

Neurocognitive Aging and the Compensation Hypothesis

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ABSTRACT—*The most unexpected and intriguing result from functional brain imaging studies of cognitive aging is evidence for age-related overactivation: greater activation in older adults than in younger adults, even when performance is age-equivalent. Here we examine the hypothesis that age-related overactivation is compensatory and discuss the compensation-related utilization of neural circuits hypothesis (CRUNCH). We review evidence that favors a compensatory account, discuss questions about strategy differences, and consider the functions that may be served by overactive brain areas. Future research directed at neurocognitively informed training interventions may augment the potential for plasticity that persists into the later years of the human lifespan.*

KEYWORDS—*plasticity; dedifferentiation; brain imaging; working memory*

Brain imaging has become a method of great importance for studying cognitive aging, which makes sense because the latter presumably results from neurobiological aging. Therefore, brain-based measurements that can be linked to cognitive processes expand the range of questions that can be addressed about the aging mind. The emerging answers have prompted new ways to think about the normal aging process and about functional brain organization across the lifespan. Before the advent of brain imaging, the behavioral methods and interpretive logic of clinical neuropsychology guided brain-based theories of cognitive aging. This approach assumes that minimal age differences in performance imply minimal alterations in underlying cognitive mechanisms and, by extension, *age-invariance* in the neural substrates that mediate them. In our assessment, one of the most far-reaching discoveries to have thus far emerged from brain imaging studies of aging is that this assumption is erroneous.

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The initial neuroimaging studies of cognitive aging, which measured brain activation via the distribution of a radioactive isotope (i.e., positron emission tomography, PET; Grady et al., 1994), noted that older adults display activation in regions that are not activated by younger adults performing the same tasks. In some studies, sites of overactivation co-occur with regions that are underactive relative to younger adults. In other studies, regions of overactivation are the only indication that older brains function differently than younger brains (for reviews, see Grady & Craik, 2000; Reuter-Lorenz, 2002). The terms overactivation and underactivation are purely relative, referring to sites that senior adults activate more or less, respectively, than their younger counterparts (Fig. 1). Overactivation is frequently observed in prefrontal sites (Cabeza et al., 2004; Reuter-Lorenz et al., 2000). Overactivation in seniors is often found in regions that approximately mirror active sites in younger adults but in the opposite hemisphere (e.g., Cabeza, 2002; Reuter-Lorenz et al., 2000; see the lower left panel of Fig. 1). This pattern of reduced asymmetry in older adults has been referred to as hemispheric asymmetry reduction in older age, or HAROLD for short (Cabeza, 2002).

INTERPRETING OVERACTIVATION

Age-related underactivation is typically interpreted as a sign of impairment due to poor or underutilized strategies or due to structural changes such as atrophy. However, the cognitive and neural mechanisms associated with age-specific regions of overactivation are more ambiguous. Determining whether overactivations are neural correlates of processes that are beneficial, detrimental, or inconsequential to cognitive function is the crux of many research efforts in the cognitive neuroscience of aging (Reuter-Lorenz & Lustig, 2005).

Because overactivation has been found for a broad range of tasks, across a variety of brain regions, with or without age differences in performance, and with or without concurrent underactivation, it is highly unlikely that all instances stem from a single cause. Unsurprisingly, when overactivation is found in association with poor performance, it is interpreted as impair-

