Overrecruitment in the Aging Brain as a Function of Task Demands: Evidence for a Compensatory View

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Abstract

■ This study used fMRI to investigate the neural effects of increasing cognitive demands in normal aging and their role for performance. Simple and complex go/no-go tasks were used with two versus eight colored letters as go stimuli, respectively. In both tasks, no-go stimuli could produce high conflict (same letter, different color) or low conflict (colored numbers) with go stimuli. Multivariate partial least square analysis of fMRI data showed that older adults overengaged a cohesive pattern of fronto-parietal regions with no-go stimuli under the specific combination of factors which progressively amplified task demands: high conflict no-go trials in the first phase of the complex task. This early neural overrecruitment was positively correlated with a lower error rate in the older group. Thus, the present data suggest that age-related extrarecruitment of neural resources can be beneficial for performance under taxing task conditions, such as when novel, weak, and complex rules have to be acquired. ■

INTRODUCTION

Cognitive changes with aging are accompanied by modifications in brain functioning, as shown by neuroimaging evidence (e.g., Grady, 2008; Park, Polk, Mikels, Taylor, & Marshuetz, 2001). Although some studies report an underrecruitment of brain regions with age (e.g., Rypma & D'Esposito, 2000), different patterns of age-related neural overrecruitment have also been often described in the literature, especially under demanding task conditions. Those patterns include activations in similar areas as those engaged by young adults but with a greater magnitude of activation, a more symmetric pattern of brain activity with additional activation in homologous areas of the opposite hemisphere in the older, or additional activation of completely different areas (Morcom, Li, & Rugg, 2007; Hedden & Gabrieli, 2004; Cabeza, 2001, 2002; Logan, Sanders, Snyder, Morris, & Buckner, 2002; Park et al., 2001).

Changes in the use of cognitive and neural resources have been associated with aging in a number of different contexts. An age-related cognitive decline often occurs in tasks involving suppression of information interfering with the present goals (Sweeney, Rosano, Berman, & Luna, 2001; Hasher, Zacks, & May, 1999). Mirroring this age-specific inhibitory deficit in cognition (Hasher & Zacks, 1988), brain imaging and electrophysiological evidence shows an increased neural activity (overrecruitment) associated with processing of interfering information in older adults (Gazzaley et al., 2008; Zysset, Schroeter, Neumann, & Yves von Cramon, 2007; Gazzaley, Cooney, Rissman, & D'Esposito, 2005; Nielson, Langenecker, & Garavan, 2002; but see Grady et al., 1995).

Moreover, age-related differences in the capacity to circumvent interference from distracting nontarget information are amplified by increasing task complexity (Gazzaley, Sheridan, Cooney, & D'Esposito, 2007; Viskontas, Morrison, Holyoak, Hummel, & Knowlton, 2004). Although common factors such as generalized slowing have been proposed to explain the disrupting effects of task complexity with age (Salthouse, 1996), significant age effects remain after adequately controlling for differences in processing speed (Verhaeghen, Cerella, & Basak, 2006; Keys & White, 2000), suggesting that a number of different mechanisms may underlie an age-related decline in information processing. Again, at the neural level, age-related overrecruitment of brain regions often accompanies more complex and demanding task conditions, such as dual versus single tasks (Smith et al., 2001), source versus item memory retrieval (Morcom et al., 2007), or high versus low selection demands in word generation tasks (Persson et al., 2004).

Poor performance under nonroutine contingencies in aging (Craik & Byrd, 1982), such as during conflicting and complex task conditions, suggests an age-related decline in task setting, a hypothesized frontally based function thought to be required to establish weak stimulus–response associations or rules (Alexander, Stuss, Shallice, Picton, & Gillingham, 2005; Stuss, Shallice, Alexander, & Picton, 1995), especially when those rules compete with more prepotent ones (Vallesi, McIntosh, Alexander, & Stuss, 2009; Alexander, Stuss, Picton, Shallice, & Gillingham, 2007; Stuss & Alexander, 2007).

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As briefly reviewed above, neural overrecruitment with aging has been associated with both suppression and task complexity, although, to the best of our knowledge, no study has combined the two factors in a single experimental design. To test whether a combination of those factors amplifies neural overrecruitment in aging (i.e., when both cognitive conflict and task complexity are high), a factorial design crossing two complexity levels with two suppression levels was adopted. Specifically, two versions of a go/no-go task were used. In the simpler version, the subjects responded to red X and blue O (go stimuli) while withholding responses to the blue X and red O (high-conflict no-go stimuli) and to numbers of either color (low-conflict no-go stimuli). Go responses were prepotent for letters because they were twice more frequent than no-go responses to letters (50% vs. 25%) and because of Stroop-like effects (Stroop, 1935). A classical Stroop interference effect arises when subjects are required to name the ink color of incongruent color words (e.g., the word "BLUE" written in red ink) because it is faster to read a word than to name a color. In the present task, likewise, participants were faster in identifying the letter than its ink color and then in combining these two kinds of information in order to make a no-go decision, when appropriate.

