

Cognitive neuroscience of aging: Contributions of functional neuroimaging

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By revealing how brain activity during cognitive performance changes as a function of aging, studies using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) are contributing to the development of a new discipline of Cognitive Neuroscience of Aging. This article reviews functional neuroimaging studies of cognitive aging in the domains of visual perception, episodic memory encoding and semantic memory retrieval, episodic memory retrieval, implicit memory, and working memory. The most consistent finding of these studies was that brain activity tends to be less lateralized in older adults than in younger adults. This finding is conceptualized in terms of a model called *Hemispheric Asymmetry Reduction in Old Adults* (HAROLD). According to a compensation hypothesis, bihemispheric involvement could help counteract age-related neurocognitive decline, whereas, according to a dedifferentiation hypothesis, it reflects a difficulty in recruiting specialized neural mechanisms.

Key words: Aging, positron emission tomography (PET), functional magnetic resonance imaging (fMRI), memory, perception, encoding, retrieval
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Until very recently, our knowledge concerning the neural basis of cognitive aging was based on two disciplines that had little contact with each other. Whereas the *neuroscience of aging* investigated the effects of aging on the brain independently of age-related changes in cognition, the *cognitive psychology of aging* investigated the effects of aging on cognition independently of age-related changes in the brain. The lack of communication between these two disciplines is rapidly being resolved as an increasing number of studies in the new discipline of *cognitive neuroscience of aging* focus on the links between cognitive and cerebral aging (for a review see, Cabeza, 2001). These studies employ a variety of methods, but the most powerful are functional neuroimaging techniques, such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). PET and fMRI studies can reveal how the neural correlates of different cognitive functions change as a function of aging. This paper reviews evidence from these studies, and then describes a model conceptualizing what is probably the most consistent finding in functional neuroimaging of cognitive aging: an age-related reduction in the lateralization of brain activity during cognitive performance.

FUNCTIONAL NEUROIMAGING STUDIES OF COGNITIVE AGING

Table 1 summarizes the results of PET and fMRI studies of cognitive aging that used an activation paradigm and measured blood flow changes (for a review resting and metabolic PET studies, see Madden & Hoffman, 1997). Black circles correspond to brain regions (e.g., Brodmann Areas) that were more activated by younger adults than by

older adults, or that were significantly activated by young adults but not by older adults. White circles correspond to brain regions that were more activated by older adults than by younger adults, or that were significantly activated by older adults but not by older adults. Stars correspond to regions similarly activated in the two groups. The studies included in Table 1, as well as others not included in this table, are briefly reviewed in the following sections.

Visual perception

The first activation study of cognitive aging was the PET study by Grady *et al.* (1994), which investigated face and location matching tasks. Consistent with the ventral/dorsal pathway distinction (Ungerleider & Mishkin, 1982), both younger and older adults showed occipitotemporal activations during face matching, and occipitoparietal activations during location matching. In both conditions, older adults showed less activity than younger adults in occipital regions, but more activity outside the occipital cortex. Grady *et al.* proposed that older adults are less efficient in recruiting visual areas before the ventral-dorsal bifurcation, and have to rely on more anterior brain regions, including the prefrontal cortex (PFC). They also suggested that recruiting anterior brain regions allowed older adults to maintain a good accuracy level at the expense of slower reaction times.

The findings of Grady *et al.* (1994) were replicated by Madden *et al.* (1997) using a target detection task. In a divided attention condition, older adults showed weaker activity than younger adults in occipital regions but stronger activity in PFC. The authors suggested that older adults were not able to perform the search task on the basis of letter identification processes mediated by the ventral

pathway, but rather had to rely on higher-order control processes (e.g., rehearsal, monitoring) that are mediated by the frontal lobes.

More recently, Grady *et al.* (2000) investigated face matching for nondegraded and degraded faces. For non-degraded faces, younger adults showed stronger activity in right PFC, as well as in bilateral occipital and parietal regions, whereas older adults showed stronger activity in left PFC, as well as in left temporal, hippocampal, insular, and thalamic regions. Degraded face matching performance (accuracy and RTs) was correlated with fusiform regions in younger adults but thalamic and hippocampal regions in older adults. These latter two regions were recruited during nondegraded face matching only by older adults, which suggests that these areas performed a compensatory role in older adults.

