CHAPTER

6

Research on Human Plasticity in Adulthood: A Lifespan Agenda

Simone Kühn[1] *and Ulman Lindenberger*[1,2]

[1]Center for Lifespan Psychology, Max Planck Institute for Human Development, Berlin, Germany
[2]Max Planck University College London Centre for Computational Psychiatry and Ageing Research, Berlin, Germany

OUTLINE

Plasticity and Stability in Lifespan Development 106

The Supply–Demand Mismatch Model of Plasticity 106

Proposition #1: Plasticity Decreases from Childhood to Old Age 108

Proposition #2: Flexibility Increases from Childhood to Middle Adulthood, and Declines Thereafter 112

Proposition #3: Relative to Childhood, Plasticity in Adulthood and Old Age is More Often Associated with Maintenance, and Less Often with Growth 113

Plasticity and Flexibility in Relation to *Gf*–*Gc* Theory 115

Open Questions and Future Research Directions 116

Investigating Age Differences in the Sequential Progression of Plasticity 116

Scrutinizing "Ribot's Law" and the "Dark Side of Plasticity" 117

Towards a Molecular Understanding of Plasticity Dynamics in Human Adults 118

References 119

K.W. Schaie & S.L. Willis (Eds)
Handbook of the Psychology of Aging, Eighth edition.

DOI: http://dx.doi.org/10.1016/B978-0-12-411469-2.00006-6

PLASTICITY AND STABILITY IN LIFESPAN DEVELOPMENT

For a long time, instances of *plasticity*, defined as long-lasting alterations in the brain's chemistry, gray matter, and structural connectivity in support of behavior, were assumed to be restricted to early periods of development. However, recent research has shown that plasticity is present throughout the lifespan, albeit to different degrees (Churchill et al., 2002; Hensch, 2005; Kempermann, 2006). Hence, the brain's potential for plasticity needs to be constantly held in check by mechanisms sustaining *stability* (Hensch, 2005). Recent research has begun to identify molecular mechanisms that promote either stability or plasticity. The dynamic interplay of these mechanisms organizes behavioral development into alternating, sequentially structured periods of plasticity and stability that permit the hierarchical organization of cerebral function and higher-order cognition. The canonical example is the sequence of sensitive periods that drives sensory and cognitive development from infancy to adolescence. According to Hensch (2005) and Takesian and Hensch (2013), plasticity in later periods of life, including adulthood and old age, is likely to be governed by similar molecular mechanisms as those regulating the opening and closing of sensitive periods during early ontogeny.

During periods of stability, behavior is far from immutable. In addition to plasticity, there is *flexibility*, defined as the adaptive reconfiguration of the existing behavioral repertoire in the absence of macroscopic structural change (cf. Lövdén, Bäckman, Lindenberger, Schaefer, & Schmiedek, 2010). At the behavioral level of analysis, the distinction between plasticity and flexibility can be traced back to Jean Piaget. In 1980, Piaget argued that cognitive development alternates between phases of structural change, in which new structures and relations are created, and phases of elaboration, in which the implications of these structures and relations are explored and instantiated.

In summary, the evolving brain strikes a balance between plasticity and stability that supports the construction, modification, and maintenance of behavioral repertoires from early ontogeny to late adulthood. We assume that the set point of the plasticity/stability equilibrium follows an overall lifespan trend from a greater relative emphasis on plasticity to a greater relative emphasis on stability. In particular, and for reasons outlined below, the transition from childhood to adulthood results in a strengthening of mechanisms that actively suppress plasticity and promote stability.

THE SUPPLY–DEMAND MISMATCH MODEL OF PLASTICITY

Lövdén, Bäckman et al. (2010) proposed the economic metaphor of neural supplies and experiential demands to further clarify the difference between plasticity and flexibility (Figure 6.1). Whereas flexibility *makes use* of existing neural supplies, plasticity *changes* them. According to Lövdén, Bäckman et al. (2010), it would be functionally maladaptive and metabolically costly if a system would always and instantaneously respond to supply–demand mismatches with plastic (structural) changes, rather than with the utilization of the range of function supported by flexibility. A central nervous system under permanent renovation would not develop a coordinated scheme of habits and skills, and would constantly consume large amounts of energy. Hence, the supply–demand mismatch has to surpass some degree of intensity to trade the goal of stability for that of plasticity. The degree of sluggishness of plastic responses to mismatch differs among various manifestations of plasticity, probably in part as a function of the metabolic cost of their implementation. For example, whereas gliogenesis and growth of capillaries may develop over

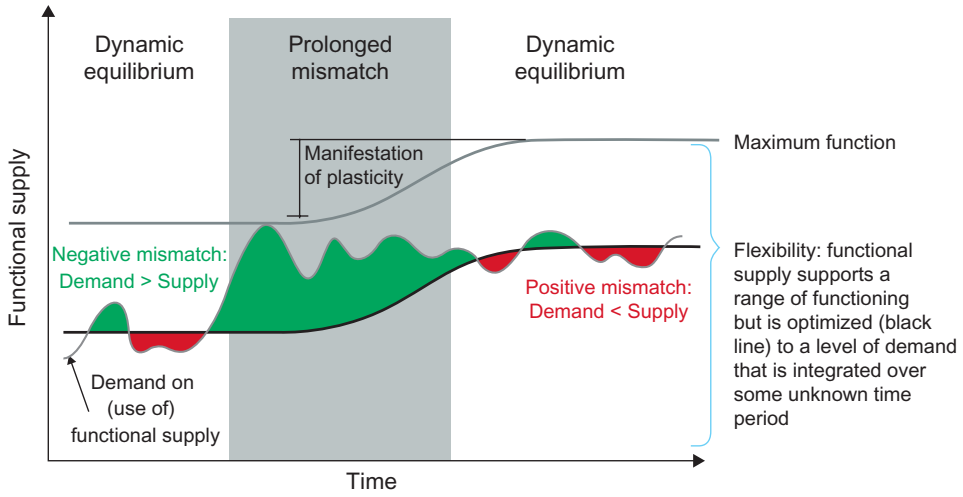

FIGURE 6.1 *The supply–demand mismatch model of plasticity*. The mismatch between functional supply and experienced environmental demands can be caused by primary changes in demand (shown here), or by primary changes in functional supply (not shown). *Functional supply* denotes structural constraints imposed by the brain on function and performance, and permits a given range of performance and functioning. *Flexibility* denotes the capacity to optimize the brain's performance within this range. Deviations in *functional demand* that are within the available range of functional supply constitute the impetus for plasticity. Mismatches between supply and demand need to be present for some period of time to overcome the system's tendency towards stability (sluggishness), and to push the system away from its current dynamic equilibrium. *Adapted from Lövdén, Bäckman et al. (2010).*

months, synaptogenesis and structural changes associated with long-term potentiation (LTP) may develop over hours, minutes, or seconds.

How does the sluggishness of plastic responses change from early ontogeny to adulthood? In the course of their lives, adults have acquired a rich model of the world that enables the flexible deployment of established behavioral repertoires. For this reason alone, the number of situations requiring a plastic response is likely to decrease with advancing adult age. In addition, putting a premium on stability also favors continuity of social structures, which in turn may facilitate the deployment of plastic potential in the next generation (cf. Lindenberger, 2014). Finally, bringing about plastic changes is metabolically costly (Kuzawa et al., 2014), and these costs are likely to be exacerbated in systems that have accumulated damage, reflecting evolved limitations in somatic maintenance, as is the case for brains in later adulthood. Primarily for these reasons, we assume that the brains of older adults are both less able and less in need of reaction to a supply–demand mismatch with a plastic response, relative to the brains of normally developing children and adolescents.

The preceding considerations motivate a set of three propositions, which we elaborate on in the remainder of this chapter:

1. *Plasticity decreases from childhood to old age.*
2. *Flexibility increases from childhood to middle adulthood, and declines thereafter.*
3. *Relative to childhood, plasticity in adulthood and old age is more associated with maintenance, and less with growth.*

Figure 6.2 illustrates these propositions. In the following, we will expand on them, with empirical examples drawn primarily from cognitive intervention studies and animal models. We then compare the

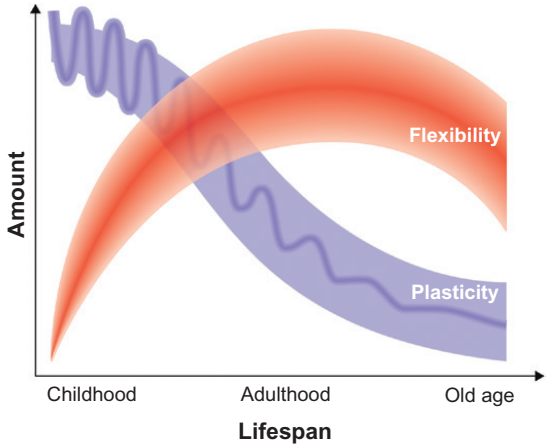

FIGURE 6.2 *Plasticity and flexibility across the lifespan.* Plasticity refers to long-lasting alterations in the brain's chemistry, gray matter, and structural connectivity in support of behavior. Flexibility denotes the capacity to optimize performance within the limits of the current functional supply. The dynamic interplay of mechanisms promoting plasticity versus stability, illustrated by the oscillating pattern of the plasticity trajectory, organizes behavioral development into alternating, sequentially structured periods that permit the hierarchical organization of cerebral function and higher-order cognition. The range of the functions at any given age denotes between-person differences and within-person modifiability.

stability–flexibility–plasticity framework to the theory of crystallized versus fluid intelligence (*Gf–Gc theory*; Cattell, 1971; Horn, 1989), and conclude by suggesting avenues for future research.

