Aging reduces neural specialization in ventral visual cortex

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The present study investigated whether neural structures become less functionally differentiated and specialized with age. We studied ventral visual cortex, an area of the brain that responds selectively to visual categories (faces, places, and words) in young adults, and that shows little atrophy with age. Functional MRI was used to estimate neural activity in this cortical area, while young and old adults viewed faces, houses, pseudowords, and chairs. The results demonstrated significantly less neural specialization for these stimulus categories in older adults across a range of analyses.

There is growing behavioral evidence that the functional architecture of cognition becomes dedifferentiated with age: A number of studies have found that correlations among distinct measures of cognitive function are more intercorrelated in older subjects than in younger adult subjects (1–5). Furthermore, markers of central sensory function (e.g., corrected visual and auditory acuity) account for virtually all age-related variance on a broad array of higher-order cognitive tasks, including speed of processing, memory, verbal fluency, and reasoning (4, 6). Based on these and related findings, Baltes and Lindenberger (6) argued that aging reduces the degree to which behavior is specialized (or differentiated) for individual tasks and that a domain-independent decline in neural integrity is the mechanism underlying this dedifferentiation. Providing a more specific mechanism for dedifferentiation, Li *et al.* (7) have argued that both empirical and computational data suggest that increased age results in a decrease in distinctiveness of neural representations due to deficient dopaminergic modulation. With the advent of neuroimaging techniques, the dedifferentiation hypothesis can be addressed more directly than is possible with behavioral techniques alone. Thus, in the present study, we test whether neural structures become dedifferentiated with age, by examining the degree of category-specificity that is present in ventral visual cortex in young and old adults.

A few recent neuroimaging studies suggest that age-related dedifferentiation may indeed apply at the neural level. Most of these studies have found that older adults exhibit bilateral prefrontal activity in tasks for which younger adults exhibit lateralized activity. This pattern has been observed in working memory tasks (8), in semantic judgments (9), and in long-term memory tasks (10). However, it is unclear whether such results imply age-related dedifferentiation. For one thing, the functions performed by different areas of prefrontal cortex are poorly understood. It is therefore difficult to interpret the functional significance of bilateral prefrontal activation in elderly subjects (11–13). Does the additional activation reflect the recruitment of more neural resources that are functionally specialized for the task being performed (which does not imply dedifferentiation of function)? Or does it reflect the involvement of areas that are specialized in young adults but perform more general functions in older subjects (which would be consistent with dedifferentiation)? Or perhaps the additional activations exhibited by old are dysfunctional and do not enhance task performance at all. Answering questions like these is difficult without knowing what functions the activated prefrontal areas perform. A second problem is that prefrontal cortex exhibits disproportionate atrophy with age compared with other cortical areas (14). It is therefore possible that the observed age-related changes in the laterality of prefrontal activity reflect an age-independent response to atrophy. A number of studies suggest that cortical damage leads to recruitment of contralateral cortical areas (15–17), so perhaps prefrontal atrophy also leads to contralateral recruitment, independent of age. Alternatively, the increased activation with age could be due to decreases in dopamine receptors, demyelination, or other aspects of neurobiological aging.

In the present study, we focus our attention on ventral visual cortex. This area exhibits clear evidence of neural differentiation in young adults. Functional neuroimaging studies of healthy young adults have revealed that different parts of ventral visual cortex respond maximally to faces (18), to places (19–20), and to orthography (21). It has also recently been demonstrated that a variety of other object categories elicit distinct neural signatures in ventral visual cortex (22). Based on these results, there is considerable debate about whether localized regions of ventral visual cortex are specialized for specific categories of visual stimuli (23), or whether processing of these categories is more distributed across much of ventral visual cortex (22). What is unquestionable, however, is that different categories of visual stimulus elicit different patterns of activity in ventral visual cortex (differentiation), and that these differences can be reliably detected with functional neuroimaging techniques.

Unlike frontal cortex, there is relatively little age-related atrophy in visual cortex with age as measured by volumetric studies (14) [although postmortem studies reveal less neural density in visual areas with age (24)]. Moreover, the functions of different areas of ventral visual cortex are better understood than are the functions of prefrontal areas. Hence, clear focal hypotheses about what constitutes evidence for age-related dedifferentiation in the ventral visual cortex can be developed. Specifically, if there is less neural specialization (more dedifferentiation) with age, the neural activity patterns elicited by different categories of visual stimuli (e.g., faces, places, and words) should be less distinctive in old adults than they are in young adults. Furthermore, evidence for age-related neural dedifferentiation in ventral visual cortex would suggest a compromised neural system at earlier stages of processing than has been demonstrated with studies of frontal function.

