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Aging Gracefully: Compensatory Brain Activity in High-Performing Older Adults

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Whereas some older adults show significant cognitive deficits, others perform as well as young adults. We investigated the neural basis of these different aging patterns using positron emission tomography (PET). In PET and functional MRI (fMRI) studies, prefrontal cortex (PFC) activity tends to be less asymmetric in older than in younger adults (Hemispheric Asymmetry Reduction in Old Adults or HAROLD). This change may help counteract age-related neurocognitive decline (compensation hypothesis) or it may reflect an age-related difficulty in recruiting specialized neural mechanisms (dedifferentiation hypothesis). To compare these two hypotheses, we measured PFC activity in younger adults, low-performing older adults, and high-performing older adults during recall and source memory of recently studied words. Compared to recall, source memory was associated with right PFC activations in younger adults. Low-performing older adults recruited similar right PFC regions as young adults, but high-performing older adults engaged PFC regions bilaterally. Thus, consistent with the compensation hypothesis and inconsistent with the dedifferentiation hypothesis, a hemispheric asymmetry reduction was found in high-performing but not in low-performing older adults. The results suggest that low-performing older adults recruited a similar network as young adults but used it inefficiently, whereas high-performing older adults counteracted age-related neural decline through a plastic reorganization of neurocognitive networks.

INTRODUCTION

As we age, our brains undergo a series of deleterious changes, including gray and white matter atrophy, synaptic degeneration, blood flow reductions, and neurochemical alterations (Raz, 2000; Cabeza, 2001). Given these changes, it is not surprising that older adults perform more poorly than young adults in a variety of cognitive tasks, including perception, attention, and memory tasks (Craik and Salthouse, 2000). However, whereas some older adults show pronounced cognitive deficits, others perform as well or better than young adults (Christensen *et al.*, 1999). An intriguing possibility is that high-performing older adults counteract age-related neural decline by reorganizing brain functions.

In positron emission tomography (PET) and functional MRI (fMRI) studies, higher-order cognitive functions, such as episodic memory, have been associated with prominent activations in the prefrontal cortex (PFC, for reviews, see Cabeza and Nyberg, 2000; Fletcher and Henson, 2001). These prefrontal cortex activations are sometimes lateralized, possibly reflecting the nature of the processes and/or the stimuli involved (e.g., Nyberg *et al.*, 1996; Smith and Jonides, 1997; Kelley *et al.*, 1998; McDermott *et al.*, 1999). Recent evidence indicates that the lateralization of PFC activations tends to be reduced by aging, and this empirical regularity was conceptualized in terms of a model called Hemispheric Asymmetry Reduction in Old Adults, or HAROLD (Cabeza, 2002). As listed in Table 1, the HAROLD model is supported by functional neuroimaging evidence in a variety of cognitive domains, including episodic memory retrieval (Bäckman *et al.*, 1997; Cabeza *et al.*, 1997; Madden *et al.*, 1999; Grady *et al.*, 2002), episodic encoding/semantic retrieval (Logan *et al.*, 2002; Morcom *et al.*, 2002; Stebbins *et al.*, 2002), working memory (Dixit *et al.*, 2000; Reuter-Lorenz *et al.*, 2000), perception (Grady *et al.*, 1994, 2000), and inhibitory control (Nielson *et al.*, 2002). Age-related asymmetry reductions have been also observed in electrophysiological (Bellis *et al.*, 2000) and behavioral (Reuter-Lorenz *et al.*, 1999) studies.

Although the evidence for age-related asymmetry reductions is strong, the function of these changes is

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TABLE 1

PET/fMRI Activity in Left and Right PFC in Younger and Older Adults

Cognitive domain Imaging technique: Materials/task (Ref.)	Younger		Older	
	Left	Right	Left	Right
Episodic retrieval				
PET: Pair cued-recall (Cabeza *et al.*, 1997)	−	++	+	+
PET: Stem cued-recall (Bäckman *et al.*, 1997)	−	+	+	+
PET: Word recognition (Madden *et al.*, 1999)	−	+	++	++
PET: Face recognition (Grady *et al.*, 2002)	−	++	+	+
Episodic encoding/semantic retrieval				
fMRI: Word—incidental (Stebbins *et al.*, 2002)	++	+	+	+
fMRI: Word—intentional (Logan *et al.*, 2002)	++	+	+	+
fMRI: Word—incidental (Logan *et al.*, 2002)	++	+	++	++
fMRI: Word—subsequent memory (Morcom *et al.*, 2002)	++	+	++	++
Working memory				
PET: Letter DR (Reuter-Lorenz *et al.*, 2000)	+	−	+	+
PET: Location DR (Reuter-Lorenz *et al.*, 2000)	−	+	+	+
PET: Number N-back: (Dixit *et al.*, 2000)	+	+++	++	++
Perception				
PET: Face matching (Grady *et al.*, 1994, Expt. 2)	−	+	++	++
PET: Face matching (Grady *et al.*, 2000)	+	+++	++	++
Inhibitory control				
fMRI: No-go trails (Nielson *et al.*, 2002)	−	+	+	+

Note. Plus signs indicate significant activity in the left or right PFC, and minus signs indicate nonsignificant activity. The number of plusses is an approximate index of the relative amount of activity in left and right PFC in each study, and it cannot be compared across studies. DR, delayed response task.