PROPOSITION #1: PLASTICITY DECREASES FROM CHILDHOOD TO OLD AGE

Early in life, children's brains are highly malleable by experience, both inside and outside the uterus (Karmiloff-Smith, 1995). In the mid-1900s, it was discovered that depriving an organism of certain experiences at an early age compromises brain function later on. In a seminal series of studies on kittens, Hubel and Wiesel (1959) surgically closed one of their eyes soon after birth. When the deprived eye was reopened a few months later, it appeared normal, but most of the nerve cells in the visual cortex no longer responded to visual input from that eye. These findings demonstrate the importance of sensitive periods, defined as developmental windows in which experience has a particularly strong effect on brain structure. Mice show similar responses to visual deprivation. The discovery of sensitive periods has led to the quest for the factors that influence their opening and closure. In particular, the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) has been found to be involved in the onset of sensitive periods (Hensch, 2005).

Both the initial overproduction of synapses and the subsequent stimulus-dependent pruning of dendritic arborization are thought to play a key role in cortical ontogeny. Early neural plasticity does not happen synchronously in all brain regions, but rather progresses like a "wave," beginning in primary sensory and motor regions and subsequently moving towards secondary association areas, parietal cortex, and finally to frontal brain regions. To explore this progression computationally, Shrager and Johnson (1996) modeled a simplified cortical array, and showed that a corticotrophic wave, in combination with a pruning mechanism, results in cortical structures with hierarchically organized representations. The model nicely illustrates that temporally and spatially structured periods of plasticity facilitate the emergence of hierarchical brain organization. The simulation provides a compelling reason why brain development within and across sensory modalities does not consist of one single period of generalized plasticity, but of an orderly sequence of sensitive periods.

Neural and behavioral evidence clearly indicates that plasticity declines with age. One kind of behavioral evidence in humans is provided by training studies, in which children, younger adults, and older adults practice the

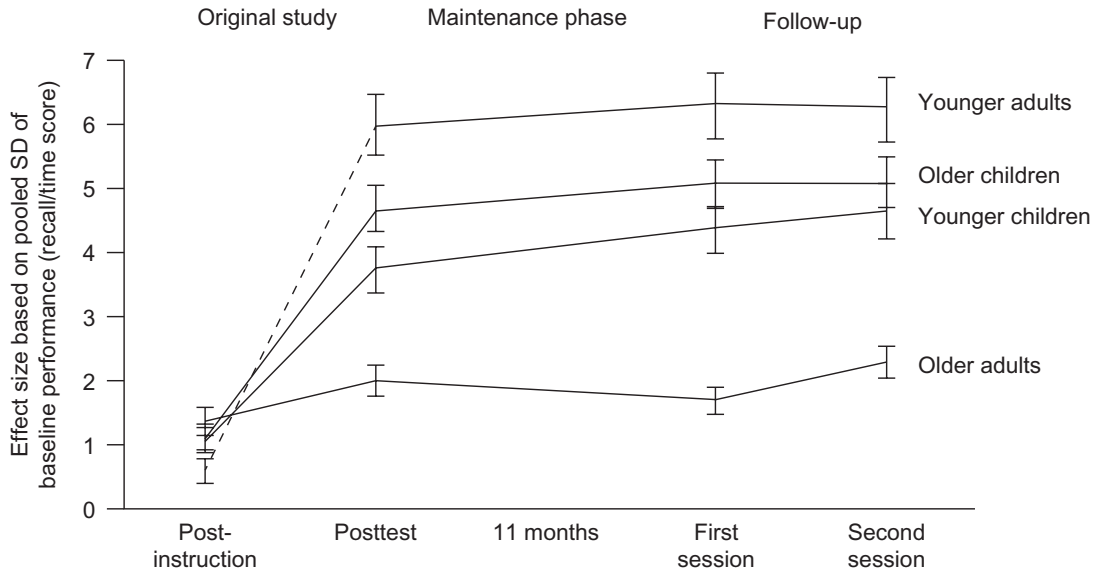

FIGURE 6.3 *Plasticity in memory performance across the lifespan.* The left part of the figure summarizes the results of a training study by Brehmer et al. (2007), whereas the right part summarizes the results of a follow-up study conducted 11 months later (Brehmer et al., 2008). In line with the trajectories shown in Figure 6.2, children profited more from mnemonic practice and reached higher levels of performance at the end of training. Younger and older adults' average performance levels were stable across the 11-month no-contact interval. In contrast, children's memory performance improved beyond originally attained levels, presumably reflecting maturational changes in the brain's functional supply. Levels of memory performance refer to the number of words recalled over log encoding times (recall/time scores) and are expressed in pooled pretest standard deviation units. For younger adults (dashed line), the post-instruction scores of the training study cannot be interpreted because of ceiling effects; all other scores are interpretable. Error bars indicate standard errors of the mean.

same cognitive skill (Shing & Lindenberger, 2011). For instance, Brehmer, Li, Müller, von Oertzen, and Lindenberger (2007) and Brehmer et al. (2008) asked participants of different ages to acquire and practice an imagery-based memory technique. Children benefited more from the intervention and reached higher levels of asymptotic performance than older adults (Brehmer et al., 2007), reflecting the reduction of plastic potential in older age. Younger and older adults' performance levels were found to be stable in a follow-up session after 11 months (Brehmer et al., 2008), suggesting that the ability to maintain acquired skills is relatively well preserved in adulthood. In contrast, children even improved their performance from posttest to follow-up session, presumably because task-relevant brain structure had matured in the meantime (Figure 6.3).

Another observation from Brehmer et al. (2007) is that younger adults showed larger performance gains than children, suggesting, at first sight, that plasticity is greater in early adulthood than in childhood. In our view, this observation points to the general difficulty of disentangling plasticity and flexibility at the behavioral level of analysis (see section on plasticity and flexibility in relation to *Gf–Gc* theory). Given the expansion of the behavioral repertoire from childhood to adulthood, the acquisition of a new mnemonic skill may depend less upon plasticity with increasing age, and more on the reconfiguration of already-existing strategies and skills. This hypothetical difference in