Methods

Subjects. We tested 13 younger adults (mean age of 20.8 years with seven males and six females) who were undergraduates at the University of Michigan and 12 older adults (minimum age of 60, mean age of 69.9 years, with five males and seven females)

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Data deposition: The neuroimaging data have been deposited with the fMRI Data Center, www.fmridc.org (accession no. 2-2004-1167W).

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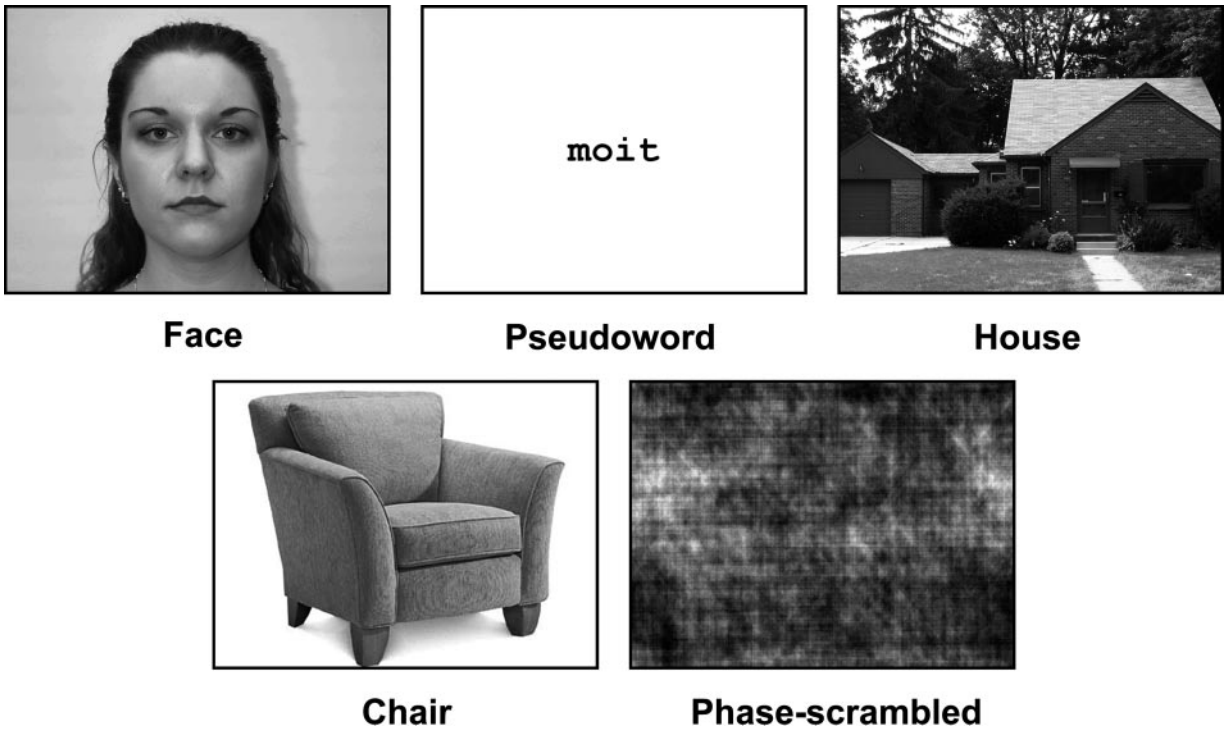

Fig. 1. Examples of stimuli from the categories of faces, houses, chairs, pseudowords, and phase-scrambled versions of the same stimuli (which served as control).

who were active residents of the Ann Arbor community. All subjects were right-handed and were screened for disease, major depression, and artificial lens implants. No subjects were taking any medications that have a known effect on brain function. Subjects had corrected 20/40 vision or better and the correction was used while scanning took place. Minimental scores for young and old adults were 29.92 and 28.08, respectively, with 30 being a perfect score. Older adults had a significantly higher vocabulary score than young adults [34.92 vs. 30.75, $t(22) = 3.68$, $P < 0.001$], but lower working memory span performance on the Wechsler Adult Intelligence Scale letter/number reordering task (4.75 vs. 6.17 for old/young, $t(22) = 3.65$, $P < 0.001$) and lower speed of processing scores [digit comparison task: 66.92 vs. 77.67 for old/young, $t(22) = 2.38$, $P < 0.05$].