still unclear. According to a compensation hypothesis (Cabeza *et al.*, 1997; Cabeza, 2002), increased bilaterality in old adults could help counteract age-related neurocognitive deficits. Consistent with this hypothesis, in the PET study by Reuter-Lorenz *et al.* (2000), older adults who displayed a bilateral pattern of PFC activity were *faster* in a verbal working memory task than those who did not. The compensation hypothesis is also supported by evidence that hemispheric asymmetry reductions may facilitate recovery from brain damage. Numerous studies have demonstrated that recovery of motor and language functions after unilateral brain damage may involve the recruitment of the unaffected nondominant hemisphere. This finding has been observed with a variety of techniques, including electrophysiological measures (Honda *et al.*, 1997; Thomas *et al.*, 1997); transcranial magnetic stimulation (Cicinelli *et al.*, 1997; Netz *et al.*, 1997), Doppler ultrasonography (Silvestrini *et al.*, 1993; Silvestrini *et al.*, 1998), Xenon-133 imaging (Brion *et al.*, 1989; Demeurisse and Capon, 1991), PET (Di Piero *et al.*, 1992; Engelien *et al.*, 1995; Weiller *et al.*, 1995; Buckner *et al.*, 1996; Ohyama *et al.*, 1996; Honda *et al.*, 1997), and functional MRI (Cao *et al.*, 1999; Thulborn *et al.*, 1999). As a result of contralateral recruitment, cognitive functions that are strongly lateralized in the healthy brain may become more bilateral following brain damage, and several studies have directly linked successful recovery of function to bihemispheric involvement. For example, a longitudinal study using Doppler ultrasonography found that after a period of speech therapy, word fluency in a group of aphasic patients was associated with a bilateral increase in flow velocity (Silvestrini *et al.*, 1993). An fMRI study found a similar result: several months after a left-hemisphere stroke, better language recovery was observed in aphasic patients who showed bilateral activations (Cao *et al.*, 1999). Because bihemispheric involvement can facilitate recovery from brain damage, it is reasonable to assume that it may also play a compensatory function in the aging brain.

However, there is an alternative account of age-related asymmetry reductions: according to a dedifferentiation hypothesis, reduced hemispheric asymmetry in old adults may reflect an age-related difficulty in recruiting specialized neural mechanisms (Li and Lindenberger, 1999). The notion of age-related dedifferentiation is supported by evidence that correlations among different cognitive measures tend to increase with age (e.g., Mitrushina and Satz, 1991; Babcock *et al.*, 1997; Baltes and Lindenberger, 1997) and by computer simulations linking age-related declines in catecholamine function to an increase in "neural noise" (Li and Lindenberger, 1999; Li *et al.*, 2000). According to the dedifferentiation hypothesis, age-related asymmetry reductions are just another example of the deleterious effects of aging on brain function.

The main goal of the present study was to contrast predictions of the compensation and dedifferentiation hypotheses. Before scanning, we tested 33 older adults

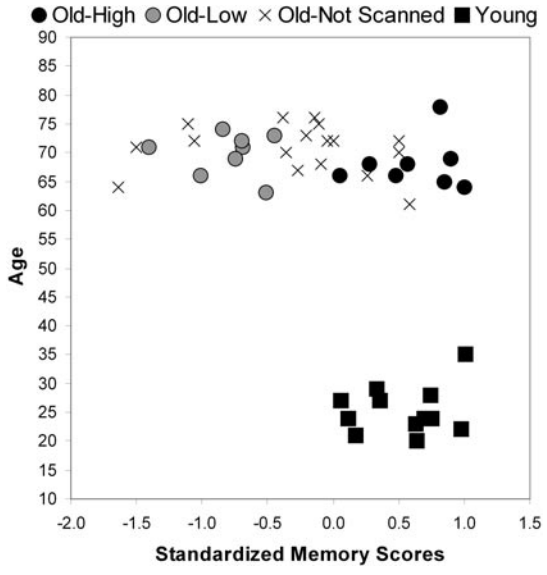

FIG. 1. Standardized composite memory scores for young and older adults that completed a battery of memory tests during a screening session. Among older adults, eight who performed as well as young adults (Old-High) and eight who performed significantly below young adults (Old-Low) were selected to be part of the PET study.

and 12 young adults (Young participants) on a battery of memory tests. As illustrated in Fig. 1, we selected 8 older adults that performed as well young adults (Old-High participants) and 8 older adults that performed significantly below than young adults (Old-Low participants). The three groups of participants were PET scanned while performing two memory tests, recall and source memory. These tests were selected because they yielded a clear dissociation in the lateralization of PFC activity in a previous PET study with young adults: whereas left PFC was more activated for recall than for source memory, right PFC showed the converse pattern (Cabeza *et al.*, 2001). Given asymmetric PFC activity in young adults, the compensation hypothesis predicts that hemispheric asymmetry reductions in PFC activity should be greater in Old-High participants than in Old-Low participants. Moreover, the compensation hypothesis predicts that these hemispheric asymmetry reductions should occur in the most demanding of the two tasks, which in the present study was the source task. In contrast, the dedifferentiation hypothesis predicts that hemispheric asymmetry should occur in the group of older adults showing more pronounced age-related cognitive decline, that is, the Old-Low participants. In summary, finding the HAROLD pattern during source memory in Old-High participants would support the compensation hypothesis, whereas finding the HAROLD pattern in Old-Low participants would support the dedifferentiation hypothesis. If the HAROLD pattern is not found in either group, the validity of the HAROLD model could be questioned.