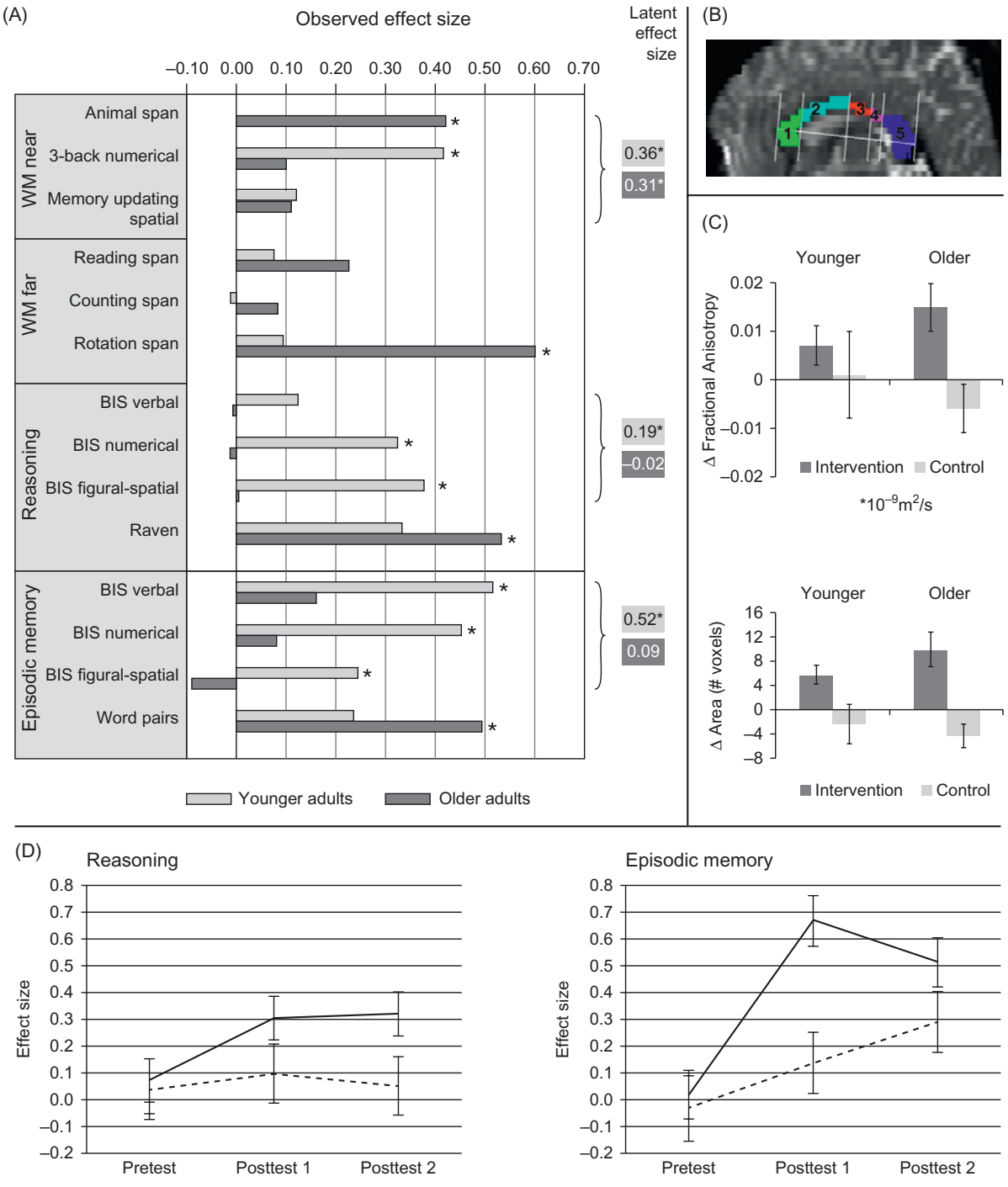

FIGURE 6.4 *Plasticity of intellectual abilities in younger and older adults.* In the COGITO study (Schmiedek et al., 2010), 101 younger and 103 older adults practiced six tests of perceptual speed, three tests of working memory, and three tests of episodic memory over a period of 6 months for 101 daily 1-h sessions. Unpracticed cognitive tests were administered before and after training to examine whether performance improvements generalize to the level of cognitive abilities (transfer).

the relative importance of plasticity and flexibility in the production of training gains would lead one to predict that transfer of training, as an indicator of plasticity, would be more prominent in children than in adults. To our knowledge, this prediction has not yet been tested directly.

Other studies have focused on age differences in plasticity within the adult age range (for a review, see Lövdén, Wenger, Mårtensson, Lindenberger, & Bäckman, 2013). In one very extensive training study (Schmiedek, Lövdén, & Lindenberger, 2010), older and younger adults practiced three working memory, three episodic memory, and six perceptual speed tasks for 100 1-h sessions (Figure 6.4). Immediately after training, both older and younger adults showed near transfer of training to working memory, and younger adults showed additional transfer to episodic memory and reasoning. Neural data obtained for subsamples of younger and older adults revealed an increase in white matter integrity in the genu of the corpus callosum in both younger and older adults (Lövdén, Bodammer, & Kühn, 2010). In younger adults, transfer effects in reasoning and episodic memory were maintained over a period of 2 years (Schmiedek, Lövdén, & Lindenberger, 2014).

Among the various regions of the brain, the hippocampus is both particularly plastic and vulnerable to risk factors (Raz, 2007). While hippocampal neurogenesis persists throughout adulthood, animal data indicate that the rate at which new neurons are generated dramatically declines with increasing age (Bizon & Gallagher, 2003; Kuhn, Dickinson-Anson, & Gage, 1996; Lee, Clemenson, & Gage, 2012). Older animals show significantly less neural progenitor proliferation, neuronal differentiation, and neural survival than younger animals (Ben Abdallah et al., 2010; Heine, Maslam, Joëls, & Lucassen, 2004). In mice, the age-related decline of neural progenitor cells begins at 1–2 months of age and progressively decreases each month thereafter, until it is barely present in aged mice (Bondolfi, Ermini, Long, Ingram, & Jucker, 2004).

Animal evidence from post-lesion plasticity after stroke shows that the expression pattern of growth-promoting genes parallels the evolution of neuritic sprouting. In contrast, in aged animals, the expression of such genes is dampened or delayed, which may account for the age-dependent decline in compensatory responses (Li et al., 2010). Several growth inhibitors are up-regulated after stroke in the aged brain, but not in the juvenile brain (Li & Carmichael, 2006). These findings fit well to the assumption that the brain strikes a balance between plasticity and stability. During the transition from childhood to adulthood, the set point of equilibrium is shifting away from plasticity towards stability, presumably reflecting the operation of molecular mechanisms that actively suppress plasticity.

FIGURE 6.4 (Continued) (A) Effect sizes (ES; standardized changes in the experimental group minus standardized changes in the control group), separately for younger adults (gray bars) and older adults (black bars). Statistically significant ES correspond to reliable interactions (*P<0.05) between group (experimental vs. control) and occasion (pretest vs. posttest). Observed ES refer to individual tests, latent ES to cognitive abilities estimated with structural equation modeling. At the level of cognitive abilities, younger and older adults show transfer of training to working memory (WM); in addition, younger adults also show transfer to reasoning and episodic memory. (B) A midsagittal slice of a mean diffusivity data set, with the corpus callosum segmented into five different regions. The first region refers to the genu, which connects the prefrontal cortices. (C) Changes in fractional anisotropy and area of the genu assessed in subsamples of younger and older COGITO participants. Changes differ reliably between intervention and control groups, but not by adult age (Lövdén, Bodammer et al., 2010). (D) Younger adults maintain transfer of training effects in reasoning and episodic memory over 2 years (Schmiedek et al., 2014).

The age-related average decrease in plasticity takes place in the presence of sizeable individual differences in plasticity at any given age, and these differences seem to increase rather than decrease with advancing age. Individual differences in older rats' ability to learn novel information are a particularly striking example. Some older animals' capacity to learn is just as great as that of younger animals (Bizon & Gallagher, 2003; Bizon, Lee, & Gallagher, 2004). Likewise, Kempermann and colleagues have repeatedly shown that enriched environments promote neurogenesis and learning in mice (Kempermann, Kuhn, & Gage, 1997), and enhance individual differences in plasticity (Freund et al., 2013; see also Bergmann & Frisén, 2013).

PROPOSITION #2: FLEXIBILITY INCREASES FROM CHILDHOOD TO MIDDLE ADULTHOOD, AND DECLINES THEREAFTER

As noted above, flexibility differs from plasticity, and denotes individuals' use of their currently available brain resources, or their "functional cerebral space" (Kinsbourne & Hicks, 1978). The available evidence indicates that flexibility increases from childhood to middle adulthood, reflecting the vast increase in knowledge, habits, and skills, but gradually declines during later stages of life, due to senescent changes in the brain's chemistry, anatomy, and function (for a summary, see Lindenberger, 2014). This decline is likely to occur for at least two reasons. First, the behavioral repertoire itself is shrinking (selection), reflecting the decline in functional supply associated with normal aging (for a summary, see Lindenberger, 2014); second, the goal-directed, top-down implementation of the remaining set of behaviorally relevant brain states becomes increasingly inefficient (Lindenberger & Mayr, 2014). For instance, adaptively switching from one task set to another becomes increasingly difficult with advancing age, presumably as a reflection of senescent changes in prefrontal circuitry and dopaminergic neuromodulation (Gazzaley, 2013).

In addition to the sheer size of the behavioral repertoire, which corresponds to the brain's functional supply, flexibility is aided by cognitive control, or the ability to adaptively switch among different task sets (Mayr, Kuhns, & Hubbard, 2014). Cognitive control increases from childhood onwards, and declines in the course of normal aging (De Luca et al., 2003). Confirmatory factor analyses suggest that the structure of executive functions progresses from unity to diversity during middle childhood and adolescence, indicating a higher differentiation over the course of development (Shing, Lindenberger, Diamond, Li, & Davidson, 2010; Span, Ridderinkhof, & van der Molen, 2004; F. Xu et al., 2013). Global switch costs, which reflect the load associated with working on more than one task set, are more pronounced in older adults than in younger adults (Kray & Lindenberger, 2000; Verhaeghen & Cerella, 2002; Wasylyshyn, Verhaeghen, & Sliwinski, 2011). Global switch costs are typically derived by comparing reaction times in single-task blocks with blocks of trials that contain two or more tasks. In line with pronounced adult age differences in global switch costs, performance in dual-task situations, where two tasks have to be accomplished in parallel, also show pronounced adult age differences (Verhaeghen & Cerella, 2002).

Lindenberger and Mayr (2014) have recently suggested that older adults rely more strongly on environmental external information than younger adults do, in part because they have difficulties in internally triggering and maintaining cognitive representations. Similar accounts have previously been proposed in the domain of memory. It has been shown that adult age differences in memory performance tend to be exacerbated when retrieval depends

on self-generated cues, whereas age differences are smaller when retrieval cues are provided by the environment (Craik, 1983, 2006).

The decline of task switching and dual-tasking as well as the increased reliance on environmental support with advancing age support the claim that flexibility declines during later periods of adulthood because the cognitive system is gradually losing cognitive, "top-down" control, or the capability to impose its goal structure upon a complex or distracting environment. For instance, Passow et al. (2012) examined adult age differences in the interplay between perceptual saliency and attentional control over auditory processing in a dichotic listening task. Perceptual saliency was manipulated by decreasing the intensity of either the right- or the left-ear input in 5-dB steps until a maximum difference of 20 dB between ears was reached. The 0-dB difference condition served as the baseline intensity and was adapted to each participant's individual hearing threshold. Twelve different dichotic syllable pairs were presented twice for each of the nine interaural intensity conditions. Attentional focus was manipulated by instructing the participants to focus on the right ear, on the left ear, or on both ears (neutral focus). When the stimulus of the attended ear is louder, then attention is facilitated by saliency; however, when the stimulus of the attended ear is softer, then attention has to overcome the saliency advantage of stimuli presented to the unattended ear. Across all interaural intensity conditions, younger adults were capable of flexibly focusing their attention on auditory inputs from either the right or left ear (see Figure 6.5A). In stark contrast to younger adults, the performance of older adults was driven almost exclusively by perceptual saliency, with attentional focus having little effect on performance (see Figure 6.5B).