Thus, we assumed that there was a need to suppress a prepotent go response in the presence of high-conflict no-go letters, whereas suppression was less required for low-conflict no-go stimuli, which were much faster to distinguish from go responses because they belonged to a different category (numbers vs. letters; see Vallesi, Stuss, McIntosh, & Picton, 2009 for event-related potential support to this assumption). In the more complex version, four vowels and four consonants replaced Os and Xs. A prediction was that neural overrecruitment would occur in older adults when task demands were maximal, that is, for the high-conflict no-go condition of the complex task.

Regarding specific predictions about the functional anatomy underlying the necessity to deal with increasing task demands, we expected an activation of left lateral prefrontal cortex, as lesions in this region are associated with an increase in false alarms to nontarget information in different domains and tasks (Alexander et al., 2007; Stuss & Alexander, 2007; see also Bunge, 2004; Fletcher, Shallice, & Dolan, 2000, for neuroimaging evidence). However, it is likely that a more extensive fronto-parietal network will be involved in acquiring weak and complex associations not only between stimuli and responses (e.g., Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008) but also between stimuli and a nonresponse (Vallesi, McIntosh, Alexander, et al., 2009).

To partially anticipate the findings of the present study, older adults did engage an extensive set of fronto-parietal regions for the high-conflict no-go stimuli similarly to the young adults but, as expected, overrecruited these regions in the complex task, suggesting a relation between overrecruitment and task complexity. There is some evidence indicating that age-related deficits with complex tasks especially emerge in the early stages of task performance (Willis & Nesselroade, 1990), and age differences are substantially reduced after practice (Kramer, Hahn, & Gopher, 1999). Thus, to further test how this network behaves in aging when task demands are further taxed, we capitalized on the assumption that task difficulty is high in novel situations and decreases with learning, further dividing the trials of the complex task into a first and a second run. The prediction was made that if overrecruitment is associated with increasing task demands, it should mostly occur in the first run.

When increased neural activity has been found with aging, two opposite accounts have been proposed to explain it (Grady, 2008). The compensatory view posits that neural overrecruitment reflects adaptive plasticity to improve or maintain performance despite age-related neurodegenerative modifications (Gutchess et al., 2005; Buckner, 2004; Reuter-Lorenz, 2002; Cabeza et al., 1997; Grady et al., 1994). An alternative view posits that this additional neural recruitment reflects a loss of neural specificity and efficiency with aging, especially when it is present despite worse performance in the older than in the young adults (Rypma, Eldreth, & Rebbechi, 2007; Zarahn, Rakitin, Abela, Flynn, & Stern, 2007; Colcombe, Kramer, Erickson, & Scalf, 2005; Park et al., 2001).

Our protocol provided the opportunity to test whether any neural overrecruitment observed in the present study reflects a compensatory or an inefficient use of neural resources with increasing task difficulty. We correlated an overall measure of the degree of recruitment of brain regions sensitive to task demands with accuracy on the high-conflict no-go condition of the complex task (where age differences mostly occurred). The compensatory account would suggest that the older adults who showed more neural overrecruitment in the first run would also be expected to perform better on this run (positive correlation). An opposite prediction can be made on the inefficiency account; that is, the older adults who overrecruited these regions more on the first run would also be the ones that show worse performance on this run (negative correlation).

METHODS

Participants

Fourteen young (8 women; mean age = 27 years, range = 20–34 years) and 14 older (9 women; mean age = 70 years, range = 60–80 years) volunteers took part in the study. All the participants had normal or corrected-to-normal vision. All were right-handed with an average score on the Edinburgh Handedness Inventory (Oldfield, 1971) of 87 and 89 for young and older, respectively. None of the participants had any history of drug or alcohol abuse, or history of psychiatric, neurological, or other medical illness, which might compromise cognitive function. None reported memory or other cognitive problems noted by either themselves or their relatives and friends. The two groups were also matched in their education level (17 and 16 years, for young and older, respectively). Given this high level of education, the results of the present study cannot be generalized to the whole aging population. Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975) was administered to older participants in order to screen them for dementia (score range: 28–30/30). Each participant signed an informed consent that was previously approved by the local Ethics Research Board, and received a compensation of $50. Part of the data of the young group (simple task) has already been reported elsewhere (Vallesi, McIntosh, Alexander, et al., 2009).