METHODS

Participants

The participants of the PET study were 12 Young participants (5 female, 7 male; age range: 20–35), 8 Old-High participants (4 female, 4 male; age range: 64–78), and 8 Old-Low participants (4 female, 4 male; age range: 63–74). The age of the two old groups (see Table 2) was similar ($P > 0.3$) and greater than the age of the young group. Old-High and Old-Low participants were selected using a composite memory score based on the results of four memory measures: Logical Memory I, Verbal Paired Associates I, and Visual Paired Associates II from the Wechsler Memory Scale-Revised (Wechsler, 1987) and the Long-Delay Cued Recall from the California Verbal Learning Test (Delis *et al.*, 1987). These tasks were selected because they previously have been shown to distinguish older adults with low and high mnemonic functioning (Glisky *et al.*, 1995). The raw and standardized scores of these screening tests are listed in Table 2. The average standardized scores, which were used for selecting participants, are listed in Table 2 and Fig. 1. Average standardized scores were similar for Young and Old-High participants ($P > 0.6$), but significantly lower for Old-Low than for Young and Old-High participants (both $P < 0.001$). Despite significant differences in memory performance, the three groups were equivalent (all $P > 0.3$) in four tests assumed to reflect executive function and general intellectual performance (see Table 2): Wisconsin Card Sorting Test (WCST), orthographic fluency test (FAS), mental arithmetic test (WAIS-R), and mental control test (WMS-R). All participants were right handed and had no history of neurological or psychiatric illness. None of the participants was taking medication or had a medical condition that could affect cerebral blood flow (e.g., high blood pressure). The study was approved by the joint Baycrest Centre/University of Toronto Research Ethics and Scientific Review Committee.

Behavioral Methods

The study consisted of two sessions, screening and PET. During the screening session, participants filled out demographic and health questionnaires and completed several neuropsychological tests including the ones used for screening (see above). At the end of the screening session, they practiced the tasks to be performed in the scanner. The PET session took place several days after the screening session and included participants selected according to their level of memory performance (see above). In both the recall and the

TABLE 2

Behavioral Data

	Young		Old-High		Old-Low	
	M	SD	M	SD	M	SD
Age	25.3	4.1	68.0	4.4	69.9	3.7
Executive tasks						
WCST test	6.0	0.0	6.0	0.0	5.6	1.1
FAS	46.8	11.9	48.3	11.1	49.4	9.4
Mental control (WAIS-R)	5.3	1.3	5.1	1.0	5.3	1.2
Mental arithmetic	13.0	3.9	15.3	2.7	14.0	3.9
Screening tasks						
Raw scores						
Logical Memory I	29.5	5.9	32.3	6.4	25.4	5.0
Pair Associates I	22.6	1.1	21.9	1.5	17.3	2.8
Pair Associates II	6.0	0.0	6.0	0.0	4.6	1.6
CVLT	14.1	1.4	14.3	1.6	9.8	1.7
Standardized scores						
Logical Memory I	0.38	0.92	0.81	0.99	−0.26	0.77
Pair Associates I	0.81	0.28	0.62	0.38	−0.57	0.72
Pair Associates II	0.34	0.00	0.34	0.00	−1.15	1.73
CVLT	0.63	0.58	0.70	0.66	−1.19	0.70
Standardized mean	0.54	0.33	0.62	0.33	−0.79	0.30
Scanned tasks						
Recall	0.75	0.14	0.86	0.07	0.64	0.19
Source	0.73	0.17	0.73	0.16	0.55	0.23

Note. CVLT, California Verbal Learning Test.

context memory conditions, subjects studied a list of items before the scan and their memory for these items was tested during the scan. At study, items were presented at a 3 s/item rate, and subjects were instructed to remember them for a subsequent memory test. In both conditions, the study list was presented once or four times, but for the present analyses we averaged across this manipulation. In the recall condition, subjects studied a visually presented list of 24 unrelated word-pairs (e.g., lawyer–window), and during the scan, they were presented the first word of each studied pair (e.g., lawyer) and tried to recall the second word (e.g., window). In the source recognition test, subjects studied two lists of 12 single words before the scan, 1 presented auditorily and 1 visually, and during the scan, they read each studied word and decided whether the word was either heard or read during the study phase. At test, words were presented for 4 s and followed by fixation for 1 s. The test list started 30 s before and continued 30 s after the 60-s scan window. In all conditions, subjects responded to each item by saying 1 word aloud: the word recalled in the recall task and "seen" or "heard" in CRN. In the recall task, if subjects could not recall a word before fixation appeared, they said "pass" so that 1 word was spoken in every trial.