Cognitive control has been linked to the integrity of the prefrontal cortex (Alvarez & Emory, 2006), and a recent meta-analysis has reported an association between executive task performance and volume of the prefrontal cortex, showing that "bigger is better" (Yuan & Raz, 2014). The prefrontal cortex is known to be among one of the last brain regions to mature during childhood (Giedd et al., 1999) and to substantially decline as humans reach older ages (Raz, 2000). Hence, the aspect of flexibility related to the pliable and goal-adequate use of existing knowledge, skills, and habits, rather than to their sheer amount, may closely follow the ontogenetic trajectory of prefrontal areas.

Senescent changes in cognitive control among animals seem to resemble those of humans. For instance, aged rats show decrements in a set-shifting task performance as compared to young rats (Beas, Setlow, & Bizon, 2013). Interestingly, the variability among older rats was considerably higher than the variability among younger rats, and some of the older rats performed at the level of the young. Relative to young monkeys, aged monkeys are impaired in learning a set-shifting task, and show a greater number of perseverative responses (Moore, Killiany, Herndon, Rosene, & Moss, 2003). Perseverative behavior has also been observed in aged mice in cases in which they are required to overcome a previously learned response (Matzel et al., 2011). The latter study also showed that the observed impairments in flexibility are not entirely immutable, as the older mice seemed to benefit from a cognitive exercise regimen.

PROPOSITION #3: RELATIVE TO CHILDHOOD, PLASTICITY IN ADULTHOOD AND OLD AGE IS MORE OFTEN ASSOCIATED WITH MAINTENANCE, AND LESS OFTEN WITH GROWTH

Several studies have found that the brains of older adults show fewer signs of growth in response to an intervention than the brains of younger adults. In a juggling training

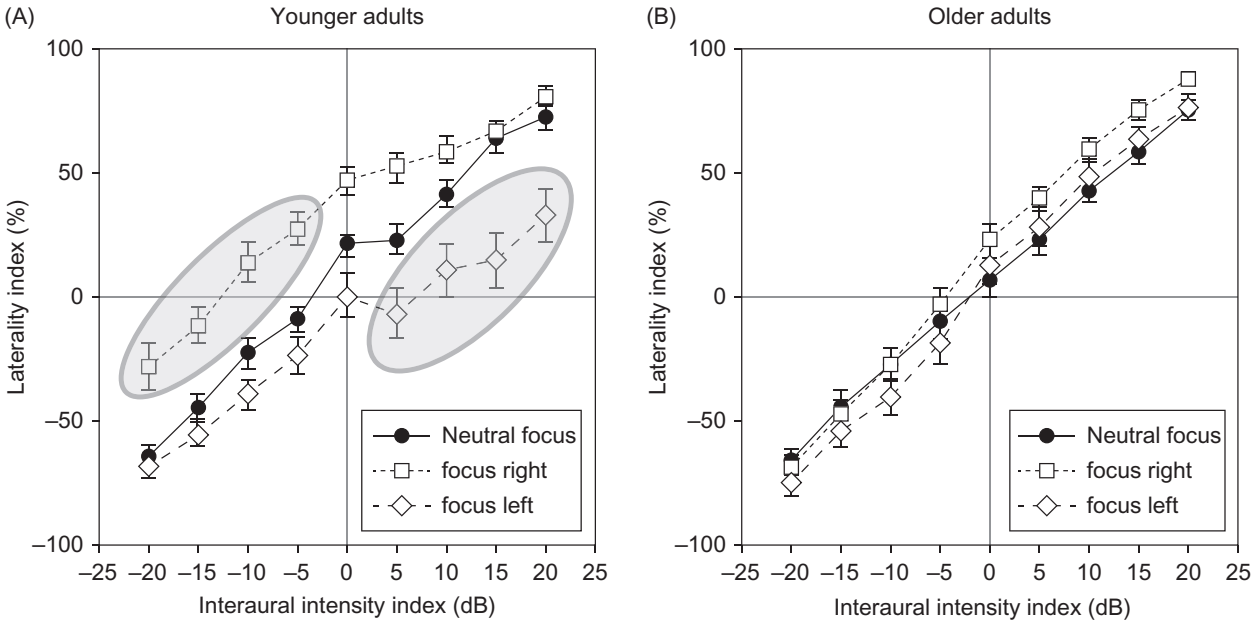

FIGURE 6.5 *Adult age differences in flexibility.* In a dichotic listening task, Passow et al. (2012) presented participants with dichotic pairs of voiced versus unvoiced syllables (e.g., /ba/ vs. /pa/), and asked them to report the syllable they heard. Perceptual saliency, shown on the *X*-axis, was manipulated by decreasing the intensity of either the right- or the left-ear input in 5-dB steps until a maximum difference of 20 dB between ears was reached. Negative values represent conditions in which left-ear stimuli were louder than right-ear stimuli, and positive values represent conditions in which right-ear stimuli were louder than left-ear stimuli. Attentional focus was manipulated by instructing participants to focus on the right ear, on the left ear, or on both ears (neutral focus). Reports are quantified by the laterality index, shown on the *Y*-axis, which expresses the amount of right-ear reports in relation to left-ear reports (i.e., [(right ear − left ear)/(right ear + left ear)] × 100). The laterality index ranges from −100% to +100%, with positive values indicating a right-ear advantage, and negative values indicating a left-ear advantage. When the stimulus of the attended ear is louder, then attention is facilitated by saliency; when the stimulus of the attended ear is softer, then the saliency advantage of the stimuli presented to the unattended ear has to be overcome by top-down attentional control. In contrast to younger adults (A), who were capable of flexibly focusing their attention on auditory inputs from either the right or left ear, performance in older adults was driven almost exclusively by perceptual saliency (B). In particular, the distance between the data highlighted and the data point from the neutral-focus condition underscore younger adults' ability to use top-down modulation to overcome conflicts between perceptual saliency and attentional focus; the overlap between the corresponding conditions among older adults indicates that this ability is severely impaired in old age. *Figure adapted from Passow et al. (2012) with permission.*

study (Boyke, Driemeyer, Gaser, Büchel, & May, 2008), older adults showed training-induced gray-matter increases in task-related brain regions, but these changes were less pronounced than those found in younger adults (Draganski et al., 2004). Lövdén et al. (2012) found that spatial navigation training was associated with maintenance of hippocampal volumes in both younger and older adults relative to younger and older adults in the control group, who showed age-related volume shrinkage. However, reliable training-induced increases in cortical thickness of the precuneus and the paracentral lobule were restricted to the group of younger adults (Wenger et al., 2012).

In line with general tenets of lifespan psychology (Baltes, 1987; Baltes, Lindenberger, & Staudinger, 2006), these findings mandate an age-comparative look at neural and behavioral

manifestations of plasticity in adulthood. In adulthood, and especially in old age, the positive effects of cognitive interventions on cognitive development may not exclusively, and perhaps not even primarily, consist in growing new tissue, or acquiring new skills. Instead, such interventions may trigger positive deviations from the modal path of cognitive aging by preventing the structural, functional, and behavioral decline that would have occurred otherwise. In this vein, Nyberg, Lövdén, Riklund, Lindenberger, and Bäckman (2012) as well as Lindenberger, Burzynska, and Nagel (2013) have proposed that the *maintenance* of brain structure and function over time may function as a key meta-mechanism of successful cognitive aging. From this point of view, effective cognitive interventions may preserve the volume of relevant brain areas during a time period in which non-trained individuals show reductions in volume.

In animals, age-related synapse loss has been shown to be reversible, for instance, in response to the administration of nicotine (Picciotto & Zoli, 2002) or estrogen (Morrison, Brinton, Schmidt & Gore, 2006), and in response to neurotrophin gene transfer in rhesus monkeys (Smith, Roberts, Gage & Tuszynski, 1999). Similarly, environmental enrichment (Darmopil, Petanjek, Mohammed, & Bogdanović, 2009) and exercise have been shown to attenuate neural and behavioral losses in older animals (Kempermann, 2008; Kronenberg et al., 2006).

PLASTICITY AND FLEXIBILITY IN RELATION TO *GF–GC* THEORY

It is instructive to compare the postulated lifespan gradients of plasticity and flexibility, as shown in Figure 6.2, with the gradients postulated by existing two-component theories of cognitive lifespan development (Baltes, 1987; Cattell, 1971; Horn, 1989; for a summary, see Lindenberger, 2001). These theories make two basic assumptions. First, they posit that cognitive development across the lifespan reflects the operation of two intertwined components, one biological and the other cultural. The biological component is construed as an expression of the neurophysiological architecture of the mind as it evolved during biological evolution and unfolds during ontogeny. The cultural component refers to bodies of knowledge available from and mediated through culture. Second, potential related to the biological component is *invested into* various cultural domains, thereby leading to the acquisition of culturally transmitted bodies of knowledge. A good example is the acquisition of reading and writing skills. Hence, at any point in time during development, two types of cognitive capacities can be distinguished: the capacity to invest (i.e., to acquire new knowledge of various sorts); and the capacity to think and act on the basis of acquired knowledge.