In summary, perception studies converged on a very interesting finding: Older adults showed weaker activity in visual cortex but more activity in PFC. In Grady *et al.* (2000), the age-related increase in left PFC activity was coupled with an age-related decrease in right PFC, which suggests a more bilateral pattern of PFC activity in older than in younger adults.

Episodic memory encoding and semantic memory retrieval

Episodic memory encoding and semantic memory retrieval are considered in the same section because they tend to co-occur during scanning and are very difficult to differentiate (Nyberg, Cabeza & Tulving, 1996; Tulving, Kapur, Craik, Moscovitch & Houle, 1994). When participants are asked to encode new information (*intentional learning*), they normally process it by retrieving information from semantic memory, and when they are asked to retrieve information from semantic memory, they normally encode the retrieval cues and retrieved information into episodic memory (*incidental learning*).

In the first study in this domain, Grady *et al.* (1995) investigated intentional face encoding. Older adults showed weaker activations than younger adults in left PFC, left medial temporal lobe (MTL), left temporal, and anterior cingulate regions. The authors suggested that older adults failed to engage the appropriate encoding network, encoded faces insufficiently, and, as a consequence, showed poorer recognition performance.

Madden *et al.* (1996) examined simple semantic retrieval (lexical decision) and passive encoding tasks. Consistent with visual perception data reviewed in the previous section, ventral pathway activity during lexical decision was weaker in older than in younger adults. An age-related decrease in ventral pathway activity was also found during passive encoding, although more anteriorly in Area 20. The passive encoding task also yielded an age-related activity reduction in medial PFC (left Areas 32/10).

Cabeza *et al.* (1997a) investigated intentional encoding of word pairs. Consistent with the previous two studies, older

adults showed weaker activity than younger adults in left PFC and occipitotemporal regions. Conversely, older adults showed more activity than younger adults in several brain regions, including the right insula. This last activation was negatively correlated with delayed recall performance, suggesting it was detrimental for encoding, and is possibly related to inhibition deficits in older adults.

In Madden *et al.* (1999b) subjects made living/nonliving decisions about words while trying to memorize them. Younger adults did not show any significant activation, but there were two regions that showed significant age-related increases in older adults: the left thalamus and the red nucleus. According to the authors, living/nonliving task was not difficult enough to elicit activations in these regions in younger adults, but it was sufficiently difficult to elicit activations in older adults. They also suggested that the thalamic activation in older adults could reflect increased attention during encoding.

Grady *et al.* (1999, not included in Table 1) examined the encoding of pictures and words during intentional, deep incidental, and shallow incidental learning. Picture encoding was associated with extrastriate and MTL regions, and word encoding, with frontotemporal regions. Although older adults showed weaker MTL activity during picture encoding, their picture memory was not impaired, which suggests that extrastriate activity may be sufficient for maintaining picture memory in older adults.

Anderson *et al.* (2000) investigated word-pair encoding under full or divided attention. Under full-attention, older adults showed weaker activity in several left PFC regions. Some of these regions were similarly affected by aging and divided attention, which is consistent with the resources theory of aging (Craik & Byrd, 1982), and with the idea that poor episodic memory performance in older adults is partly due to impaired encoding operations mediated by the left PFC (Cabeza *et al.*, 1997a; Grady *et al.*, 1995). Several right PFC regions showed age-related increases in activity, suggesting a reduction in the left lateralized pattern shown by younger adults.

Stebbins *et al.* (in press) examined age-related differences in PFC activity during deep (concrete/abstract) and shallow (uppercase/lowercase) incidental encoding of words. In younger adults, left PFC activity was nearly twice as large as right PFC activity. In older adults, left PFC activity was reduced but right PFC was not, and as a result, the asymmetry shown by younger adults was eliminated.