Stimulus Materials. Five categories of stimuli were used: faces, places (pictures of houses), pseudowords, pictures of chairs, and phase-scrambled control stimuli. We used faces, places, and pseudowords because some of the best evidence for neural specialization in young adults has been found using these stimulus categories. Some researchers have argued that the visual recognition of these three categories is subserved by localized neural tissue (18–20), although, as mentioned earlier, these claims are controversial (22, 23). We included chairs so that we would have one category of stimulus for which no such claims of localization have been made [although chairs do elicit a specific but distributed neural signature in the ventral visual area that can be distinguished from the patterns produced by the other stimuli (22)].

The experimenters developed a library of gray-scale photographs of faces, houses, and chairs. Examples of stimuli are presented in Fig. 1. The face library was created by photographing several hundred paid adult volunteers at a shopping mall in Ohio. The photographs of chairs were taken off furniture web sites. Houses were photographed from various locations across the U.S. In addition, a series of four- to six-letter pseudowords, used in Polk and Farah (25), were used for the orthographic condition. Finally, control pictures were created by scrambling the phase information present in all of the experimental stimuli so that the spatial frequency information was otherwise preserved (the power spectra were identical), but the visual information was meaningless.

Procedure. All subjects were tested in a Signa 3 Tesla scanner. Neural activity was estimated based on the blood oxygenation level-dependent signal by using a spiral acquisition sequence (2,000-ms repetition time, 30 5-mm axial slices, 24-cm field of view, 30-ms echo time, and 90° flip angle). Stimuli were presented in three runs with 15 20-sec blocks per run. Each run contained three blocks of each of the five categories of stimuli (faces, chairs, houses, pseudowords, and phase-scrambled pictures) that were presented in a pseudorandom order. Subjects were instructed to view each picture and to try to remember them (we did so only to ensure attention to the pictures, subjects were not given a subsequent memory test).

Each run began with a 20-sec rest period to allow tissue magnetization to reach steady state and to allow participants to become acclimated to the noise. Each 20-sec block consisted of 10 items from the same category presented for 1,500 msec each, followed by a 500-msec intertrial interval. Structural images were high-resolution T1-weighted images collected in 30 5-mm-thick axial slices parallel to the anterior commissure to the posterior commissure line.

Results

After reconstruction, the data were preprocessed to correct for differences in the acquisition times of each of the slices, to correct for motion, and to eliminate data outside the brain. The data were then analyzed on a voxel-by-voxel basis by using a general linear model corrected to deal with temporal autocorrelation in the data. Regressors were included in the general