Arguably the most influential two-component theory of cognitive lifespan development is the theory of *fluid* versus *crystallized* intelligence (*Gf–Gc* theory) introduced by Raymond B. Cattell (Cattell, 1971) and modified by John Horn (Horn, 1989). Fluid intelligence represents the biological component; it is called fluid because it can be invested into various cultural domains. In contrast, crystallized intelligence represents the cultural component; it is called crystallized because it has solidified into knowledge.

In light of these assumptions, one may gain the impression that the *Gf–Gc* distinction is virtually identical to the distinction between plasticity and flexibility proposed in this chapter. And, indeed, the hypothesized lifespan trajectories for flexibility and *Gc* are identical (Figure 6.2). However, the trajectories for plasticity and *Gf* deviate from each other: whereas overall plasticity, on average, is assumed to decline across the lifespan, *Gf* shows a sharp increase up to late adolescence and early adulthood, followed by accelerated decline during adulthood

and old age. In fact, the trajectories postulated by *Gf–Gc* theory summarize a vast amount of psychometric evidence obtained through standardized behavioral testing and factor analysis (Jones & Conrad, 1933). Abilities subsumed under *Gf*, such as reasoning, memory, spatial orientation, and perceptual speed, generally show a sharp increase in childhood and adolescence, followed by roughly linear decline during adulthood, and accelerated decline in very old age. In contrast, abilities subsumed under *Gc*, such as verbal knowledge and certain facets of numerical ability, remain stable or increase up to the sixth or seventh decades of life, and evince some decline in advanced old age.

In our view, the discrepancy between plasticity and *Gf* points to the hybrid nature of measured *Gf*. In contrast to theoretical assumptions, the empirical indicators used to assess *Gf* are not, as postulated, a pure expression of biological potential; if they were, the lifespan trajectory for *Gf* would, in fact, coincide with the trajectory postulated for plasticity. Instead, indicators of *Gf* represent a mixture of plastic potential and flexibility (e.g., invested plasticity), and this hybrid nature of *Gf* places its trajectory in an intermediate position between plasticity and flexibility. This reinterpretation of *Gf* helps to explain the massive performance gains on IQ tests across historical time, also known as the "Flynn effect" (Flynn, 1987). This gain is more likely to reflect secular changes in the realization of plastic potential, or gene–environment correlations, than changes in the potential itself (for a similar line of reasoning, see Beam & Turkheimer, 2013; Dickens & Flynn, 2001).

OPEN QUESTIONS AND FUTURE RESEARCH DIRECTIONS

We end this chapter by highlighting three open research questions, and suggesting future directions in the study of human adult plasticity.

Investigating Age Differences in the Sequential Progression of Plasticity

Developmental findings, animal models, and conceptual considerations indicate that plasticity-induced gray matter changes take an inverse quadratic course (Lövdén et al., 2013). For example, in-vivo microscopic imaging of dendritic spines in mice reveals new spines after a few hours of motor training in mice (T. Xu et al., 2009), which is followed by selective stabilization of new and partial elimination of old spines (see Fu & Zuo, 2011, for review). Learning-related cortical map expansion has also been shown to occur quite rapidly, such as within a few days, and then renormalize during further training despite stable performance (Molina-Luna, Hertler, Buitrago, & Luft, 2008; Reed et al., 2011). It has been proposed that an initial "overshoot" may increase the pool of neural resources from which the most efficient wiring can then be selected (Reed et al., 2011). At an ontogenetic timescale, Changeux and Dehaene have suggested that brain plasticity during early ontogeny goes through cycles that are marked by an initial increase in the number of synapses followed by experience-dependent selective stabilization of behaviorally relevant connections (Changeux & Dehaene, 1989; see also Edelman, 1987). Based on these findings and concepts, Lövdén et al. (2013) recently proposed that expansion followed by partial renormalization may be a common principle that unites different manifestations of plasticity.

From a design perspective, one may argue that an expansion–renormalization process is presumably a more efficient way for the brain to reorganize and adjust than a constant growth process. In stark contrast to this conjecture, available evidence on macroscopic manifestations of plasticity in humans is generally restricted to pretest–posttest designs, with one scan taken before and another taken after the termination of the intervention. Such designs do not discriminate between monotonic and

non-monotonic manifestations of plasticity. In a recent study, Wenger et al. (submitted) acquired up to 16 magnetic resonance images during a 7-week period in which 15 right-handed young men practiced left-hand writing and drawing. After 4 weeks of training, the authors observed increases in gray matter of both left and right primary motor cortices relative to a control group; 3 weeks later, these differences were no longer reliable. Gray matter in the primary motor cortices expanded during the first 4 weeks, and then partially renormalized, in particular in the right hemisphere, despite continued practice and further performance improvements. Based on these promising findings, it seems highly desirable to compare the time course of intervention-induced plastic changes across different age groups to gain a more dynamic view of age-graded changes in plasticity.

Scrutinizing "Ribot's Law" and the "Dark Side of Plasticity"

For a long time, researchers have speculated that senescent changes in the mammalian brain late in life are a mirror-image of maturational changes early in life. The general idea was introduced by the French philosopher Théodule Ribot, who noted that episodic memory loss in old age progresses from newly acquired memories to older memories (Ribot, 1881). Transferring this observation to the neural level of analysis, Ribot postulated that senescent brain changes would follow the reverse order of maturational changes during development. According to this hypothesis, brain regions that would develop late—during ontogeny and possibly also during phylogeny—would be those that degenerate early (Hill et al., 2010), following a "last in, first out" rule (Raz, 2000).

In line with Ribot's law, Raz (2000) noted that regional differences in volume shrinkage are inversely related to the order in which intracortical fibers of different brain regions myelinate during early ontogeny. Using lifespan cross-sectional data and VBM-based analyses, Douaud et al. (2014) recently reported a set of brain regions that show signs of late maturation and early senescence in an inverted-U-shape relationship between structural variation and age. The regions following this mirror-image pattern were transmodal regions including heteromodal cortex as well as limbic and paralimbic regions; in particular, lateral prefrontal cortex, frontal eye field, intraparietal sulcus, superior temporal sulcus, posterior cingulate cortex, and the medial temporal lobe. Based on separate analyses, the authors discovered that the very same brain regions that matured late and senesced early also showed a heightened vulnerability to clinical disorders such as schizophrenia and Alzheimer's disease.

Based on the notion that ontogeny is characterized by temporally ordered, hierarchically nested cycles of plasticity (Shrager & Johnson, 1996), one may speculate whether late-maturing brain regions are more susceptible to the detrimental effects of aging exactly because their construction and operation builds on earlier cycles of plasticity. In this context, it is interesting to note that brain regions with greater plastic potential in adulthood tend to show greater age-related decline, and to be particularly vulnerable to vascular and metabolic risk factors. One such region is the hippocampus, which is critically involved in spatial orientation, and in many forms of learning and memory. The hippocampus is both particularly plastic and highly susceptible to risk factors such as stress, vascular conditions, and metabolic syndrome, suggesting that plasticity comes at a price (Raz, 2001, 2007).

To further explore the association between regional differences in plasticity and regional differences in age-related decline, we conducted a quantitative meta-analysis, using methods that are described in detailed in Eickhoff et al. (2009). The meta-analysis was based on 27 studies for which training-induced

gray matter changes have been observed (Lövdén et al., 2013). Despite large variation in the skills that were trained, we observed considerable concordance across studies in right occipital cortex (27, −84, −3), left precentral gyrus (−37, −21, 58), left cerebellum (−27, −41, −46), right cuneus (19, −84, 28), right postcentral gyrus (41, −27, 39), left inferior parietal lobe (−54, −32, 27), left parahippocampal gyrus (−17, −10, −16), left superior frontal gyrus (−22, 52, 20), right thalamus (23, −38, 8), right superior temporal gyrus (58, 6, −12) and left insula (−42, −8, 16) ($P<0.05$ FDR corrected, cluster > 200 mm^3). Age-related atrophy of brain areas has consistently been reported for prefrontal cortex, insula, caudate nucleus, thalamus, and sensorimotor cortex in a meta-analysis (Di, Rypma, & Biswal, 2014) as well as hippocampus, cerebellum, and parietal cortex (Raz, 2004; Raz, Ghisletta, Rodrigue, Kennedy, & Lindenberger, 2010). When focusing on the overlap between the two sets of brain regions, 8 of the 11 brain areas showing structural plasticity across training studies were located within brain regions that have been reported to show pronounced age-related decline in volume. If this association between plasticity and vulnerability holds true, it would call for interventions that target brain regions showing large, rather than little, age-related decline (Raz, 2009).