Finally, Grady *et al.* (in press) investigated encoding of faces under intentional, deep, and shallow conditions. Compared to recognition, all encoding conditions in younger adults, as well as intentional and deep conditions in older adults, were associated with bilateral ventral occipitotemporal regions, including the hippocampus, and the anterior cingulate. Left temporal regions were less activated in older adults.

In summary, age-related decreases in activation were typically found in left PFC, which possibly reflects

age-related deficits in episodic encoding and/or semantic retrieval operations. In contrast, right PFC activity in older adults was as strong as, or stronger than, in younger adults. These results suggest that PFC activity was less asymmetric in older adults than in younger adults; an effect specifically noted in some studies (e.g., Stebbins *et al.*, in press).

Episodic memory retrieval

In the first activation study in this area, Grady *et al.* (1995) investigated face recognition. Right parietal and occipital activity was weaker in older adults than in younger adults, whereas right PFC activity was similar in both groups. This latter finding contrasts with the significant age-related decrease in left PFC found in the same study during face encoding. The authors suggested that age effects on the neural correlates of episodic memory are more pronounced during encoding than during retrieval.

However, a subsequent study by Schacter *et al.* (1996) found significant age-related differences in PFC activity during retrieval using a word-stem cued recall test. High and Low levels of recall performance were produced by varying encoding conditions. In the Low-High contrast, bilateral anterior PFC regions were more activated in younger than in older adults, whereas left posterior PFC (Broca's area) showed the reverse pattern. This age-related difference was attributed to a shift from memory strategies, mediated by anterior PFC, to inappropriate phonological strategies, mediated by Broca's area. In the High-Low contrast, younger and older adults showed similar hippocampal activations, which implies that this region reflects a commonality in the way younger and older adults remember past events.

Cabeza *et al.* (1997a) investigated word-pair cued recall and recognition. Consistent with Schacter *et al.* (1996), we found an age-related increase in left PFC activity during recall. Due to this activation, PFC activity during recall was right-lateralized in younger adults but bilateral in older adults. We interpreted bilateral activity in older adults as compensatory. During recognition, there was an age-related increased activation in the precuneus region. In both tests, older adults showed weaker activations in right PFC and right parietal regions, and stronger activations in left temporal and right anterior cingulate regions.

Bäckman *et al.* (1997) used a word-stem cued recall task similar to the one used by Schacter *et al.* (1996). Compared to younger adults, older adults showed weaker activations in the cerebellum—possibly reflecting a deficit in self-initiated retrieval and processing speed, and in Wernicke's area—possibly reflecting a deficit in visual-auditory recoding. Interestingly, MTL was more activated in older than in younger adults. As in Cabeza *et al.* (1997a), there was a left PFC activation in older but not in younger adults, and as a result, PFC activity was right lateralized in younger adults but bilateral in older adults.

Madden *et al.* (1999b) investigated word recognition, and again, as in Cabeza *et al.* (1997a) and Bäckman *et al.* (1997), PFC activity was right-lateralized in younger subjects but bilateral in older subjects. Activation data was subsequently analyzed using a stepwise regression method that distinguished between exponential (*tau*) and Gaussian (*mu*) components of RT distributions (Madden *et al.*, 1999a). During recognition, younger adults' right PFC activity was related only to *mu* (right BA 10), whereas older adults showed activations related to both *mu* and *tau* (right BA 10, left BA 41). Since *tau* is associated with task-specific decision processes, and *mu*, with residual sensory coding and response processes, the authors concluded that attentional demands were greater for older adults, possibly leading to the recruitment of additional regions.

Older adults tend to be more impaired on context memory than on item memory tests (Spencer & Raz, 1995). To investigate the neural basis of this differential effect, Cabeza *et al.* (2000) compared item (recognition) and temporal-order (recency) memory tests. There were three main results. First, there was an age-related decrease in right PFC activity during temporal-order retrieval, consistent with the notion that impaired context memory in older adults reflects PFC dysfunction. Second, MTL activity during item memory was similar in younger and older adults, consistent with evidence that age-related atrophy is relatively minor in MTL (Raz *et al.*, 1997). Finally, replicating the results of Cabeza *et al.* (1997a), older adults showed weaker activations than younger adults in the right PFC, but stronger activations in the left PFC. The age-related increase in left PFC activity was again interpreted as compensatory.