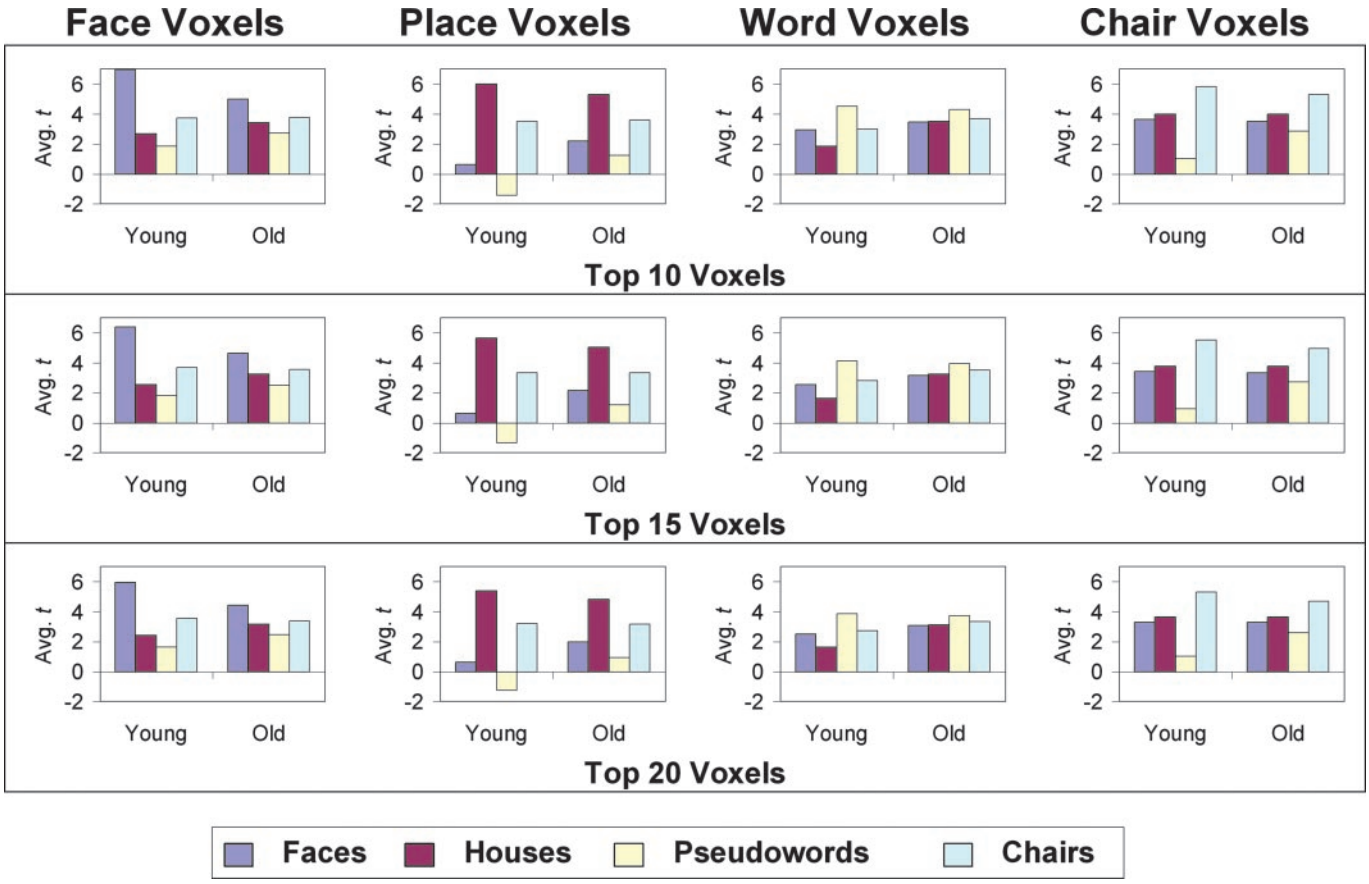

Fig. 2. Mean *t* values as a function of age and stimulus category. (*Top*) The 10 voxels most activated by faces, places, pseudowords, and chairs. (*Middle*) The 15 voxels most activated by faces, places, pseudowords, and chairs. (*Bottom*) The 20 voxels most activated by faces, places, pseudowords, and chairs.

linear model for each of the major stimulus conditions: faces, places, chairs, pseudowords, and phase-scrambled stimuli.

Analysis of Neural Selectivity to Categories as a Function of Age. We analyzed data within an anatomical mask of ventral visual cortex that included the parahippocampal gyrus, the inferior temporal gyrus, and the portion of the fusiform gyrus anterior to the level of the anterior occipital sulcus. Within this masked area, for each subject we isolated the 10, 15, and 20 most active voxels for faces, places, pseudowords, and chairs relative to the phase-scrambled control stimuli. In the first analysis, the voxels were selected from the ventral visual mask based only on level of activation and without regard to contiguity among voxels. We used three different sizes for these functionally defined sets of active voxels to ensure that our results were not affected by thresholding artifacts. We then measured the response (mean *t* value) of these functionally defined face, place, word, and chair areas to each of the stimulus categories relative to the phase-scrambled control stimuli.