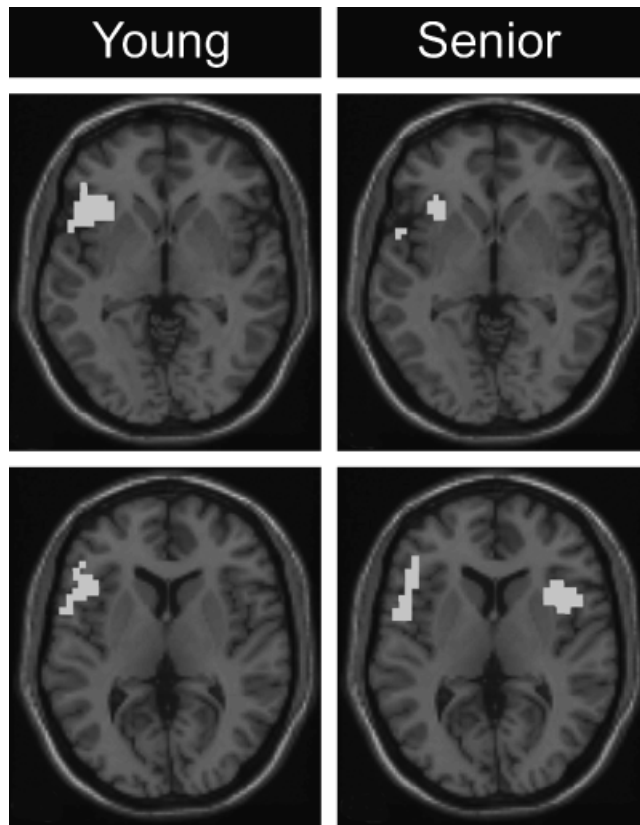


Fig. 1. Results typically referred to as “underactivation” (top) and “overactivation” (bottom). When older adults activate a brain region at lower levels or show a smaller extent of activation compared to younger adults, as illustrated in the top pair of images, the results are often interpreted to indicate that the older group is functionally deficient in the processing operations mediated by this region. The overactivation pattern in the bottom pair of images illustrates the hemispheric asymmetry reduction in older age (or HAROLD) effect: Younger adults show activation that is lateralized to the left hemisphere, whereas the older adults are activating homologous brain regions in the opposite hemisphere also. See Reuter-Lorenz and Lustig (2005) for examples of studies reporting these age-specific activation patterns.

ment and is typically attributed to any of several potentially related mechanisms: the use of multiple and/or inefficient cognitive strategies; disinhibition because communication between the left and right hemispheres declines; or dedifferentiation, whereby the specificity and selectivity of neural processors break down.

In many studies, however, overactivation is accompanied by age-equivalent performance, raising the possibility that the additional activity serves a beneficial, compensatory function without which performance decrements would result (see Fig. 1). Regardless of whether performance matching is achieved by selecting younger and older subgroups that perform at equivalent levels, providing different amounts of training, adopting age-tailored stimulus parameters, or otherwise altering task demands for each age group, overactivation has been found consistently across perceptual, motoric, mnemonic, verbal, and spatial domains. The compensation hypothesis predicts that,

even while performance is matched at the group level, overactivation across individuals should be correlated with higher performance in the older group. Although significant correlations may sometimes be lacking due to insufficient variability or a lack of statistical power, positive activation–performance correlations have been reported, lending support to the compensatory account of age-specific overactivations (Fig. 1; Cabeza et al., 2004; Reuter-Lorenz & Lustig, 2005).

Establishing that overactive sites in older adults contribute to and are necessary for successful performance would provide especially strong support for the compensation hypothesis. Transcranial magnetic stimulation (TMS) is a technique that applies a series of focally directed magnetic pulses to the scalp to stimulate the underlying neural tissue. TMS can be applied in either a deactivating or an activating mode. In the deactivating mode, TMS temporarily disrupts the underlying neural signals, producing a virtual, transient lesion. Using this mode, Rossi et al. (2005) showed that overactive sites in seniors contributed to performance success: Older adults, who typically show bilateral prefrontal activation during recognition memory, were impaired by TMS to either hemisphere, suggesting that recognition relies on both sides. Younger adults, who activate unilaterally during recognition memory, were impaired by TMS to only one side. When used in the activating mode, TMS increases the contribution of the underlying tissue. Another study found that, when TMS was applied prefrontally in the activating mode, a group of low-performing elderly showed improvement; furthermore, functional magnetic resonance imaging (fMRI) showed their brain activation to be unilateral before TMS and bilateral after TMS, in association with their improved performance (Sole-Padulles et al., 2006).

COMPENSATION FOR WHAT?

The compensation hypothesis assumes that overactive sites in older adult brains are “working harder” than the corresponding regions in their younger counterparts. In the aging brain, a network may work harder, and thus overactivate, to make up either for its own declining efficiency or for processing deficiencies elsewhere in the brain. Although definitive support for the first possibility is currently lacking, such support could come from work using multiple measures to assess structural and functional integrity within the same subjects. For example, volumetric measures could reveal age-related atrophy in a region that also displays overactivation. When also coupled with preserved performance, such a pattern would suggest that increased recruitment compensates for decline (cf., Persson et al., 2006).