Anderson *et al.* (2000) investigated word-pair recall under full and divided attention conditions. Under full attention, older adults showed weaker activations primarily in right PFC but stronger activations primarily in left PFC, which suggests an attenuation of the right-lateralized pattern shown by younger adults.

Finally, in Grady *et al.*'s (in press) study, older adults showed more activity in left anterior PFC during face recognition than younger adults. Replicating Cabeza *et al.* (1997a), this age-related increase in left PFC made PFC activity more bilateral in older adults than in younger adults.

To sum up, during episodic memory retrieval, age-related decreases in activation were typically found in right PFC and right parietal regions, whereas age-related increases in activation were typically found in left PFC, as well as in bilateral anterior cingulate and cuneus/precuneus regions. Given that PFC activity was usually right lateralized in younger adults, age-related decreases in right PFC activity coupled with age-related increases in left PFC activity often led to a more symmetric pattern of PFC activity in older adults. In contrast with PFC, MTL activity was preserved in older adults (Bäckman *et al.*, 1997; Cabeza *et al.*, 2000; Schacter *et al.*, 1996), consistent with evidence that MTL

regions show less age-related structural decline than PFC (Raz *et al.*, 1997).

Implicit memory

Older adults tend to be impaired in explicit but not in implicit memory tests. Bäckman *et al.*'s (1997, not shown in Table 1) investigated age-related changes on the neural correlates of implicit memory. As expected, the amount of priming in a word-stem completion test was equivalent in younger and older adults. Consistent with the behavioral pattern, priming in a word-stem completion test was associated with a similar right occipital deactivation in younger and older adults. Taken together with the significant behavioral and activation differences found in the recall condition of the same study, these results support the idea that aging alters the neural correlates of explicit memory but not those of implicit memory.

Working memory

Grady *et al.* (1998) investigated a face working memory task and varied the maintenance interval between 1 and 21 sec. There were three interesting findings. First, activity in right PFC area 45 was greater in younger than in older adults, and increased with longer delays only for younger adults, which suggests that only younger adults were better able to engage this region as task difficulty increased. Second, older adults showed greater activity in left frontal BA 9/45, possibly reflecting a compensatory mechanism or increased task demands. Finally, as delay extended from 1 to 6 sec, left MTL activity increased in younger adults but decreased in older adults, which implies that older adults have difficulties initiating memory strategies mediated by MTL or sustaining MTL activity beyond very short retention intervals.

In McIntosh *et al.*'s (1999, not included in Table 1) study, subjects maintained a target sine wave grating in visual short-term memory for either 0.4 or 4 sec, and then compared its spatial frequency to a probe grating. The difference in spatial frequency between targets and probes was adjusted for each subject, thereby matching performance across subjects. Despite equivalent performance, older adults showed weaker interactions among the regions underlying task performance. Conversely, they recruited unique PFC and MTL regions, which were related to task performance only in older adults. These results suggest that older adults compensated for reduced network interactions by recruiting additional brain regions.

Reuter-Lorenz *et al.* (2000) investigated verbal and spatial working memory tasks. The main finding of the study was that in younger adults, PFC activity was left-lateralized in the verbal task but right lateralized in the spatial task, whereas in older adults, PFC activity was bilateral in both tasks. As in Cabeza *et al.* (1997a), this age-related hemispheric asymmetry reduction was interpreted as compensa-

tory. Supporting this hypothesis, in the verbal working memory tasks, those older adults who showed a bilateral activation pattern were faster than those that did not.