We conducted an ANOVA on the data displayed in each of the 12 bar graphs of Fig. 2. For each of these analyses, Age was a between-subject variable and Stimulus Category Viewed (faces, places, pseudowords, and chairs) was a within-subject variable. Each of the 12 bar graphs displayed in Fig. 2 yielded a significant Age × Category interaction. In every case, the interaction occurred because younger adults exhibited more category-specificity in the top voxels activated to a category than older adults did. The results for the top 10 voxels analyses are $F(3,69) = 9.13$, $P < 0.0001$ in the face voxels; $F(3,69) = 7.73$, $P < 0.0005$ in the place voxels; $F(3,69) = 4.04$, $P < 0.05$ in the word voxels; and $F(3,69) = 4.11$, $P < 0.01$ in the chair voxels. For the top 15 voxels analyses, the results are $F(3,69) = 10.1$, $P < 0.0001$ in the face voxels; $F(3,69) = 8.70$, $P < 0.0001$ in the place voxels; $F(3,69) = 5.71$, $P < 0.005$ in the word voxels; and $F(3,69) = 4.57$, $P < 0.01$ in the chair voxels. For the top 20 voxels analyses the results are $F(3,69) = 11.1$, $P < 0.0001$ in the face voxels; $F(3,69) = 6.97$, $P < 0.0005$ in the place voxels; $F(3,69) = 5.51$, $P < 0.005$ in the word voxels; and $F(3,69) = 4.92$, $P < 0.005$ in the chair voxels. Consider the face voxels in the top left bar graph in Fig. 2. The dark blue bar represents the response (mean *t* value) of the top 10 face voxels to the face stimuli. For young adults, these 10 voxels were significantly less active to pictures of houses, pseudowords, and chairs. In contrast, in the older adults the top voxels that responded to faces were also active to houses, pseudowords, and chairs, indicating shared activation to these different categories. This pattern can be seen in every bar graph of Fig. 2. We also note that for the chair voxels (last column of Fig. 2), young adults' top chair voxels only showed differentiation between chairs and words. In keeping with the pattern of dedifferentiation with age, in old adults these chair voxels showed little differentiation between words and chairs, and this difference is the basis of the significant interactions reported for the chair voxels.

To further explore these effects, three further ANOVAs were conducted; one on each row of the data displayed in Fig. 2. The overall three-way Age × Stimulus Category Viewed × Voxel Type (face, place, word, or chair) interaction was highly significant in all three cases. Younger adults displayed a significantly larger Stimulus Category Viewed × Voxel Type interaction (more distinct activation pattern for each voxel type) than the older adults. Again, this finding was true for the 10-, 15-, and 20-voxel analyses [$F(6,138) = 11.5$, $P < 0.0001$ for 10 voxels; $F(6,138) = 14.8$, $P < 0.0001$ for 15 voxels; and $F(6,138) = 14.6$,

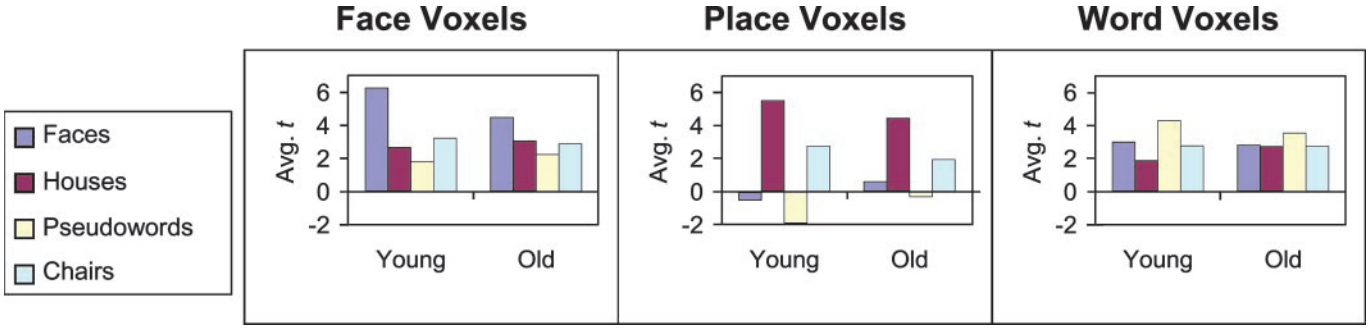

Fig. 3. Mean *t* values as a function of age and stimulus category in the 10 voxels most active in the fusiform face area (*Left*), the parahippocampal place area (*Center*), and the left fusiform word form area (*Right*).

$P < 0.0001$ for 20 voxels]. Note that the older subjects exhibited just as much overall activation as the younger subjects, as the average *t* value of the activation to all four categories vs. control across all four brain areas was actually slightly higher in the older adults (10 voxels, 3.62; 15 voxels, 3.40; 20 voxels, 3.24; average: 3.42) compared with the younger adults (10 voxels, 3.18; 15 voxels, 2.98; 20 voxels, 2.85; average: 3.00). (These differences were not significant.) Therefore, the results cannot be attributed to a floor effect or other type of scaling artifact.