PET Methods

Two PET scans were conducted for each of the two tasks, and the order of two tasks was counterbalanced across subjects. The PET session included other scans that are not reported here. PET scans were obtained with a GEMS-Scanditronix PC2048-15B head scanner using a bolus injection of 35.5 mCi of $15O–H_2O$. Image processing and statistical analyses were performed using SPM99b (Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab (Mathworks Inc., Sherborn, MA). First, the different images from each subject were realigned to the first image. Second, the realigned images from each subject were transformed into a standard space (Talairach and Tournoux, 1988) and smoothed using a 10-mm isotropic Gaussian kernel. Third, the effects of the conditions on the regional cerebral blood flow at each voxel were estimated using a general linear model, wherein the changes in global counts are considered as a covariate. The effects of each comparison were estimated using linear contrasts, which yield a t statistic (expressed as a Z-score) for a given comparison at each voxel. Statistical comparisons were performed in two steps. (1) PFC regions showing significant task effects (recall vs source) were identified at a threshold of $Z \geq 3.09$ ($P < 0.001$ uncorrected). (2) For the handful of PFC regions identified in Step 1, task × group interactions were identified with a threshold of $Z \geq 2.66$ ($P < 0.005$ uncorrected). Since in all these regions one group was different than the other two, task × group interactions compared one group to the average of the other two groups. Table 3 reports the results for the grouping that yielded the significant interaction, such as Young

TABLE 3

PFC Regions Showing Significant Task Effects and Task × Group Interactions

Contrast PFC region	BA	Task effects: Young				Old-Low				Old-High				Task × group interactions				
		x	*y*	*z*	*Z*	*x*	*y*	*z*	*Z*	*x*	*y*	*z*	*Z*	Pattern	*x*	*y*	*z*	*Z*
Recall > source																		
Left dorsolateral	9	−30	44	36	3.9									Y > OL/OH	−26	44	36	3.3
Left ventrolateral/insula	47/44	−28	4	−4	3.6	−34	0	8	3.9	−28	28	−8	3.1	Y/OL > OH	−28	22	−4	4.7
Source > recall																		
Right dorsolateral	9/45	44	20	28	5.5	42	18	40	4.2					Y > OL/OH	42	14	20	3.5
Right anterior	10	34	50	8	3.6	24	56	12	4.3	26	56	−4	4.6	OL/OH > Y	22	56	−4	4.1
Left anterior	10									−38	50	4	4.1	OH > Y/OL	−38	50	4	2.7

Note. Y, young; OL, old-low; OH, old-high.

vs Old-High/Old-Low (e.g., SPM contrast: 2, −2, −1, 1, −1, 1). In both steps, the risk of false-positive activations was further reduced by setting a minimum activation size of 10 contiguous voxels.

RESULTS

Behavioral Data

Memory performance during scanning was consistent with the screening data. Recall accuracy and source memory accuracy adjusted by chance are shown in Table 2. A 3 (group) × 2 (task) ANOVA yielded reliable main effects of group ($F = 4.8$, $P < 0.002$) and task ($F = 5.2$, $P < 0.04$) and a nonsignificant group × task interaction ($F < 1$). The main effect of task reflected lower accuracy for source memory than for recall. Although the group × task interaction was not reliable, the recall–source difference was numerically greater in the older adults groups than in the young adults group. To investigate significant main effect of group, Fisher PLSD contrasts were performed between each pair of groups. These contrasts showed that performance for Young ($P < 0.03$) and Old-High ($P < 0.01$) was significantly higher than for Old-Low, whereas the difference between Young and Old-High ($P > 0.4$) was not significant. Therefore, consistent with subject selection, Old-High participants performed as well as Young participants whereas Old-Low participants performed reliably below Young participants. Given differences in group size, the results were checked using nonparametric tests. A Kruskal–Wallis test confirmed a significant group effect ($P < 0.02$), a Kolmogorov–Smirnov test confirmed the critical difference between Old-High and Old-Low groups ($P < 0.03$), and a Wilcoxon test confirmed that accuracy was lower for source than for recall memory ($P < 0.05$).

PET Data

PFC regions showing significant effects of task and task × group interactions are listed in Table 3. All the regions that showed a significant task effects in one or more of the groups (Young, Old-Low, and Old-High columns) also showed a significant task × group interaction (rightmost column). In the recall-minus-source contrast, Young adults showed significant activations in left dorsolateral (Brodmann area (BA) 9) and ventrolateral (BA 47/44) regions. Old-Low and Old-High adults showed only the left ventrolateral activation, which was weaker in Old-High participants than in the other two groups. Confirming these impressions, group × task interactions indicated that the left dorsolateral activation was greater in Young than in Old-Low and Old-High participants and that the left ventrolateral activation was greater in Young and Old-Low participants than in Old-High participants.

In the source-minus-recall contrast, Young adults showed significant PFC activations in right dorsolateral (9/45) and right anterior (BA 10) regions. Old-Low participants showed activations in the same two right PFC regions, although the dorsolateral activation was weaker than in Young adults and the anterior activation was stronger than in Young adults. Old-High participants also showed stronger activity than Young adults in right anterior PFC, but this group did not show the right dorsolateral activation. More importantly, Old-High participants showed a left anterior PFC activation not shown by either Young or Old-Low participants. Group × task interactions confirmed that the right dorsolateral PFC activation was greater in Young than in Old-Low and Old-High participants, whereas the right anterior PFC activation was greater in Old-High and Old-Low participants than in Young participants. Group × task interactions also confirmed the critical finding that the left anterior activation was significantly greater in Old-High than in Young and Old-Low participants.