Rypma *et al.* (in press) examined working memory for different memory loads (1 vs. 6 letters). The six-minus-one contrast yielded three main findings. First, left-lateralized ventrolateral PFC activity was similar in younger and older adults. Second, right-lateralized dorsolateral PFC was weaker in older than in younger adults. Finally, a left anterior PFC region was more activated in older than in younger adults. The authors suggested that aging impairs executive aspects of working memory mediated by dorsolateral PFC, but not maintenance operations (e.g., phonological loop) mediated by ventrolateral PFC. Additionally, as in Cabeza *et al.* (1997a), the age-related increased left PFC activity was attributed to functional compensation.

Taking advantage of event-related fMRI, Rypma and D'Esposito (2000) differentiated the effects of aging on the encoding, maintenance, and retrieval stages of working-memory. The main result was that ventrolateral PFC did not show significant age-related differences during any stage, whereas dorsolateral PFC showed an age-related decrease during the retrieval stage. These results are consistent with the aforementioned idea that aging affects executive aspects of working memory mediated by dorsolateral PFC rather than maintenance operations mediated by ventrolateral PFC (Rypma *et al.*, in press), and additionally suggest that the retrieval phase is more sensitive to aging than encoding and maintenance phases. Another interesting result of this study was that dorsolateral PFC activity during retrieval was positively correlated with response speed in older adults but negatively correlated in younger adults, which indicates that greater PFC activity may be beneficial for older adults but detrimental for younger adults.

Two working memory studies—not included in Table 1—focused on specific cognitive processes during working memory. Jonides *et al.* (2000) investigated inhibition processes by comparing an interference condition, in which distractors were previously presented letters that had to be inhibited, to a control condition, in which distractors were novel. The interference-control contrast yielded a left ventrolateral PFC activation, which was significantly weaker in older adults. Since older adults were more impaired by the interference manipulation than younger adults, this result suggest that aging diminishes the efficacy of the left PFC in inhibiting the interfering effects of prepotent processes.

Mitchell *et al.* (2000) investigated the binding of object and spatial information. In each trial, participants were presented an object in a particular screen location and had to hold in working memory the object, its location, or both (combination trials). In younger, but not in older adults, left anterior hippocampal activity was greater for combination trials than for object and location trials, which suggests that hippocampal dysfunction underlies age-related binding deficits.

Finally, two studies investigated problem-solving tasks dependent on executive functions. Nagahama *et al.* (1997) examined a modified version of the Wisconsin Card Sorting Test (WCST). This test was associated with left dorsolateral PFC, bilateral frontopolar, and cuneus regions in both groups. Age-related reductions in activation were found in several regions, including left PFC, bilateral parietal, and cerebellar gyrus, possibly reflecting strategy differences. The right ventrolateral PFC was activated in older adults but not in younger adults, although the age effect was nonsignificant. Nagahama *et al.* suggested that this activation could reflect greater effort to maintain selective attention. The age-related decrease in left PFC activity, coupled with the age-related increase in right PFC, suggests a more bilateral pattern of PFC activity in older adults.

Esposito *et al.* (1999) examined the WCST and the Raven's Progressive Matrices (RPM) test on a relatively large group of subjects evenly distributed from 18 to 80 years of age. During RPM, regions that were activated in younger adults (e.g., parahippocampal, fusiform, and parietal regions) were less activated in older adults, whereas regions deactivated in younger adults (e.g., frontopolar and superior temporal regions) were less deactivated in older adults. The authors suggested this attenuation of activation/deactivation patterns could reflect an age-related reduction in mental flexibility. During WCST, however, older adults also showed activations (e.g., anterior PFC, cuneus, MTL) and deactivations (e.g., left PFC, anterior cingulate, and cerebellar regions) not shown by the younger adults. According to Esposito *et al.*, these age-related differences may reflect a failure to engage appropriate networks and suppress inappropriate networks, or a compensatory use of alternative networks. Using a method reported by Cabeza *et al.* (1997b), Esposito *et al.* found that PFC-parietal interactions within the working-memory system and temporal-parietal-hippocampal interactions within posterior visuospatial processing systems were altered in older adults. The authors interpreted this finding in terms of disconnectivity and systems failure.