Experimental Material and Design

Stimuli were presented centrally against a gray background. Participants viewed the stimuli through a mirror placed on the head coil. Go/no-go stimuli were letters and numbers written in Times New Roman font and colored in blue or red (50% each). In the simple task, go stimuli were "red O" and "blue X," and no-go stimuli were "blue O" and "red X" (*high-conflict no-go*) on the one side, and red and blue numbers 2 and 3 (*low-conflict no-go*) on the other side. In the complex task, go stimuli were red vowels (A, E, I, U) and blue consonants (L, N, P and Z), and no-go stimuli were blue vowels and red consonants (*high-conflict no-go*), or red and blue numbers 4, 5, 6, and 7 (*low-conflict no-go*). In both tasks, the association between color and go/no-go letters was counterbalanced across subjects. Participants were briefly familiarized with the task and stimuli before entering the scanner room to ensure that they understood the instructions and to reduce anxiety.

Each trial began with a go or no-go stimulus lasting 300 msec. The deadline for the go response was 2 sec after stimulus onset. A blank screen followed the stimulus presentation. Interstimulus interval varied randomly and continuously between 2.2 and 4.2 sec. This manipulation was important to sample the whole hemodynamic response function. Participants performed two consecutive runs for each task. Each run had 64 *go* (50%), 32 *high-conflict no-go* (25%), and 32 *low-conflict no-go* (25%) stimuli. Although there was an equal number of go and no-go trials, when one only considers the conflicting go/no-go stimuli belonging to the same category (letters), no-go letters were half as frequent as the go letters, a typical manipulation in the go/no-go literature meant to produce prepotent go responding (e.g., Hester, Murphy, & Garavan, 2004; Nielson et al., 2002; Rubia et al., 2001).

The total number of test trials was 512. Participants were instructed to press a button with the index finger of their dominant hand as soon as they saw a go stimulus, and refrain from responding when a no-go stimulus appeared. Thus, the experiment consisted of a 2 Task (simple vs. complex) × 3 Condition (*go*, *high-conflict and low-conflict no-go*) × 2 Run (first and second runs) design. Six familiarization trials preceded each run. During the presentation of these initial trials only, participants received visual feedback about their performance. The order of presentation of the two tasks was counterbalanced across participants.

Analysis of the Behavioral Data

The familiarization trials and the first test trial were discarded from the analyses. Moreover, the low-conflict no-go condition was discarded from subsequent behavioral analyses because performance on those conditions was at ceiling in both groups and tasks (see Figure 1). Accuracy data on the go and high-conflict no-go stimuli were analyzed separately by means of a 2 × 2 × 2 mixed ANOVA with task (simple vs. complex) and run (first vs. second) as the within-subject factors, and age (young vs. older) as the between-subjects factor.

RT analysis was limited to the go conditions only because not enough commission errors occurred for the no-go conditions. A 2 × 2 × 2 mixed ANOVA was carried out on the go RTs, with task (simple vs. complex) and run (first vs. second) as the within-subject factors, and age (young vs. older) as the between-subjects factor.

Image Acquisition and Data Preprocessing

Images were acquired on a 3-T Siemens Magnetom Trio scanner with a matrix 12-channel head coil. Functional volumes were obtained using a whole-head T2*-weighted EPI sequence (repetition time [TR] = 2 sec, echo time [TE] = 30 msec, flip angle [FA] = 70°, 28 oblique axial slices with interleaved acquisition, 3.1 × 3.1 × 5 mm voxel resolution, field of view [FOV] = 20 cm, acquisition matrix [AM] = 64 × 64). The first 5 volumes were discarded to allow the magnetization to reach steady state. Physiological data (heart and respiration rate) were acquired during the scanning session. Anatomical images were acquired using an MP-RAGE sequence (TR = 2 sec, TE = 2.63 sec, 160 oblique axial slices, with a 1-mm^3 voxel size, FOV = 25.6 cm, AM = 256 × 256), either before or after the functional images (counterbalanced across subjects). Stimuli were presented visually through a mirror mounted on the coil that reflected images from a projector located at the bottom of the scanner. Finger-press responses were recorded with an MRI-compatible response pad. T2 Fluid Attenuated Inversion Recovery sequences (TR = 9 sec, TE = 96 msec, FA = 165°, FOV = 2.2 cm, AM = 256 × 162) were acquired at the beginning of the MR session to assess the presence of white matter disease, especially in the older adults. No participant was found with white matter hyperintensities outside the normal range.