Alternatively, a network may need to work harder and thus becomes overactive because the input it receives is degraded or compromised. By this account, overactivation is compensating for functional declines elsewhere. We see three types of evidence as being consistent with this possibility. First, several studies

report overactive sites accompanied by, and in some cases inversely correlated with, sites of underactivation (Reuter-Lorenz & Lustig, 2005). For example, in a study of incidental memory for complex scenes, Gutchess et al. (2005) compared the neural correlates of successfully remembered items to those of forgotten items in younger and older adults. Compared to the older group, successful memory in younger adults was associated with greater activation in medial temporal lobe (MTL) regions. In contrast, when older adults were successful, the prefrontal cortex was overactivated and was inversely correlated with MTL activation. Prefrontal activity appears to compensate for MTL declines to support successful memory with age. Likewise, in a recent study using functional connectivity analyses to measure intercorrelations between brain regions (Daselaar, Fleck, Dobbins, Madden, & Cabeza, 2006), younger adults were more confident in their memory performance and showed greater connectivity between the hippocampus and a posterior, midline network associated with detailed, contextual memory; older adults with equal but less confident memories showed more activation and greater connectivity in a different network that included the prefrontal cortex and was associated with familiarity. A tendency to rely more on familiarity signals in the aging brain presumably serves to compensate for decreased availability of hippocampally mediated context memory.

Second, overactivation may compensate for increased “noise” or the declining precision of perceptual processes. For example, representational codes or receptive field properties may be less specific in senior adults. Single-unit recordings in aged animals and brain-imaging studies in older humans reveal broader tuning curves and declining precision of attribute- and category-specific coding in posterior cortices (Reuter-Lorenz & Lustig, 2005). Consequently, higher cognitive operations that utilize these codes may have to “work harder” to perform the same tasks. Consistent with this possibility, Denise Park’s group has shown that deficient domain selectivity in ventral visual association cortex in older adults is associated with overactive prefrontal cortex (Payer, Marshuetz, Sutton, Hebrank, Welsh, & Park, 2006) in a visual working memory task (see also Cabeza et al., 2004; Grady et al., 1994; Madden et al., 1996). Likewise, greater noise or interference may result from age-related difficulties suppressing or inhibiting irrelevant information due to alterations in top-down, controlled processing (e.g., Gazzaley, Cooney, Rissman, & D’Esposito, 2005).

Finally, the aging brain may also have to contend with noise from nonperceptual processes. A growing body of evidence indicates that older adults have difficulty attenuating activity in the so-called “default network.” This network shows correlated activations during nontask periods (e.g., passive fixation baseline or rest) and deactivations during engagement in experimental tasks. The default network is thought to mediate unconstrained self-referential thought about past and future events that occurs when cognition is not being dictated by external demands, such as those imposed by an experimental task.

Activity in task-related regions is inversely correlated with default-network activity, suggesting that default-network quiescence focuses neural and cognitive resources on the task at hand: More demanding cognitive tasks are associated with greater levels of deactivation. However, across a variety of cognitive tasks, older adults show less deactivation of the default network than their younger counterparts do. Moreover, age differences in deactivation magnitudes increase at higher levels of task demand (Persson, Lustig, Nelson, & Reuter-Lorenz, 2007), indicating that older brains are particularly deficient at silencing the default network when faced with tasks requiring greater cognitive effort.

ARE OLDER BRAINS SIMPLY YOUNGER BRAINS WORKING HARDER?

Are patterns of overactivation observed in the aging brain “equivalent” to those found when the younger brain contends with increased task demand? Although this model is surely incomplete, it may accurately characterize some aspects of neurocognitive aging. In our lab, using variable verbal working memory loads, we found that older adults activated regions of the dorsolateral prefrontal cortex at lower loads, whereas younger adults activated these same sites only at higher loads. Importantly, at the lower loads, age differences in performance were minimal. At the higher loads, activation in the younger group exceeded that observed in the older group, and elderly performance was relatively deficient as well (Cappell, Gmeindl, & Reuter-Lorenz, 2006). Mattay et al. (2006) report a similar result using a different verbal task. At the lowest level of task demand, senior adults overactivate the prefrontal cortex while performing equivalently to younger adults. With increasing demand, this prefrontal site becomes underactivated in seniors, and performance becomes impaired.

