations between different cognitive abilities: Studies conducted since the 1920s have shown that as people age, performance levels on different tasks become more correlated with each other. These phenomena can also be accounted for by reduction in mean *G*, suggesting that aging-related increases in intraindividual performance variability, interindividual diversity, and ability dedifferentiation might in part be associated with declining neuromodulation (Li et al., 2000). For example, Figure 2d shows the results of a simulation in which intranetwork variability was tested. Performance variability across different study lists in four conditions of paired associate learning was larger in the old than in the young networks.

COEVOLVING FIELDS VIA CROSS-LEVEL DATA SYNTHESIS AND HYPOTHESIS GENERATION

Accumulating evidence indicates that catecholaminergic neuromodulation is an influential biological underpinning of many cognitive aging deficits. However, details of the effects causing this neurobiological-behavior link remain to be unraveled. Pieces of the puzzle are emerging from the various subfields, but the field as a whole needs overarching frameworks to integrate existing data and guide concerted research efforts. The cross-level computational theory described in this article is only an initial attempt to arrive at such integrative frameworks. Indeed, the theory's main tenet—that attenuated neuromodulation leads to increased neuronal noise and less distinctive cortical representations in the aging brain, and in turn to cognitive aging deficits—awaits more direct and vigorous empirical scrutiny in the future. However, the computational simulations conducted thus far integrate evidence of aging-related decline in catecholaminergic modulation with a broad range of cognitive aging effects that have been observed in humans—an integrative task that still cannot be easily implemented in animal neurobiological or human neuroimaging studies alone.

In addition to synthesizing data, the theory generates some cross-level hypotheses for future research. For instance, it suggests that neuromodulation might influence aging-related increases in intraindividual performance variability