Thus, consistent with the compensation hypothesis, only Old-High participants showed a reduction in hemispheric asymmetry, and this reduction was found during the most demanding memory task, that is, the

source memory task. As depicted in Fig. 2, PFC activity during source memory was right lateralized in Young and Old-Low participants but bilateral in Old-High participants. Old-Low participants showed stronger activity than Young participants in right anterior PFC, but the location and lateralization of PFC activity during source memory were the same as in Young adults. In contrast, Old-High participants did not show the right dorsolateral PFC activation shown by Young and Old-Low participants and showed instead a left anterior PFC activation that was not displayed by the other two groups.

DISCUSSION

The present results provide strong support for the compensation hypothesis of age-related hemispheric asymmetry reductions. As shown in Fig. 2, PFC activity during source memory was right lateralized in Young and Old-Low participants but bilateral in Old-High participants. Thus, consistent with the compensation hypothesis, an age-related asymmetry reduction was found for the best performing group during the most demanding task. This finding suggests that Old-High participants responded to the retrieval demands of the source memory task by recruiting bilateral PFC regions. In contrast, the results are not consistent with the dedifferentiation hypothesis of age-related asymmetry reductions. If reduced lateralization is just another example of the deleterious effects of aging on the brain (e.g., atrophy), then it should have occurred in the group of elderly adults displaying more pronounced age-related cognitive deficits (Old-Low participants), but it did not. On the contrary, reduced lateralization was found in the group of elderly that performed as well as young adults, suggesting that it is a beneficial rather than a detrimental change.

The present results suggest that in terms of functional compensation additional activity within the same hemisphere is less effective than the recruitment of homologous regions in the contralateral hemisphere. During source memory, both groups of older adults showed greater activity in the same right anterior PFC region recruited by young adults. If one assumes that this age-related increase in within-hemisphere activation reflected an attempt of functional compensation, one would have to conclude that the attempt was unsuccessful because Old-Low participants performed significantly more poorly than Young adults in the source memory task. In contrast, the recruitment of a homologous region in the contralateral hemisphere was only shown by Old-High participants, who performed as well as Young adults in the source memory task. Thus, the present results suggest that whether age-related increases in activity are successful in terms of compensation depends on whether they involve the same regions engaged by young adults or additional

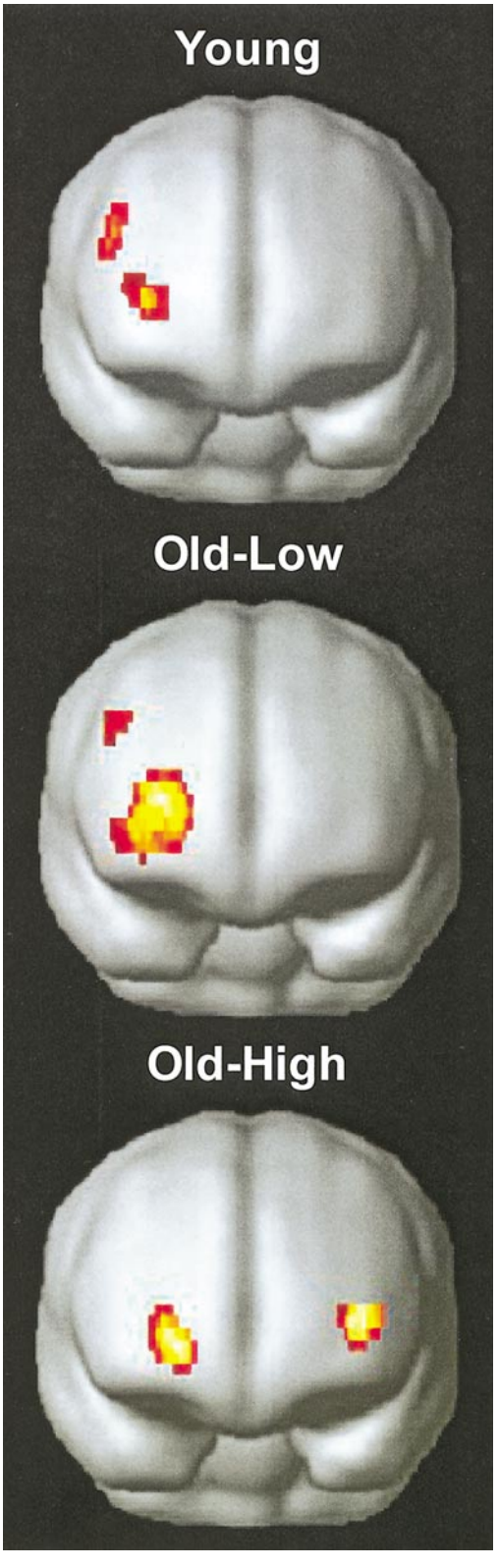

FIG. 2. PFC activity during source memory was right lateralized in Young and Old-Low participants but bilateral in Old-High participants.

regions in the contralateral hemisphere. One possible explanation is that additional within-hemisphere activity does not involve a network modification, whereas additional contralateral activity involves the recruitment of an alternative network. In those terms, the present results suggest that Old-Low engaged a similar memory network as Young participants but used it less efficiently, whereas Old-High participants compensated age-related memory decline by reorganizing memory networks.