To sum up working memory results, older adults tended to show weaker PFC activations in the hemisphere primarily engaged by the young, but stronger PFC activations in the contralateral hemisphere. The effects of aging on PFC activity were found for dorsolateral rather than for ventrolateral regions, and during the retrieval phase, rather than during encoding and maintenance phases. Age-related inhibition deficits were associated with weaker activity in left ventrolateral PFC, and age-related binding deficits, with weaker activity in MTL regions.

Regional summary

Previous sections reviewed age-related changes in activation according to cognitive functions, but one may also consider these changes according to brain regions. For example,

Table 1 indicates that left temporal and anterior cingulate activity tended to show age-related increases during perception but age-related decreases during encoding. Parietal activity often displayed right-lateralized decreases during episodic retrieval, and left-lateralized decreases during executive tasks. Occipital activity typically showed decreases during perception. Cerebellar activity frequently showed decreases during executive working memory tasks. However, age-related changes in temporal, parietal, occipital, and cerebellar activity do not appear very regular when compared to those in PFC activity.

Age-related changes on PFC activity are remarkably consistent. PFC activity typically showed bilateral age-related increases during perception, left-lateralized decreases during episodic encoding/semantic retrieval, and left-lateralized increases during episodic retrieval. During working memory, age-related decreases in PFC activity were typically found in the hemisphere primarily engaged by the young, and age-related increases, in the contralateral hemisphere. The most parsimonious way of describing age-related changes on PFC activity is in terms of their effects on the overall lateralization of PFC activity. Since PFC activity during episodic encoding/semantic retrieval is typically left-lateralized in younger adults, age-related reductions in left PFC activity often led to a more bilateral pattern of PFC activity in older adults. Likewise, since PFC activity during episodic retrieval is usually right-lateralized in younger adults, age-related increases in left PFC activity also tended to make PFC activity more bilateral in older adults. Finally, since age-related increases in PFC activity during working memory usually occurred in the hemisphere less activated in young adults, these changes also tended to produce a less asymmetric pattern of PFC activity in older adults. Thus, the effects of aging on PFC activity during these three functions can be summarized in a very simple statement: PFC activity was less asymmetric in older adults than in younger adults. This is the most consistent finding of all functional neuroimaging studies of cognitive aging, and the topic of the second part of this paper.

HEMISPHERIC ASYMMETRY REDUCTION IN OLDER ADULTS

In our 1997 study, we noted that PFC activity was right lateralized in younger adults but bilateral in older adults (Cabeza *et al.*, 1997a). Since 1997, this finding has been replicated many times. Thus, this finding was recently postulated as a general aging phenomenon, which was called Hemispheric Asymmetry Reduction in Old Adults or HAROLD (Cabeza, 2001; Cabeza, submitted). Below, functional neuroimaging data (see Table 2) and other evidence supporting the HAROLD model, is summarized and two possible explanations are discussed: the compensation and the dedifferentiation hypotheses.

Table 2. Functional neuroimaging evidence for the HAROLD model

Study	Younger		Older	
	Left	Right	Left	Right
Episodic Retrieval				
Pair Cued Recall: Cabeza <i>et al.</i> (1997)	–	++	+	+
Stem Cued Recall: Bäckman <i>et al.</i> (1997)	–	+	+	+
Word Recognition: Madden <i>et al.</i> (1999)	–	+	++	++
Face Recognition: Grady <i>et al.</i> (in press)	–	++	+	+
Perception				
Face matching: Grady <i>et al.</i> (2000)	+	+++	++	++
Episodic Encoding/Semantic Retrieval				
Word—incidental: Stebbins <i>et al.</i> (in press)	++	+	+	+
Word—intentional: Buckner <i>et al.</i> (submitted)	++	+	+	+
Word—incidental: Buckner <i>et al.</i> (submitted)	++	+	++	++
Working Memory				
Letter WM: Reuter-Lorenz <i>et al.</i> (2000)	+	–	+	+
Location WM: Reuter-Lorenz <i>et al.</i> (2000)	–	+	+	+
Number N-back: Dixit <i>et al.</i> (2000)	+	+++	++	++

Note. Plus signs indicate significant activity in the left or right PFC, and minus signs indicate nonsignificant activity. The number of pluses is an index of the amount of neural activity *within each study* but not across studies.