The preceding analyses did not require that the top 10, 15, or 20 voxels that activated to a category be contiguous, and in general, they were not. We performed an additional analysis in which regions of interest were constrained to contain contiguous voxels. Once again, there was a highly significant Age × Stimulus Category interaction in each of the four functionally defined sets of voxels, with younger adults exhibiting more category specificity than older adults. These interactions were all significant whether the regions of interest were based on the top 10, 15, or 20 voxels [10 voxels: $F(3,69) = 10.7, P < 0.0001$ in the face voxels; $F(3,69) = 10.4$, $P < 0.0001$ in the place voxels; $F(3,69) = 4.34$, $P < 0.01$ in the word voxels; and $F(3,69) = 3.60$, $P < 0.05$ in the chair voxels; 15 voxels: $F(3,69) = 7.80$, $P < 0.0005$ in the face voxels; $F(3,69) = 7.67$, $P < 0.0005$ in the place voxels; $F(3,69) = 6.97$, $P < 0.0005$ in the word voxels; and $F(3,69) = 3.29$, $P < 0.05$ in the chair voxels; 20 voxels: $F(3,69) = 9.47$, $P < 0.0001$ in the face voxels; $F(3,69) = 9.78$, $P < 0.0001$ in the place voxels; $F(3,69) = 5.70$, $P < 0.005$ in the word voxels; and $F(3,69) = 2.86$, $P < 0.05$ in the chair voxels]. The three-way Age × Stimulus Category × Voxel Type interaction was also again significant, with younger adults exhibiting a larger Stimulus Category × Voxel Type interaction than the older adults [10 voxels: $F(6,138) = 11.6$, $P < 0.0001$; 15 voxels: $F(6,138) = 10.9$, $P < 0.0001$; and 20 voxels: $F(6,138) = 11.7$, $P < 0.0001$].

Some of the voxels in the preceding analyses were outside the brain areas in which neural specialization has been argued to exist in young adults (e.g. the fusiform gyrus bilaterally for faces, the parahippocampal gyrus bilaterally for places, and the left fusiform gyrus and collateral sulcus for words). We therefore performed another analysis in which we excluded voxels outside of these areas. (Chairs were not included in this particular analysis as there are no reports in the literature of a "chair area.") For this set of analyses, we again functionally defined face, place, and word areas based on the most active voxels, but we restricted the region of interest to narrowly defined anatomical regions within the ventral visual cortex: the fusiform gyrus bilaterally for faces, the parahippocampal gyrus bilaterally for places, and the left fusiform gyrus and collateral sulcus for words. Because there were far fewer potentially relevant voxels than before in these regions of interest, we initially conducted this more restrictive analysis based on only the 10 most active voxels for faces, places, and words. After isolating the top 10 most active voxels in each of these anatomical areas, we then measured the average response of these top voxels to each of the stimulus categories vs. the phase-scrambled control stimuli. The results are presented in Fig. 3. Once again, we observed a significant Age × Stimulus Category interaction in each of the three brain areas with younger adults exhibiting more category specificity than older adults [$F(3,69) = 5.06, P < 0.005$ in the face area; $F(3,69) = 6.23$, $P < 0.001$ in the place area; and $F(3, 69) = 4.019$, $P < 0.05$ in the word area]. The most pronounced effects were in the face and place areas. And again, the three-way Age × Stimulus Category × Voxel Type interaction was also highly significant [$F(6,138) = 11.16, P < 0.0001$] due to significantly less category specificity in the old. When we increased the number of voxels to the top 15 and the top 20, all of the interactions reported for 10 voxels were significant and were of the same form as those presented in Fig. 3.

In a final set of analyses, we asked how often a voxel that was included in a functionally defined set of voxels for one of the categories was also activated by another category. To the extent that neural activation to categories is well differentiated, one would expect fewer top voxels activated to a given category to be activated by other categories. For each subject, we thresholded the functional maps so that only the top 15 voxels for a category (e.g., faces) survived. We then applied that same threshold to the functional maps for each of the