The cognitive functions of the particular PFC regions showing age-related changes in activation can be inferred from previous functional neuroimaging research. It is generally held that episodic retrieval involves two processes: generate processes in which candidate information is retrieved and recognize processes that select from among the retrieved information. We have recently proposed that the left PFC is more involved in production processes, whereas the right PFC is more involved in monitoring processes (Cabeza *et al.*, 2001). Accordingly, the present results suggest that during source memory, Old-Low participants tried to compensate memory deficits by recruiting additional monitoring processes mediated by right PFC, while Old-High participants also tapped additional production processes mediated by left PFC. These ideas are consistent with the present behavioral results because additional monitoring processes are less likely to counteract insufficient information recovery than are additional production processes. As for the age-related decreases in dorsolateral PFC activity (left BA 9 during recall and right BA 9/45 during recall) shown by both groups of older participants, they are consistent with evidence that dorsolateral PFC activity is particularly sensitive to aging (Rypma and D'Esposito, 2000; Rypma *et al.*, 2001). Age-related reductions in dorsolateral PFC may reflect working memory deficits associated with cognitive aging (Rypma and D'Esposito, 2000; Zacks *et al.*, 2000; Rypma *et al.*, 2001).

Although the present study focused on PFC activity, there is some evidence that age-related asymmetry reductions can occur beyond PFC. For example, in a PET study on face encoding (Grady *et al.*, 2002), age-related asymmetry reductions were found not only in PFC but also in temporal and parietal regions. Also, in a PET study on face perception (Grady *et al.*, 2000), positive correlations between temporoparietal activity and memory performance were found in the left hemisphere for young adults but bilaterally for old adults. Moreover, in an fMRI study on inhibitory control (Nielson *et al.*, 2002), young adults showed a more bilateral activation pattern in PFC as well as parietal regions. Thus, several functional neuroimaging studies suggest that age-related asymmetry reductions may also apply to temporal and parietal regions.

If reduced hemispheric asymmetry in old adults can have a compensatory function, how could we take advantage of this mechanism in order to attenuate age-related cognitive decline? The answer to this question depends on whether age-related asymmetry reductions have a cognitive or a neural origin (for a discussion, see Cabeza, 2002). If age-related asymmetry reductions reflect a change in cognitive strategies, then strategies that lead to bilateral PFC recruitment could be identified and taught to low-performing older adults. However, it is unlikely that age-related asymmetry reductions are primarily cognitive in origin, because they have been observed for simple perceptual (Grady *et al.*, 1994, 2000) and motor (Calautti *et al.*, 2001) tasks in which cognitive strategies play little or no role. Moreover, there is evidence that manipulations of cognitive strategies may affect the overall level of PFC activity in older adults without affecting age-related asymmetry reductions (Logan *et al.*, 2002). If age-related asymmetry reductions have a neural origin, then a good understanding of the neural mechanisms underlying these reductions may eventually lead to the development of drugs and other therapies. Regardless of whether the interventions are made at the cognitive or neural level, functional neuroimaging techniques could provide non-invasive measures to guide the intervention process.

In summary, during a source memory task, young adults and low-performing older adults recruited similar right PFC regions, whereas high-performing older adults engaged PFC regions bilaterally. These results suggest that low-performing older adults recruit a similar network of brain regions as young adults but use them inefficiently, whereas high-performing older adults counteract age-related neural decline by reorganizing brain functions.

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REFERENCES

Babcock, R. L., Laguna, K. D., and Roesch, S. C. 1997. A comparison of the factor structure of processing speed for younger and older adults: Testing the assumption of measurement equivalence across age groups. *Psychol. Aging* **12:** 268–276.

Bäckman, L., Almkvist, O., Andersson, J., Nordberg, A., Windblad, B., Rineck, R., and Lågström, B. 1997. Brain activation in young and older adults during implicit and explicit retrieval. *J. Cogn. Neurosci.* **9:** 378–391.

Baltes, P. B., and Lindenberger, U. 1997. Emergence of a powerful connection between sensory and cognitive functions across the adult life span: A new window to the study of cognitive aging? *Psychol. Aging* **12:** 12–21.

Bellis, T. J., Nicol, T., and Kraus, N. 2000. Aging affects hemispheric asymmetry in the neural representation of speech sounds. *J. Neurosci.* **20:** 791–797.

Brion, J. P., Demeurisse, G., and Capon, A. 1989. Evidence of cortical reorganization in hemiparetic patients. *Stroke* **20:** 1079–1084.

Buckner, R. L., Corbetta, M., Schatz, J., Raichle, M. E., and Petersen, S. E. 1996. Preserved speech abilities and compensation following prefrontal damage. *Proc. Natl. Acad. Sci. USA* **93:** 1249–1253.

Cabeza, R. 2001. Functional neuroimaging of cognitive aging. In *Handbook of Functional Neuroimaging of Cognition* (R. Cabeza and A. Kingstone, Eds.), pp. 331–377. MIT Press, Cambridge, MA.

Cabeza, R. 2002. Hemispheric asymmetry reduction in old adults: The HAROLD Model. *Psychol. Aging* **17:** 85–100.

Cabeza, R., Grady, C. L., Nyberg, L., McIntosh, A. R., Tulving, E., Kapur, S., Jennings, J. M., Houle, S., and Craik, F. I. M. 1997. Age-related differences in neural activity during memory encoding and retrieval: A positron emission tomography study. *J. Neurosci.* **17:** 391–400.