Functional neuroimaging evidence

Episodic Retrieval. In younger adults, PFC activity during episodic memory tends to be left lateralized during encoding and right lateralized during retrieval, a pattern known as Hemispheric Encoding/Retrieval Asymmetry (HERA) model (Nyberg *et al.*, 1996; Nyberg, Cabeza & Tulving, 1998; Tulving *et al.*, 1994). In our 1997 study (Cabeza *et al.*, 1997a), we found that PFC activity during word-pair cued-recall was right lateralized in younger adults (consistent with the HERA model), but bilateral in older adults (inconsistent with the HERA model). We interpreted this age-related change as compensatory. In just three years, this finding has been replicated three times: It was found for word-stem cued-recall (Bäckman *et al.*, 1997), word recognition (Madden *et al.*, 1999b), and face recognition (Grady *et al.*, in press). Thus, age-related asymmetry reductions during episodic memory retrieval have been demonstrated for different kinds of tests (recall and recognition) and different kinds of stimuli (verbal and pictorial), and hence, they appear to be a robust and general phenomenon.

Perception. In the aforementioned study by Grady *et al.* (2000) on perception of degraded and nondegraded faces, right hemisphere activity was greater in younger than in older adults. According to the authors: “This finding, coupled with that of greater left-hemisphere activation in older adults, may indicate a more bilateral involvement of the brain in nondegraded face matching with increasing age” (p. 180). In this study, the age-related hemispheric asymmetry reduction applies to both PFC and temporal regions.

Episodic Encoding and Semantic Retrieval. As mentioned above, Stebbins *et al.* (in press) found that an age-related reduction in PFC activity in left PFC but not in right PFC. “The age-associated reduction in left prefrontal activation eliminated the left hemisphere asymmetry evident in younger participants who exhibited twice as much activation in left relative to right prefrontal activation”. This finding was recently replicated by Buckner *et al.* (in preparation) during intentional encoding. Interestingly, providing older adults with a semantic processing strategy (i.e., increased environmental support) increased older adult’s PFC activity in both hemispheres, but did not increase their hemispheric asymmetry.

Working Memory. The aforementioned working memory study by Reuter-Lorenz and collaborators (2000) provided strong support for HAROLD, particularly because the reduction in asymmetry was found both when PFC activity was left lateralized in younger adults (verbal working memory) and when it was right lateralized in younger adults (spatial working memory). An age-related asymmetry reduction during working memory was also found in a recent study Dixit and colleagues (2000). Middle-aged participants showed weaker activity in the region most robustly activated by younger adults, right PFC, but showed stronger activity in several regions, including left PFC. The fact that this change had occurred prior to age 50 suggests that HAROLD onsets in middle age.

Electrophysiological and behavioral evidence Evidence for HAROLD has also been provided by electrophysiological

and behavioral studies. In event-related potentials (ERPs) studies, language-related effects tend to be greater over left hemisphere electrodes (e.g., Elmo, 1987; Nelson, Collins & Torres, 1990). Consistent with this pattern, Bellis *et al.* (2000) have recently found that, in children and younger adults, a N1 effect associated with auditory processing of syllables occurred only in the left hemisphere. In older adults, however, the N1 effect was bilateral. Thus, HAROLD may occur not only for perception and memory functions, but also for language functions.

Evidence for HAROLD can be found in behavioral experiments. Reuter-Lorenz *et al.* (1999) performed an experiment in which subjects matched letters projected either to the same or to the opposite visual field (hemisphere). There were three levels of task complexity: low, medium, and high. In younger adults, within-hemisphere matching was faster when complexity was low, across-hemisphere matching was faster when complexity was high, and they were equivalent when complexity was medium. These results are consistent with the idea that at high levels of complexity the benefits of engaging resources from both hemispheres outweigh the costs of interhemispheric communication (Banich, 1998). In older adults, however, the benefits of bilateral processing were evident at lower levels of complexity; they showed an advantage for across-hemisphere matching in both medium and high complexity conditions. Thus, older adults benefit from bihemispheric processing at levels of task complexity for which unilateral processing is enough in younger adults (Reuter-Lorenz *et al.*, 1999).