These studies have several important implications. First, some sites of overactivation displayed by older adults are neurologically “normal” in that they are also activated by younger adults. Older adults merely recruit them sooner in the load-activation function. Some overactivations may therefore reflect the brain’s response to increased task difficulty by which “reserve” resources are recruited (Stern et al., 2005). Second, at lower levels of task demand, region-specific overactivation in seniors is associated with good performance and presumably is compensatory because performance differences are minimal despite activation differences. Third, beyond a certain level of task demand, the senior brain falls short of sufficient activation levels, and performance declines relative to the younger group. We (e.g., Reuter-Lorenz & Lustig, 2005; Cappell et al., 2006) have referred to this tradeoff as the compensation-related utilization of neural circuits hypothesis (or CRUNCH; see Fig. 2). According to CRUNCH, processing inefficiencies cause the aging brain to recruit more neural resources to achieve computational output equivalent to that of a younger brain. The resulting

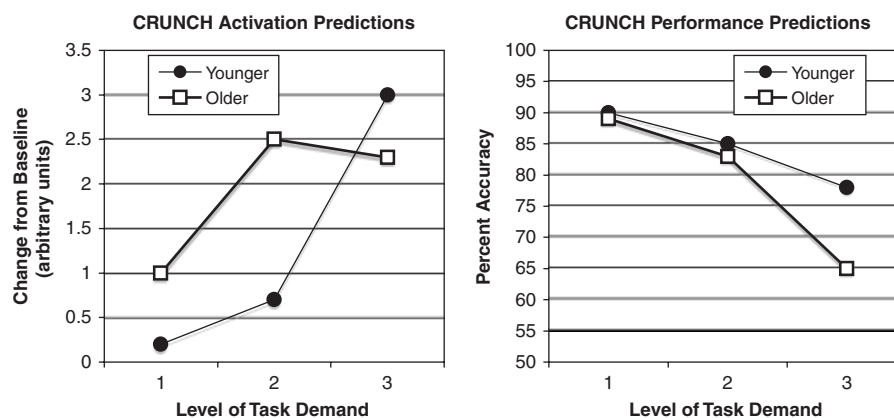


Fig. 2. Patterns of activation (in arbitrary units; left graph) and performance levels (right graph) predicted by the compensation-related utilization of neural circuits hypothesis (CRUNCH). Increased recruitment in response to increasing task demand is a “normal” neural response, evident in younger adults; what varies with age, according to CRUNCH, is the slope of the function relating activation to demand and the level at which activation asymptotes. The left graph shows how, relative to younger adults, older adults progress from overactivation at lower levels of task demand to underactivation at higher levels of task demand within the same region of interest. According to CRUNCH, compensatory recruitment at low demand maintains seniors’ performance at levels that are equivalent to or minimally different from younger adult levels. The right graph shows how, as task demands increase, older adults reach a resource ceiling, and performance levels drop, especially in comparison to those of younger groups. At peak levels of demand, errors may be sufficiently frequent that the task is met with frustration or approached with ineffective strategies, or other factors may prevail that lead to underactivation of this region compared to younger groups (cf. Mattay et al., 2006).

compensatory activation is effective at lower levels of task demand, but as demand increases, a resource ceiling is reached, leading to insufficient processing and age-related decrements for harder tasks. Training, exercise, and other interventions applied in older age or throughout the life course (Reuter-Lorenz & Mikels, 2006) may increase available resources and compensatory potential (e.g., cognitive reserve, Stern et al., 2005). Conversely, sleep deprivation, neurological damage, or genetic vulnerabilities may lower the resource ceiling, leading to underactivation and performance decrements.