In this context, the issue of excessive plasticity needs to be addressed as well. There are indications that plasticity can disrupt neural representations and behavior. A particularly compelling case is focal dystonia, a neurological condition associated with involuntary muscular contractions in particular parts of the body. Focal dystonia is commonly characterized by prevailing facilitation of synaptic potentiation, and a loss of synaptic inhibitory processes (Quartarone & Pisani, 2011). Accordingly, highly trained musicians are disproportionately affected by focal dystonia (Altenmüller & Jabusch, 2010). Though the motto, "use it or lose it," aptly summarizes the positive association between active lifestyles and cognitive functioning in old age (Hertzog, Kramer, Wilson, & Lindenberger, 2008), focal dystonia and related conditions remind us that plasticity itself may be a risk factor for behavioral development.

Towards a Molecular Understanding of Plasticity Dynamics in Human Adults

Human ontogeny is structured by a progressive sequence of sensitive periods (Michel & Tyler, 2005). These periods are not confined to basic aspects of sensory development but extend to higher-order cognitive functions, such as language (Werker & Tees, 2005) and music (Bailey & Penhune, 2012; Penhune, 2011). Inhibitory GABA neural circuits have been identified as drivers of the onset of sensitive periods (Hensch, 2005). At the same time, plasticity is constrained by two main classes of "brakes." First, the resulting structures, such as myelin and perineuronal nets, limit further plasticity. Second, the balance between excitatory and inhibitory transmitter release put constraints on plasticity (Bavelier, Levi, Li, Dan, & Hensch, 2010). A case illustrating the active suppression of plasticity comes from individuals who suffer from amblyopia. These individuals' eyes appear normal, but one eye's vision is impaired because it was not stimulated properly and did not develop its full visual potential during the sensitive period. When amblyopic patients lose vision in the normally functioning eye, the amblyopic eye sometimes improves spontaneously (Bavelier, Achtman, Mani, & Föcker, 2012; Rahi et al., 2002). This observation is consistent with the notion that the connections from the amblyopic eye are actively suppressed rather than destroyed entirely, so that the loss of vision in the other eye may reactivate existing connections.

Conceptually and empirically, it is highly attractive to apply the molecular insights gained from the study of sensitive (also called critical) periods in animals and humans to the study of adult plasticity (cf. Bavelier et al., 2010). In particular, it is intriguing to examine whether sensitive periods can be reopened or prolonged in adult humans. Attempts to reopen windows of plasticity in adulthood may combine behavioral interventions (Lövdén et al., 2013) with targeted pharmacological manipulations (Gervain, Vines, Chen, & Seo, 2013) or with stimulation of relevant brain areas (Ferreri & Rossini, 2013).

One question that will accompany this work is whether mechanisms of plasticity change with age and experience. For instance, one may wonder about age-graded differences in the mechanisms and meaning of neurogenesis in the hippocampus. Once hippocampal circuits have been formed, the need for cellular plasticity may decrease (Couillard-Despres, Iglseder, & Aigner, 2011). Upon exposure to new stimuli, younger (or un-experienced) individuals may require more neurogenesis to improve the circuitry than older (or more experienced) animals. Based on this example, one may speculate that the degree of plasticity required for meeting new environmental demands is inversely related to previous exposures to similar challenges (cf. Schaie, 1962). In line with this speculation, long-term adaptive changes in dendritic spines have been found to be abundant in young animals, but virtually absent in adult animals (Grutzendler, Kasthuri, & Gan, 2002). This difference may be related to age differences in transfer of training. In younger individuals, plasticity may operate on a wide scale, and more easily transfer to untrained skills. In older individuals, plasticity may operate at a more local level, with little evidence of transfer to untrained skills. Clearly, age-comparative intervention studies are needed to validate these claims.

To conclude, the molecular mechanisms that regulate plasticity during adulthood may be more or less similar to the mechanisms that regulate sensitive periods in early ontogeny. Delineating these commonalities and differences may turn out to be the most important research question in the study of human adult plasticity for the next decade.

Acknowledgments

UL thanks Martin Lövdén and Naftali Raz for valuable discussions on the topic of this chapter.

References

Ben Abdallah, N. M., Slomianka, L., Vyssotski, A. L., & Lipp, H. P. (2010). Early age-related changes in adult hippocampal neurogenesis in C57 mice. *Neurobiology of Aging*, *31*(1), 151–161.

Altenmüller, E., & Jabusch, H.-C. (2010). Focal dystonia in musicians: Phenomenology, pathophysiology, triggering factors, and treatment. *Medical Problems of Performing Artists*, *25*(1), 3–9.

Alvarez, J. A., & Emory, E. (2006). Executive function and the frontal lobes: A meta-analytic review. *Neuropsychology Review*, *16*(1), 17–42.

Bailey, J., & Penhune, V. B. (2012). A sensitive period for musical training: Contributions of age of onset and cognitive abilities. *Annals of the New York Academy of Sciences*, *1252*, 163–170.

Baltes, P. B. (1987). Theoretical propositions of life-span developmental psychology: On the dynamics between growth and decline. *Developmental Psychology*, *23*(5), 611–626.

Baltes, P. B., Lindenberger, U., & Staudinger, U. M. (2006). Life-span theory in developmental psychology. In W. Damon & R. M. Lerner (Eds.), *Handbook of child psychology: Vol. 1. Theoretical models of human development* (pp. 569–664). New York: Wiley.

Bavelier, D., Achtman, R. L., Mani, M., & Föcker, J. (2012). Neural bases of selective attention in action video game players. *Vision Research*, *61*, 132–143.

Bavelier, D., Levi, D. M., Li, R. W., Dan, Y., & Hensch, T. K. (2010). Removing brakes on adult brain plasticity: From molecular to behavioral interventions. *Journal of Neuroscience*, *30*(45), 14964–14971.

Beam, C. R., & Turkheimer, E. (2013). Phenotype–environment correlations in longitudinal twin models. *Development and Psychopathology*, *25*(1), 7–16.

Beas, B. S., Setlow, B., & Bizon, J. L. (2013). Distinct manifestations of executive dysfunction in aged rats. *Neurobiology of Aging*, *34*(9), 2164–2174.

Bergmann, O., & Frisén, J. (2013). Why adults need brain cells. *Science*, *340*(6133), 695–696.

Bizon, J. L., & Gallagher, M. (2003). Production of new cells in the rat dentate gyrus over the lifespan: Relation to cognitive decline. *European Journal of Neuroscience*, *18*(1), 215–219.

Bizon, J. L., Lee, H. J., & Gallagher, M. (2004). Neurogenesis in a rat model of age-related cognitive decline. *Aging Cell*, *3*(4), 227–234.

Bondolfi, L., Ermini, F., Long, J. M., Ingram, D. K., & Jucker, M. (2004). Impact of age and caloric restriction on neurogenesis in the dentate gyrus of C57BL/6 mice. *Neurobiology of Aging*, *25*(3), 333–340.

Boyke, J., Driemeyer, J., Gaser, C., Büchel, C., & May, A. (2008). Training-induced brain structure changes in the elderly. *Journal of Neuroscience*, *28*(28), 7031–7035.

Brehmer, Y., Li, S.-C., Müller, V., von Oertzen, T., & Lindenberger, U. (2007). Memory plasticity across the life span: Uncovering children's latent potential. *Developmental Psychology*, *43*(2), 465–478.

Brehmer, Y., Li, S.-C., Straube, B., Stoll, G., von Oertzen, T., Müller, V., et al. (2008). Comparing memory skill maintenance across the life span: Preservation in adults, increase in children. *Psychology and Aging*, *23*(2), 227–238.

Cattell, R. B. (1971). *Abilities: Their structure, growth, and action*. Boston, MA: Houghton Mifflin Harcourt (HMH).

Changeux, J. P., & Dehaene, S. (1989). Neuronal models of cognitive functions. *Cognition*, *33*(1–2), 63–109.

Churchill, J. D., Galvez, R., Colcombe, S., Swain, R. A., Kramer, A. F., & Greenough, W. T. (2002). Exercise, experience and the aging brain. *Neurobiology of Aging*, *23*(5), 941–955.

Couillard-Despres, S., Iglseder, B., & Aigner, L. (2011). Neurogenesis, cellular plasticity and cognition: The impact of stem cells in the adult and aging brain—A mini review. *Gerontology*, *57*(6), 559–564.

Craik, F. I. M. (1983). On the transfer of information from temporary to permanent memory. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *302*(1110), 341–359.

Craik, F. I. M. (2006). Remembering items and their contexts: Effects of aging and divided attention. In H. Zimmer, A. Mecklinger, & U. Lindenberger (Eds.), *Handbook of binding and memory: Perspectives from cognitive neuroscience* (pp. 571–594). New York: Oxford University Press.

Darmopil, S., Petanjek, Z., Mohammed, A. H., & Bogdanović, N. (2009). Environmental enrichment alters dentate granule cell morphology in oldest-old rat. *Journal of Cellular and Molecular Medicine*, *13*(8B), 1845–1856.

Di, X., Rypma, B., & Biswal, B. B. (2014). Correspondence of executive function related functional and anatomical alterations in aging brain. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *48*, 41–50.

Dickens, W. T., & Flynn, J. R. (2001). Heritability estimates versus large environmental effects: The IQ paradox resolved. *Psychological Review*, *108*(2), 346–369.