Explanations of HAROLD

In 1997, we suggested that age-related asymmetry reductions reflect a compensation mechanism: To counteract neurocognitive deficits, older adults engage both hemispheres for tasks that require basically one hemisphere in younger adults (Cabeza *et al.*, 1997a). Consistent with this compensation hypothesis, those older adults who displayed a bilateral pattern of PFC activity in Reuter-Lorenz *et al.*'s (2000) study were *faster* in the verbal working memory task than those who did not. The compensation hypothesis is also consistent with evidence that recovery of function after unilateral brain damage is facilitated by the recruitment of homologous regions in the unaffected hemisphere. Evidence of the involvement of the healthy hemisphere during recovery of motor and language functions has been found using a variety of techniques, including PET (Buckner, Corbetta, Schatz, Raichle & Petersen, 1996; Di Piero, Chollet, MacCarthy, Lenzi & Frackowiak, 1992; Engelen *et al.*, 1995; Honda *et al.*, 1997; Ohyama *et al.*, 1996; Weiller *et al.*, 1995) and fMRI (Cao, Vikingstad, Paige George, Johnson & Welch, 1999; Thulborn, Carpenter & Just, 1999). For example, an fMRI study showed that several months after a left-hemisphere stroke, better language recovery

was observed in aphasic patients who showed bilateral activations (Cao *et al.*, 1999).

An alternative view is that age-related asymmetry reductions reflect a difficulty to recruit specialized neural mechanisms. This view is implied by the hypothesis of an age-related dedifferentiation of cognitive abilities (for a review, see Li & Lindenberger, 1999). The dedifferentiation hypothesis is primarily supported by evidence that correlations among different cognitive measures, and between cognitive and sensory measures, tend to increase with age. For example, Baltes and Lindenberger (1997) found that median intercorrelations between five cognitive measures increased from 0.37 in younger adults to 0.71 in older adults (see also, Babcock, Laguna & Roesch, 1997; Mitrushina & Satz, 1991).

Compensation and dedifferentiation views can both account for the activation data in Table 2. The compensation view can more easily accommodate evidence linking age-related asymmetry reduction to improved cognitive performance (Reuter-Lorenz *et al.*, 2000), whereas the dedifferentiation view fits better with other findings (e.g., Buckner *et al.*, submitted). However, available evidence is not enough to distinguish between these two views. Also, it is possible that compensation and dedifferentiation accounts are both correct. For example, fusing cognitive functions together could help counteract age-related neurocognitive deficits. Although it is implicitly assumed that age-related increases in inter-measure correlations are detrimental for performance, there is no definite evidence available that this is the case. Conversely, a compensatory reduction in hemispheric asymmetry would tend to increase similarity across tasks (e.g., bilateral activity for both verbal and spatial working memory; Reuter-Lorenz *et al.*, 2000), possibly accounting for an age-related increase in inter-measure correlations.

CONCLUSIONS

Despite its young age, the field of functional neuroimaging of cognitive aging has already identified several reliable patterns of results. In the case of PFC activity, most studies are consistent with the notion that neural activity is less asymmetric in older adults than in younger adults. Although the neural mechanisms and function of this hemispheric asymmetry reduction in old adults (HAROLD) are still unknown, the consistency of the pattern is noteworthy, particularly when one takes into account the small number of studies surveyed. As noted before, in the case of parietal, occipital, temporal, and subcortical regions, results have not been as consistent as in the case of PFC. Moreover, the complexity of age effects on brain activity increments exponentially if one considers not only regional increases and decreases in activation but also age-related changes in connectivity (e.g., Cabeza *et al.*, 1997b; McIntosh *et al.*, 1999). At any rate, even if we are far from a clear

understanding of age-related changes in neurocognitive function, the remarkable level of convergence that has been achieved in only six years is very encouraging.

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