Cabeza, R., Locantore, J. K., and Anderson, N. D. 2001. Lateralization of prefrontal cortex activity during episodic memory retrieval: Evidence for the production-monitoring hypothesis. *J. Cognit. Neurosci.*, in press.

Cabeza, R., and Nyberg, L. 2000. Imaging Cognition II: An empirical review of 275 PET and fMRI studies. *J. Cogn. Neurosci.* **12:** 1–47.

Calautti, C., Serrati, C., and Baron, J.-C. 2001. Effects of age on brain activation during auditory-cued thumb-to-index opposition: A positron emission tomography study. *Stroke* **32:** 139–146.

Cao, Y., Vikingstad, E. M., Paige George, K., Johnson, A. F., and Welch, K. M. A. 1999. Cortical language activation in stroke patients recovering from aphasia with functional MRI. *Stroke* **30:** 2331–2340.

Christensen, H., Mackinnon, A. J., Korten, A. E., Jorm, A. F., Henderson, A. S., Jacomb, P., and Rodgers, B. 1999. An analysis of diversity in the cognitive performance of elderly community dwellers: Individual differences in change scores as a function of age. *Psychol. Aging* **14:** 365–379.

Cicinelli, P., Traversa, R., and Rossini, P. M. 1997. Post-stroke reorganization of brain motor output to the hand: A 2–4 month follow-up with focal magnetic transcranial stimulation. *Electroencephalogr. Clin. Neurophysiol.* **105:** 438–450.

Craik, F. I. M., and Salthouse, T. A. 2000. *Handbook of Aging and Cognition II.* Erlbaum, Mahwah, NJ.

Delis, D. C., Kramer, J. H., Kaplan, E., and Ober, B. A. 1987. *California Verbal Learning Test: Adult Version Manual.* The Psychological Corporation, San Antonio, TX.

Demeurisse, G., and Capon, A. 1991. Brain activation during a linguistic task in conduction aphasia. *Cortex* **27:** 285–294.

Di Piero, V., Chollet, F. M., MacCarthy, P., Lenzi, G. L., and Frackowiak, R. S. 1992. Motor recovery after acute ischaemic stroke: A metabolic study. *J. Neurol. Neurosurg. Psychiatry* **55:** 990–996.

Dixit, N. K., Gerton, B. K., Dohn, P., Meyer-Lindenberg, A., and Berman, K. F. 2000. Age-related changes in rCBF activation during an N-Back working memory paradigm occur prior to age 50. *NeuroImage* **5**(Part 2): S94.

Engelien, A., Silbersweig, D., Stern, E., Huber, W., Doring, W., Frith, C., and Frackowiak, R. S. 1995. The functional anatomy of recovery from auditory agnosia. A PET study of sound categorization in a neurological patient and normal controls. *Brain* **118:** 1395–1409.

Fletcher, P. C., and Henson, R. N. A. 2001. Frontal lobes and human memory: Insights from functional neuroimaging. *Brain* **124:** 849–881.

Glisky, E. L., Polster, M. R., and Routhieaux, B. C. 1995. Double dissociation between item and source memory. *Neuropsychology* **9:** 229–235.

Grady, C. L., Bernstein, L. J., Beig, S., and Siegenthaler, A. L. 2002. The effects of encoding strategy on age-related changes in the functional neuroanatomy of face memory. *Psychol. Aging* **17:** 7–23.

Grady, C. L., Maisog, J. M., Horwitz, B., Ungerleider, L. G., Mentis, M. J., Salerno, J. A., Pietrini, P., Wagner, E., and Haxby, J. V. 1994. Age-related changes in cortical blood flow activation during visual processing of faces and location. *J. Neurosci.* **14:** 1450–1462.

Grady, C. L., McIntosh, A. R., Horwitz, B., and Rapoport, S. I. 2000. Age-related changes in the neural correlates of degraded and nondegraded face processing. *Cogn. Neuropsychol.* **217:** 165–186.

Honda, M., Nagamine, T., Fukuyama, H., Yonekura, Y., Kimura, J., and Shibasaki, H. 1997. Movement-related cortical potentials and regional cerebral bllod flow in patients with stroke after motor recovery. *J. Neurol. Sci.* **146:** 117–126.

Kelley, W. M., Miezin, F. M., McDermott, K. B., Buckner, R. L., Raichle, M. E., Cohen, N. J., Ollinger, J. M., Akbudak, E., Conturo, T. E., Snyder, A. Z., and Petersen, S. E. 1998. Hemispheric specialization in human dorsal frontal cortex and medial temporal lobe for verbal and nonverbal memory encoding. *Neuron* **20:** 927–936.

Li, S., Lindenberger, U., and Frensch, P. A. 2000. Unifying cognitive aging: From neuromodulation to representation to cognition. *Neurocomputing* **32–33:** 879–890.

Li, S.-C., and Lindenberger, U. 1999. Cross-level unification: A computational exploration of the link between deterioration of neurotransmitter systems dedifferentiation of cognitive abilities in old age. In *Cognitive Neuroscience of Memory* (L.-G. Nilsson and H. J. Markowitsch, Eds.), pp. 103–146. Hogrefe & Huber, Seattle.

Logan, J. M., Sanders, A. L., Snyder, A. Z., Morris, J. C., and Buckner, R. L. 2002. Under-recruitment and nonselective recruitment: Dissociable neural mechanisms associated with aging. *Neuron* **33:** 827–840.