Douaud, G., Groves, A. R., Tamnes, C. K., Westlye, L. T., Duff, E. P., Engvig, A., et al. (2014). A common brain network links development, aging, and vulnerability to disease. *Proceedings of the National Academy of Sciences of the United States of America*, *111*(49), 17648–17653.

Draganski, B., Gaser, C., Busch, V., Schuierer, G., Bogdahn, U., & May, A. (2004). Neuroplasticity: Changes in grey matter induced by training. *Nature*, *427*(6972), 311–312.

Edelman, G. E. (1987). *Neural Darwinism: The theory of neuronal group selection*. New York: Basic Books.

Eickhoff, S. B., Laird, A. R., Grefkes, C., Wang, L. E., Zilles, K., & Fox, P. T. (2009). Coordinate-based activation likelihood estimation meta-analysis of neuroimaging data: A random-effects approach based on empirical estimates of spatial uncertainty. *Human Brain Mapping*, *30*(9), 2907–2926.

Ferreri, F., & Rossini, P. M. (2013). TMS and TMS-EEG techniques in the study of the excitability, connectivity, and plasticity of the human motor cortex. *Reviews in the Neurosciences*, *24*(4), 431–442.

Flynn, J. R. (1987). Massive IQ gains in 14 nations: What IQ tests really measure. *Psychological Bulletin*, *101*(2), 171–191.

Freund, J., Brandmaier, A. M., Lewejohann, L., Kirste, I., Kritzler, M., Krüger, A., et al. (2013). Emergence of individuality in genetically identical mice. *Science*, *340*(6133), 756–759.

Fu, M., & Zuo, Y. (2011). Experience-dependent structural plasticity in the cortex. *Trends in Neurosciences*, *3*(4), 177–187.

Gazzaley, A. (2013). Top-down modulation deficit in the aging brain: An emerging theory of cognitive aging. In D. T. Stuss & R. T. Knight (Eds.), *Principles of frontal lobe function* (pp. 593–608, 2nd ed.). New York: Oxford University Press.

Gervain, J., Vines, B. W., Chen, L. M., & Seo, R. J. (2013). Valproate reopens critical-period learning of absolute pitch. *Frontiers in Systems Neuroscience*, *7*, 102.

Giedd, J. N., Blumenthal, J., Jeffries, N. O., Castellanos, F. X., Liu, H., Zijdenbos, A., et al. (1999). Brain development during childhood and adolescence: A longitudinal MRI study. *Nature Neuroscience*, *2*(10), 861–863.

Grutzendler, J., Kasthuri, N., & Gan, W.-B. (2002). Long-term dendritic spine stability in the adult cortex. *Nature*, *420*(6917), 812–816.

Heine, V. M., Maslam, S., Joëls, M., & Lucassen, P. J. (2004). Prominent decline of newborn cell proliferation, differentiation, and apoptosis in the aging dentate gyrus,

in absence of an age-related hypothalamus–pituitary–adrenal axis activation. *Neurobiology of Aging*, *25*(3), 361–375.

Hensch, T. K. (2005). Critical period plasticity in local cortical circuits. *Nature Reviews Neuroscience*, *6*(11), 877–888.

Hertzog, C., Kramer, A. F., Wilson, R. S., & Lindenberger, U. (2008). Enrichment effects on adult cognitive development: Can the functional capacity of older adults be preserved and enhanced? *Psychological Science in the Public Interest*, *9*(1), 1–65.

Hill, J., Inder, T., Neil, J., Dierker, D., Harwell, J., & Van Essen, D. (2010). Similar patterns of cortical expansion during human development and evolution. *Proceedings of the National Academy of Sciences of the United States of America*, *107*(29), 13135–13140.

Horn, J. L. (1989). Models of intelligence. In R. L. Linn (Ed.), *Intelligence: Measurement, theory, and public policy* (pp. 29–73). Urbana, IL: University of Illinois Press.

Hubel, D. H., & Wiesel, T. N. (1959). Receptive fields of single neurones in the cat's striate cortex. *Journal of Physiology*, *148*, 574–591.

Jones, H. E., & Conrad, H. (1933). The growth and decline of intelligence: A study of a homogeneous group between the ages of 10 and 60. *Genetic Psychological Monographs*, *13*, 223–298.

Karmiloff-Smith, A. (1995). Annotation: The extraordinary cognitive journey from foetus through infancy. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *36*(8), 1293–1313.

Kempermann, G. (2006). *Adult neurogenesis*. New York: Oxford University Press.

Kempermann, G. (2008). The neurogenic reserve hypothesis: What is adult hippocampal neurogenesis good for? *Trends in Neurosciences*, *31*(4), 163–169.

Kempermann, G., Kuhn, H. G., & Gage, F. H. (1997). More hippocampal neurons in adult mice living in an enriched environment. *Nature*, *386*(6624), 493–495.

Kinsbourne, M., & Hicks, R. E. (1978). Functional cerebral space: A model for overflow, transfer, and interference effects in human performance: A tutorial review. In J. Requin (Ed.), *Attention and Performance VII* (pp. 345–362). Hillsdale, NJ: Erlbaum.

Kray, J., & Lindenberger, U. (2000). Adult age differences in task switching. *Psychology and Aging*, *15*(1), 126–147.

Kronenberg, G., Bick-Sander, A., Bunk, E., Wolf, C., Ehninger, D., & Kempermann, G. (2006). Physical exercise prevents age-related decline in precursor cell activity in the mouse dentate gyrus. *Neurobiology of Aging*, *27*, 1505–1513.

Kuhn, H. G., Dickinson-Anson, H., & Gage, F. H. (1996). Neurogenesis in the dentate gyrus of the adult rat: Age-related decrease of neuronal progenitor proliferation. *Journal of Neuroscience*, *16*, 2027–2033.

Kuzawa, C. W., Chugani, H. T., Grossman, L. I., Lipovich, L., Muzik, O., Hof, P. R., et al. (2014). Metabolic costs and evolutionary implications of human brain development. *Proceedings of the National Academy of Sciences of the United States of America*, *111*(36), 13010–13015.

Lee, S. W., Clemenson, G. D., & Gage, F. H. (2012). New neurons in an aged brain. *Behavioural Brain Research*, *227*(2), 497–507.

Li, S., & Carmichael, S. T. (2006). Growth-associated gene and protein expression in the region of axonal sprouting in the aged brain after stroke. *Neurobiology of Disease*, *23*(2), 362–373.

Li, S., Overman, J. J., Katsman, D., Kozlov, S. V., Donnelly, C. J., Twiss, J. L., et al. (2010). An age-related sprouting transcriptome provides molecular control of axonal sprouting after stroke. *Nature Neuroscience*, *13*(12), 1496–1504.

Lindenberger, U. (2001). Lifespan theories of cognitive development. In N. J. Smelser & P. B. Baltes (Eds.), *International encyclopedia of the social and behavioral sciences* (pp. 8848–8854). Oxford, England: Elsevier.

Lindenberger, U. (2014). Human cognitive aging: Corriger la fortune? *Science*, *346*(6209), 572–578.

Lindenberger, U., Burzynska, A. Z., & Nagel, I. E. (2013). Heterogeneity in frontal lobe aging. In D. T. Stuss & R. T. Knight (Eds.), *Principles of frontal lobe functions* (pp. 609–627, 2nd ed.). New York: Oxford University Press.

Lindenberger, U., & Mayr, U. (2014). Cognitive aging: Is there a dark side to environmental support? *Trends in Cognitive Sciences*, *18*(1), 7–15.

Lövdén, M., Bäckman, L., Lindenberger, U., Schaefer, S., & Schmiedek, F. (2010). A theoretical framework for the study of adult cognitive plasticity. *Psychological Bulletin*, *136*(4), 659–676.

Lövdén, M., Bodammer, N. C., Kühn, S., Tempelmann, C., Heinze, H.-J., Düzel, E., et al. (2010). Experience-dependent plasticity of white-matter microstructure extends into old age. *Neuropsychologia*, *48*(13), 3878–3883.

Lövdén, M., Schaefer, S., Noack, H., Bodammer, N. C., Kühn, S., Heinze, H. -J., et al. (2012). Spatial navigation training protects the hippocampus against age-related changes during early and late adulthood. *Neurobiology of Aging*, *33*, 620.e9–620.e22.

Lövdén, M., Wenger, E., Mårtensson, J., Lindenberger, U., & Bäckman, L. (2013). Structural brain plasticity in adult learning and development. *Neuroscience and Biobehavioral Reviews*, *37*, 2296–2310.

De Luca, C. R., Wood, S. J., Anderson, V., Buchanan, J.-A., Proffitt, T. M., Mahony, K., et al. (2003). Normative data from the CANTAB. I: Development of executive function over the lifespan. *Journal of Clinical and Experimental Neuropsychology*, *25*(2), 242–254.

Matzel, L. D., Light, K. R., Wass, C., Colas-Zelin, D., Denman-Brice, A., Waddel, A. C., et al. (2011).