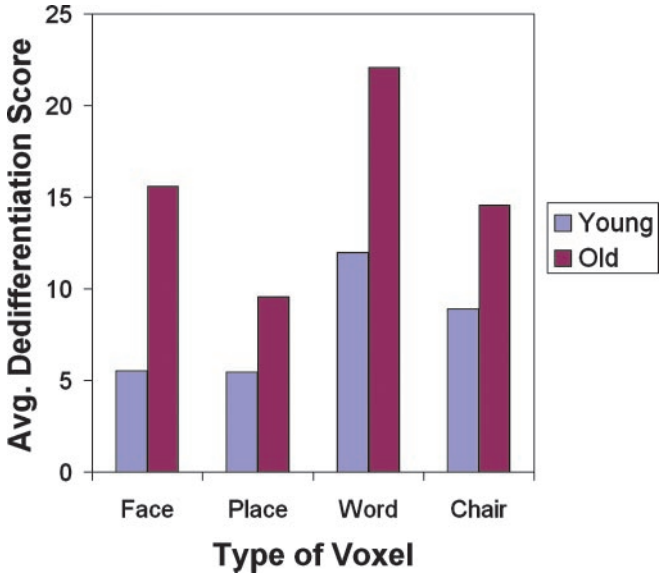

Fig. 4. Dedifferentiation score for each category type. A higher number reflects more dedifferentiation.

other three categories and calculated a ''dedifferentiation score'' for each of the 15 voxels from the original map. Specifically, we counted how often a top voxel for one category had a t value above threshold to one of the other three categories. Each voxel received a score ranging from 0 (never showed activation above threshold to another category) to 3 (activated to all three of the other categories as well as the target category). We then summed the scores for each of the 15 voxels for each subject for each category (the sums could range from 0 to 45). The results of this dedifferentiation analysis are displayed in Fig. 4. Fig. 4 demonstrates that older adults had more shared voxels across categories than young adults, and achieved higher dedifferentiation scores than young adults in all four sets of voxels [$F(1,23) = 12.882$, $P < 0.001$ in the face voxels; $F(1,23) = 3.277$, $P < 0.05$ in the place voxels; $F(1, 23) = 7.293$, $P < 0.01$ in the pseudoword voxels; and $F(1,23) = 7.930$, $P < 0.005$ in the chair voxels; the main effect of age was also highly significant after collapsing across the four sets of voxels due to the larger number of voxels to which older adults showed shared activations compared to younger adults: $F(1,23) = 21.305$, $P < 0.0001$; these tests were one-tailed].

Discussion

These findings represent clear evidence for dedifferentiation of neural response in ventral visual cortex as a result of age. Young adults, across multiple analyses, exhibited significantly more category-specific activity in ventral visual cortex compared with older adults. Behavioral dedifferentiation appears to have a basis in the brain, as originally hypothesized by Baltes and Lindenberger (6).

This finding may also provide a basis for understanding perhaps the most ubiquitous and reliable finding in all of the cognitive aging literature, that perceptual speed decreases with age (26). Perceptual speed [typically measured by the speed with which same/different judgments are made about pairs of geometric figures or pairs of digit strings or by the Wechsler Adult Intelligence Scale digit-symbol test (27)] not only declines reliably with age, but it mediates most age-related variance on a broad range of cognitive tasks (26, 28–30). Despite the powerful behavioral results demonstrating the centrality of speed for cognition in older adults, it has been difficult to identify the neural analog of decreased speed with age. Up to this point, demyelination and decreases in dopamine receptors have been the primary neural candidates accounting for age-related declines in perceptual speed (5, 11), but these accounts fail to explain why simple choice reaction time does not account for as much age-related variance in cognition as perceptual speed does (30). The present findings suggest that perceptual comparison times may be slower in older subjects due to functional dedifferentiation in high-level sensory cortex that results in more time needed to disambiguate similarities between visual stimuli. Although admittedly speculative, future work in this direction appears promising, particularly because the magnitude of dedifferentiation at the neural level is readily quantifiable and can be used as an individual differences variable.

Is the neural dedifferentiation reported here simply a result of experience as opposed to being the result of aging *per se*? Perhaps the findings arise simply because older adults have more extensive experience with visual object recognition than do young adults. We think this explanation is unlikely, particularly because it is experience that likely builds the selectivity of the neural response for some of the stimulus categories (especially pseudowords). Polk *et al.* (21) reported selective responding of ventral visual cortex in young adults for letters compared to digits. This specialization presumably arose due to experience because the distinction between letters and digits is arbitrary and culturally defined. It is therefore difficult to imagine why continued experience would undermine the very specialization it initially helped to produce.

Age-related dedifferentiation may occur in multiple neurocognitive structures. Besides the well documented increase in distributed processing in frontal cortex (8–12), which may (or may not) reflect dedifferentiation, there is also evidence for decreased distinctiveness between ventral and dorsal visual pathways in older adults (31, 32). The present findings also demonstrate decreased neural selectivity within the object recognition pathway. These data together make a compelling case for less differentiated neural architecture as a ubiquitous characteristic of aging.

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