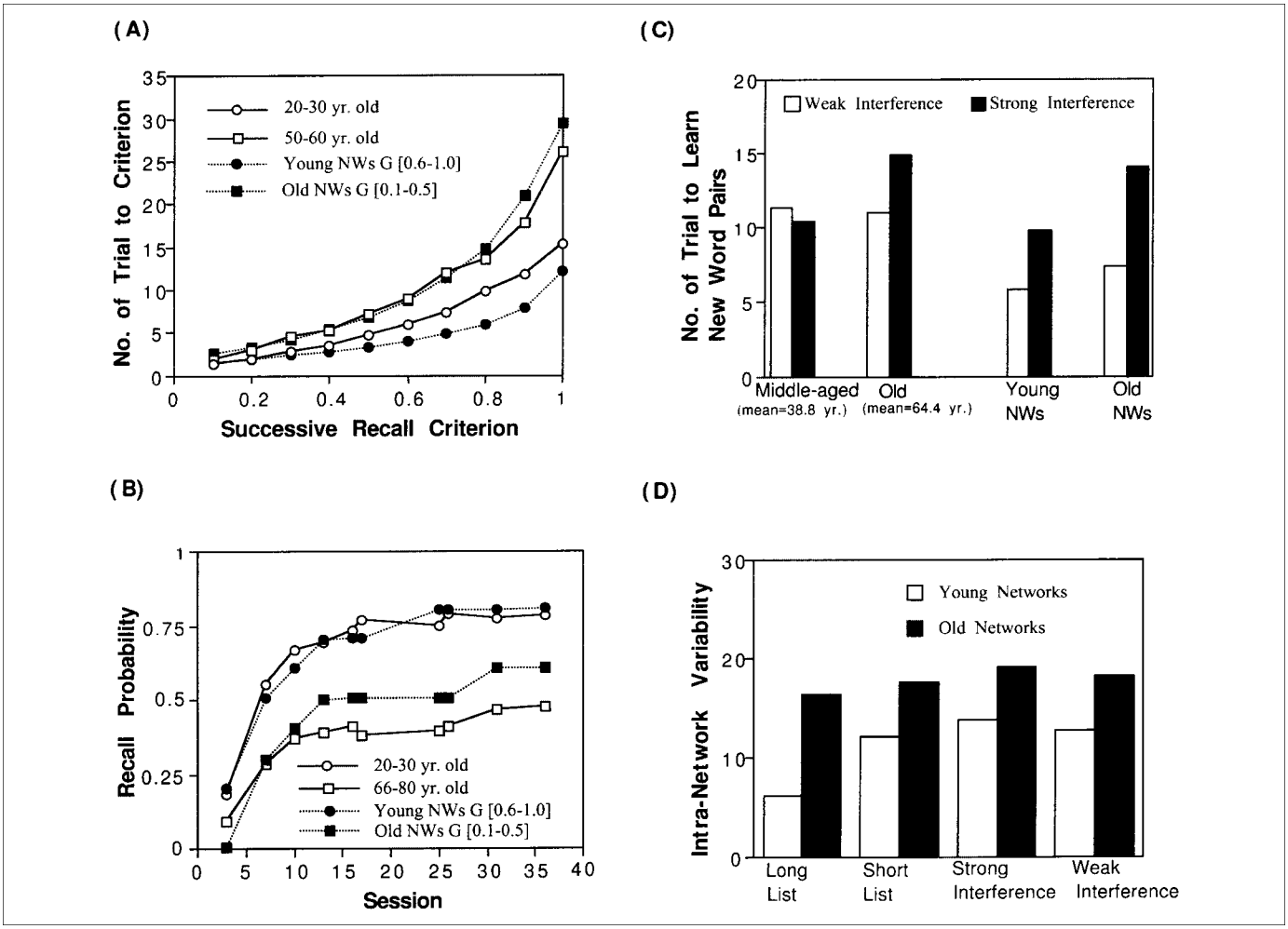

Fig. 2. Comparison of empirical data from human studies and neural network simulations of aging-related cognitive deficits. The graph in (a) shows the number of trials needed to reach increasingly stringent criteria in paired associate learning, for young and older adults and for networks (NWs) with the *G* parameter set to high and low values (the empirical results can be found in Monge, 1971). Asymptotic performance of young and old adults and networks in paired associate learning is illustrated in (b), which shows the number of training sessions required to reach maximum-possible recall performance (the empirical results can be found in Baltes & Kliegl, 1992). Aging-related increase in susceptibility to interference during paired associate learning is illustrated in (c), which shows performance under conditions of weak and strong interference (the empirical results can be found in Lair, Moon, & Kausler, 1969). The effect of reduction in mean *G* on intranetwork performance variability across different study lists in four conditions is shown in (d). Intranetwork variability is reported in units of coefficient of variance (i.e., standard deviation divided by the mean). (Reviews of aging-related increase in intraindividual variability can be found in Li & Lindenberger, 1999.) Adapted from "Unifying Cognitive Aging: From Neuromodulation to Representation to Cognition," by S.-C. Li, U. Lindenberger, and P.A. Frensch, 2000, *Neurocomputing*, *32–33*, pp. 884, 886. Copyright 2000 by Elsevier Science. Adapted with permission.

and interindividual diversity. Contrary to the traditional focus on average performance, this hypothesis motivates investigations of aging and intraindividual variability, an issue that is just now starting to be more broadly examined. Recent studies showed that intraindividual fluctuations in 60- to 80-year-olds' reaction times could be used to predict whether they had dementia (Hultsch, MacDonald, Hunter, Levy-Bencheton, & Strauss, 2000). In another study, fluctuations in 60- to 80-year-olds' gait and balance performance predicted verbal and spatial memory (Li, Aggen, Nesselroade, & Baltes, 2001). These results affirm that understanding aging-related performance variability and its sources may offer insight into aging-related changes in the brain-behavior link. At a different level, animal pharmacological studies could directly examine the effects of catecholamine agonists (drugs that facilitate the effects of catecholamines) on both intraindividual performance fluctuations and diversity

of performance across individuals. Questions about how a drug affects performance levels and intraindividual fluctuations are commonly examined. However, issues relating to diversity across individuals are more rarely systematically addressed because individual differences traditionally play little role in animal research, despite the fact that such diversity is often observed in clinical settings.

Recent neuroimaging evidence suggests that many aspects of cortical information processing that involve either the left or the right hemisphere separately in young adults become less differentiated and involve activation of both hemispheres as people age. For instance, in several studies, people in their 60s and beyond showed activity in both brain hemispheres during memory retrieval and during both verbal and spatial working memory tasks. In young adults, verbal memory is processed primarily by the left hemisphere, and spatial memory is processed by the right hemisphere (see Cabeza, in press, for a comprehensive review). The fact that attenuating the average values of the *G* parameter causes less distinctive internal representations indicates that aging-related reduction in the extent to which the two hemispheres deal separately with different processes might, in part, be related to neurochemical changes in the aging brain. This suggests a new line of inquiry into how neuromodulation of the distinctiveness of cortical representations might affect the distribution of information processing across different neural circuitry, in addition to affecting working memory, attention regulation, and processing speed. Finally, given catecholamines' involvement in developmental attentional disorders (see Arnsten, 1998), investigations of whether normal cognitive development in children might be conceived as an increase in the efficacy of neuromodulation and cortical representations could aid the search for unifying accounts of cognitive development and aging.

Recommended Reading

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Acknowledgments—With this review, I would like to commemorate Alan T. Welford (1914–1995), who more than four decades ago ventured to speculate about the neuronal-noise hypothesis. I thank the Max Planck Institute and Paul Baltes for sponsoring this research.

Note

1. Address correspondence to Shu-Chen Li, Max Planck Institute for Human Development, Lentzeallee 94, D-14195 Berlin, Germany; e-mail: shuchen@mpib-berlin.mpg.de.

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