Longitudinal attentional engagement rescues mice from age-related cognitive declines and cognitive inflexibility. *Learning & Memory*, *18*(5), 345–356.
Mayr, U., Kuhns, D., & Hubbard, J. (2014). Long-term memory and the control of attentional control. *Cognitive Psychology*, *72*, 1–26.
Michel, G. F., & Tyler, A. N. (2005). Critical period: A history of the transition from questions of when, to what, to how. *Developmental Psychobiology*, *46*(3), 156–162.
Molina-Luna, K., Hertler, B., Buitrago, M. M., & Luft, A. R. (2008). Motor learning transiently changes cortical somatotopy. *NeuroImage*, *40*(4), 1748–1754.
Moore, T. L., Killiany, R. J., Herndon, J. G., Rosene, D. L., & Moss, M. B. (2003). Impairment in abstraction and set shifting in aged rhesus monkeys. *Neurobiology of Aging*, *24*(1), 125–134.
Morrison, J. H., Brinton, R. D., Schmidt, P. J., & Gore, A. C. (2006). Estrogen, menopause, and the aging brain: How basic neuroscience can inform hormone therapy in women. *Journal of Neuroscience*, *26*(41), 10332–10348.
Nyberg, L., Lövdén, M., Riklund, K., Lindenberger, U., & Bäckman, L. (2012). Memory aging and brain maintenance. *Trends in Cognitive Sciences*, *16*, 292–305.
Passow, S., Westerhausen, R., Wartenburger, I., Hugdahl, K., Heekeren, H. R., Lindenberger, U., et al. (2012). Human aging compromises attentional control of auditory perception. *Psychology and Aging*, *27*(1), 99–105.
Penhune, V. B. (2011). Sensitive periods in human development: Evidence from musical training. *Cortex*, *47*(9), 1126–1137.
Piaget, J. (1980). Introduction. In J. Piaget (Ed.), *Les formes élémentaires de la dialectique* (pp. 9–13). Paris, France: Editions Gallimard.
Picciotto, M. R., & Zoli, M. (2002). Nicotinic receptors in aging and dementia. *Journal of Neurobiology*, *53*(4), 641–655.
Quartarone, A., & Pisani, A. (2011). Abnormal plasticity in dystonia: Disruption of synaptic homeostasis. *Neurobiology of Disease*, *42*(2), 162–170.
Rahi, J. S., Logan, S., Borja, M. C., Timms, C., Russell-Eggitt, I., & Taylor, D. (2002). Prediction of improved vision in the amblyopic eye after visual loss in the non-amblyopic eye. *The Lancet*, *360*(9333), 621–622.
Raz, N. (2000). Ageing of the brain and its impact on cognitive performance: Integration of structural and functional findings. In F. I. M. Craik & T. A. Salthouse (Eds.), *Handbook of aging and cognition* (pp. 1–90). Mahwah, NJ: Erlbaum.
Raz, N. (2001). Ageing and the brain. In *eLS*. Chichester: Wiley. http://dx.doi.org/doi:10.1038/npg.els.0004063
Raz, N. (2004). The aging brain: Structural changes and their implications for cognitive aging. In R. Dixon & L. G. Nilsson (Eds.), *New frontiers in cognitive aging* (pp. 115–134). New York: Oxford University Press.
Raz, N. (2007). Comment on Greenwood (2007): Which side of plasticity? *Neuropsychology*, *21*(6), 676–677.
Raz, N. (2009). Decline and compensation in aging brain and cognition: Promises and constraints. *Neuropsychology Review*, *19*(4), 411–414.
Raz, N., Ghisletta, P., Rodrigue, K. M., Kennedy, K. M., & Lindenberger, U. (2010). Trajectories of brain aging in middle-aged and older adults: Regional and individual differences. *NeuroImage*, *51*(2), 501–511.
Reed, A., Riley, J., Carraway, R., Carrasco, A., Perez, C., Jakkamsetti, V., et al. (2011). Cortical map plasticity improves learning but is not necessary for improved performance. *Neuron*, *70*(1), 121–131.
Ribot, T. (1881). *Les maladies de la mémoire*. Paris: Bailliere.
Schaie, K. W. (1962). A field-theory approach to age changes in cognitive behavior. *Vita Humana*, *5*(3), 129–141.
Schmiedek, F., Lövdén, M., & Lindenberger, U. (2010). Hundred days of cognitive training enhance broad cognitive abilities in adulthood: Findings from the COGITO Study. *Frontiers in Aging Neuroscience*, *2*, 27
Schmiedek, F., Lövdén, M., & Lindenberger, U. (2014). Younger adults show long-term effects of cognitive training on broad cognitive abilities over 2 years. *Developmental Psychology*, *50*(9), 2304–2310.
Shing, Y. L., & Lindenberger, U. (2011). The development of episodic memory: Lifespan lessons. *Child Development Perspectives*, *5*(2), 148–155.
Shing, Y. L., Lindenberger, U., Diamond, A., Li, S.-C., & Davidson, M. C. (2010). Memory maintenance and inhibitory control differentiate from early childhood to adolescence. *Developmental Neuropsychology*, *35*(6), 679–697.
Shrager, J., & Johnson, M. H. (1996). Dynamic plasticity influences the emergence of function in a simple cortical array. *Neural Networks*, *9*(7), 1119–1129.
Smith, D. E., Roberts, J., Gage, F. H., & Tuszynski, M. H. (1999). Age-associated neuronal atrophy occurs in the primate brain and is reversible by growth factor gene therapy. *Proceedings of the National Academy of Sciences of the United States of America*, *96*(19), 10893–10898.
Span, M. M., Ridderinkhof, K. R., & van der Molen, M. W. (2004). Age-related changes in the efficiency of cognitive processing across the life span. *Acta Psychologica*, *117*(2), 155–183.
Takesian, A. E., & Hensch, T. K. (2013). Balancing plasticity/stability across brain development. *Progress in Brain Research*, *207*, 3–34.
Verhaeghen, P., & Cerella, J. (2002). Aging, executive control, and attention: A review of meta-analyses. *Neuroscience and Biobehavioral Reviews*, *26*(7), 849–857.
Wasylyshyn, C., Verhaeghen, P., & Sliwinski, M. J. (2011). Aging and task switching: A meta-analysis. *Psychology and Aging*, *26*(1), 15–20.

Wenger, E., Kühn, S., Verrel, J., Mårtensson, J., Bodammer, N. C., Lindenberger, U., et al. (submitted). *Repeated structural imaging reveals non-linear progression of experience-dependent volume changes in human motor cortex*.

Wenger, E., Schaefer, S., Noack, H., Kühn, S., Mårtensson, J., Heinze, H.-J., et al. (2012). Cortical thickness changes following spatial navigation training in adulthood and aging. *NeuroImage*, *59*(4), 3389–3397.

Werker, J. F., & Tees, R. C. (2005). Speech perception as a window for understanding plasticity and commitment in language systems of the brain. *Developmental Psychobiology*, *46*(3), 233–251.

Xu, F., Han, Y., Sabbagh, M. A., Wang, T., Ren, X., & Li, C. (2013). Developmental differences in the structure of executive function in middle childhood and adolescence. *PLoS One*, *8*(10), e77770.

Xu, T., Yu, X., Perlik, A. J., Tobin, W. F., Zweig, J. A., Tennant, K., et al. (2009). Rapid formation and selective stabilization of synapses for enduring motor memories. *Nature*, *462*, 915–919.

Yuan, P., & Raz, N. (2014). Prefrontal cortex and executive functions in healthy adults: A meta-analysis of structural neuroimaging studies. *Neuroscience and Biobehavioral Reviews*, *42*, 180–192.

HANDBOOK OF THE PSYCHOLOGY OF AGING

EIGHTH EDITION

Edited by

K. Warner Schaie and Sherry L. Willis

Associate Editors

Bob G. Knight, Becca Levy, and Denise C. Park

ELSEVIER

AMSTERDAM • BOSTON • HEIDELBERG • LONDON
NEW YORK • OXFORD • PARIS • SAN DIEGO
SAN FRANCISCO • SINGAPORE • SYDNEY • TOKYO

Academic Press is an imprint of Elsevier

Academic Press is an imprint of Elsevier
32 Jamestown Road, London NW1 7BY, UK
525 B Street, Suite 1800, San Diego, CA 92101-4495, USA
225 Wyman Street, Waltham, MA 02451, USA
The Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, UK

Seventh edition 2011
Eighth edition 2016

Notices
Knowledge and best practice in this field are constantly changing. As new research and experience broaden our understanding, changes in research methods, professional practices, or medical treatment may become necessary.

Practitioners and researchers must always rely on their own experience and knowledge in evaluating and using any information, methods, compounds, or experiments described herein. In using such information or methods they should be mindful of their own safety and the safety of others, including parties for whom they have a professional responsibility.

To the fullest extent of the law, neither the Publisher nor the authors, contributors, or editors, assume any liability for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein.

ISBN: 978-0-12-411469-2

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library

Library of Congress Cataloging-in-Publication Data
A catalog record for this book is available from the Library of Congress

Publisher: Nikki Levy
Acquisition Editor: Emily Ekle
Editorial Project Manager: Barbara Makinster
Production Project Manager: Melissa Read
Designer: Matthew Limbert

Printed and bound in the United States of America