Madden, D. J., Turkington, T. G., Provenzale, J. M., Denny, L. L., Hawk, T. C., Gottlob, L. R., and Coleman, R. E. 1999. Adult age differences in functional neuroanatomy of verbal recognition memory. *Hum. Brain Mapp.* **7:** 115–135.

McDermott, K. B., Buckner, R. L., Petersen, S. E., Kelley, W. M., and Sanders, A. L. 1999. Set- and code-specific activation in frontal cortex: An fMRI study of encoding and retrieval of faces and words. *J. Cogn. Neurosci.* **11:** 631–640.

Mitrushina, M., and Satz, P. 1991. Analysis of longitudinal covariance structures in assessment of stability of cognitive functions in elderly. *Brain Dysfunction* **4:** 163–173.

Morcom, A. M., Good, C. D., Frackowiak, R. S., and Rugg, M. D. 2002. Age effects on the neural correlates of successful encoding. *Brain*, in press.

Netz, J., Lammers, T., and Homberg, V. 1997. Reorganization of motor output in the non-affected hemisphere after stroke. *Brain* **120:** 1579–1586.

Nielson, K. A., Langenecker, S. A., and Garavan, H. P. 2002. Differences in the functional neuroanatomy of inhibitory control across the adult lifespan. *Psychol. Aging* **17:** 56–71.

Nyberg, L., Cabeza, R., and Tulving, E. 1996. PET studies of encoding and retrieval: The HERA model. *Psychonomic Bull. Rev.* **3:** 135–148.

Ohyama, M., Senda, M., Kitamura, S., Ishii, K., Mishina, M., and Terashi, A. 1996. Role of the nondominant hemisphere and undamaged area during word repetition in poststroke aphasics. *Stroke* **47:** 897–903.

Raz, N. 2000. Aging of the brain and its impact on cognitive performance: Integration of structural and functional findings. In *Handbook of Aging and Cognition—II* (F. I. M. Craik and T. A. Salthouse, Eds.). Erlbaum, Mahwah, NJ.

Reuter-Lorenz, P., Jonides, J., Smith, E. S., Hartley, A., Miller, A., Marshuetz, C., and Koeppe, R. A. 2000. Age differences in the frontal lateralization of verbal and spatial working memory revealed by PET. *J. Cogn. Neurosci.* **12:** 174–187.

Reuter-Lorenz, P. A., Stanczak, L., and Miller, A. C. 1999. Neural recruitment and cognitive aging: Two hemispheres are better than one, especially as you age. *Psychol. Sci.* **10:** 494–500.

Rypma, B., and D'Esposito, M. 2000. Isolating the neural mechanisms of age-related changes in human working memory. *Nat. Neurosci.* **3:** 509–515.

Rypma, B., Prabhakaran, V., Desmond, J. D., and Gabrieli, J. D. E. 2001. Age differences in prefrontal cortical activity in working memory. *Psychol. Aging* **16:** 371–384.

Silvestrini, M., Cupini, L. M., Placidi, F., Diomedi, M., and Bernardi, G. 1998. Bilateral hemispheric activation in the early recovery of motor function after stroke. *Stroke* **29:** 1305–1310.

Silvestrini, M., Troisi, E., Matteis, M., Razzano, C., and Caltagirone, C. 1993. Correlations of flow velocity changes during mental activity and recovery from aphasia in ischemic stroke. *Neurology* **50:** 191–195.

Smith, E. E., and Jonides, J. 1997. Working memory: A view from neuroimaging. *Cogn. Psychol.* **33:** 5–42.

Stebbins, G. T., Carrillo, M. C., Dorman, J., Dirksen, C., Desond, J., Turner, D. A., Bennett, D. A., Wilson, R. S., Glover, G., and Gabrieli, D. E. 2002. Aging effects on memory encoding in the frontal lobes. *Psychol. Aging* **17:** 44–55.

Talairach, J., and Tournoux, P. 1988. *A Co-planar Sterotactic Atlas of the Human Brain.* Thieme, Stuttgart, Germany.

Thomas, C., Altenmuller, E., Marckmann, G., Kahrs, J., and Dichgans, J. 1997. Language processing in aphasia: Changes in lateralization patterns during recovery reflect cerebral plasticity in adults. *Electroencephalogr. Clin. Neurophysiol.* **102:** 86–97.

Thulborn, K. R., Carpenter, P. A., and Just, M. A. 1999. Plasticity of language-related brain function during recovery from stroke. *Stroke* **30:** 749–754.

Wechsler, D. 1987. *Wechsler Memory Scale—Revised.* The Psychological Corporation, San Antonio, TX.

Weiller, C., Isensee, C., Rijntsjes, M., Huber, W., Müller, S., Bier, D., Dutschka, K., Woods, R. P., Noth, J., and Diener, H. C. 1995. Recovery from Wernicke's Aphasia: A positron emission tomography study. *Ann. Neurol.* **37:** 723–732.

Zacks, R. T., Hasher, L., and Li, K. Z. H. 2000. Human memory. In *Handbook of Aging and Cognition II.* (F. I. M. Craik and T. A. Salthouse, Eds.), Vol. 293–357. Erlbaum, Mahwah, NJ.