COGNITIVE “CORRELATES” OF OVERACTIVATION

What cognitive operations are supported by sites of age-related overactivation? Do older adults engage different cognitive strategies than younger adults do, especially where the “younger brain working harder” model will not suffice? Prefrontal regions show the greatest evidence for age-related atrophy, and yet, paradoxically, these are the sites where overactivation and evidence for compensation tend to be most pronounced. Executive control functions mediated by lateral and inferior prefrontal sites (e.g., attentional selection, inhibition, rule switching, maintenance, and context processing) can be recruited adaptively to meet the challenges of changing environmental and task demands. Executive recruitment may also be the primary means by which the brain adapts both neurally and cognitively to its own aging. Executive processes account for a wide range of individual differences and are a likely source of age-related variations as well.

Yet, evidence linking age-related changes in activation to specific age differences in cognitive strategies remains sparse. Some tasks are not amenable to strategy analyses, and some studies that have attempted to relate age differences in activation to differences in strategy have failed to find such links. One example (Fera et al., 2005) comes from a weather-prediction task that permitted strategy analysis. Despite pronounced age-related activation differences, including parietal overactivation that correlated positively with performance in seniors, no age differences in accuracy or strategy use were found.

Nevertheless, assuming that neural indices have cognitive correlates, there must be some yet unidentified cognitive differences that distinguish younger and older approaches to the same tasks. Available imaging methods can be better utilized to characterize age differences in neural activity and examine the possibility of age-altered strategy use. New fMRI task designs that can distinguish activation patterns sustained over a block of trials from transient, within-trial changes in activity may be successful in identifying age differences in strategies. As in the study by Daselaar et al. (2006; see above), functional-connectivity analyses can reveal dysfunctional or compensatory networks that can be linked to age-related changes in reliance on different psychological processes.

Also, despite the low temporal resolution of fMRI, time-course information alone or combined with event-related potential methods can reveal the timing of age-related activation differences, thereby providing some insight into what mental operations they mediate. A recent study (Velanova, Lustig, Jaccoby, & Buckner, 2006) demonstrated that prefrontal overactivity in

older adults was most evident in the latter part of a trial, suggesting a shift in strategic, effortful processing operations from earlier to later stages of the task. This temporal pattern suggests that prefrontally mediated processes may be recruited “reactively,” as if to perform clean-up operations due to failure to exert adequate control in a proactive manner (Braver, Gray, & Burgess, 2007).

FUTURE DIRECTIONS

As a dynamic biological process, aging reveals an enduring neural capacity for functional reorganization or redistribution of resources in response to metabolic and neurobiological declines. As such, brain aging may share compensatory principles with other neurobiological perturbations, including epilepsy and stroke, developmental disorders such as attention-deficit-hyperactivity disorder, and sleep deprivation. The brain is exceedingly clever, not only in the social, affective, and cognitive states it supports, but in the neural strategies it invokes to develop and maintain these states effectively over the lifespan. A major research frontier concerns the neural effects of training and practice of cognitive skills early in life, throughout life, and late in life (e.g., Eriksen et al., 2007; Persson & Reuter-Lorenz, in press). Can we foster cognitive success and resilience in later life by discovering ways to forestall or reverse declines, and otherwise optimize the brain’s response to its own aging?

Recommended Reading

- Cabeza, R., Nyberg, L., & Park, D. (2005). *The cognitive neuroscience of aging*. Oxford, UK: Oxford University Press. An edited volume that includes comprehensive contributions from major researchers using neuroscientific approaches to cognitive aging.
- Greenwood, P. (2007). Functional plasticity in cognitive aging: Review and hypothesis. *Neuropsychology, 21*, 657–673. A thorough, up-to-date treatment of the interplay between decline and compensation.
- Hedden, T., & Gabrieli, J.D. (2005). Healthy and pathological processes in adult development: New evidence from neuroimaging of the aging brain. *Current Opinion in Neurology, 18*, 740–747. A comprehensive review of research addressing functional, structural, pharmacological and genetic factors that characterize the fine line between healthy and pathological aging.
- Reuter-Lorenz, P.A., & Lustig, C. (2005). (See References). A highly accessible overview of research on the cognitive neuroscience of aging.
- Reuter-Lorenz, P.A., & Mikels, J.A. (2006). (See References). A further discussion of CRUNCH within a broad treatment of cognitive aging that takes an interdisciplinary approach to analyze the reciprocal interactions of cultural, psychological and biological influences on development, decline, and compensation across the lifespan.
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