Part of the preprocessing was performed with AFNI software (http://afni.nimh.nih.gov/; Cox, 1996). EPI time-series data were corrected for cardiac and respiratory parameters (program 3dretroicor) and for difference in the timing of slice acquisition (program 3dTshift). Six-parameter rigid

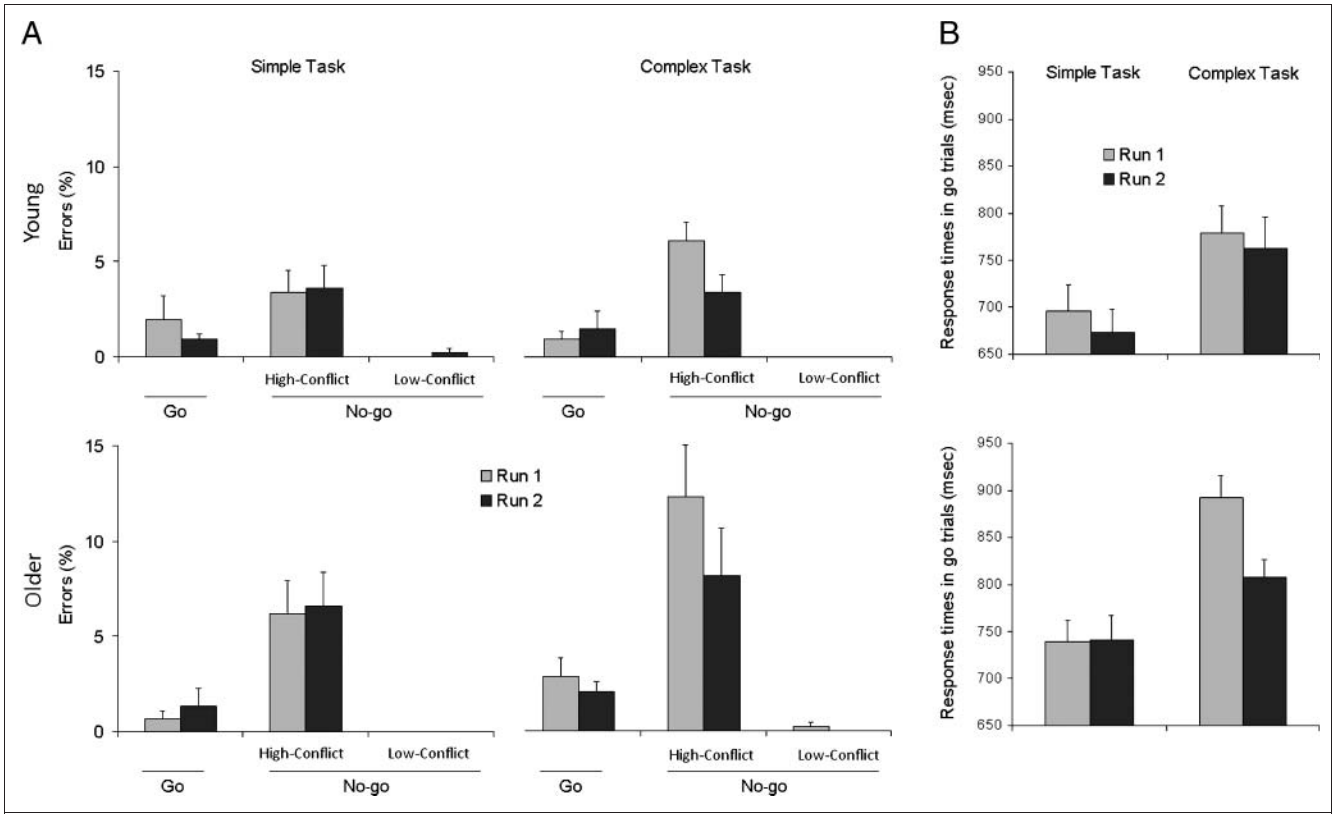

Figure 1. Behavioral data. (A) Percentage of errors (and standard errors of the mean) as a function of task, run, go/no-go conditions, and age. (B) Mean RTs (and standard errors of the mean) of correct responses (in milliseconds) to go stimuli as a function of task, run, and age.

body inter- and intra-run motion correction was then performed by coregistering volumes to a reference EPI volume (AFNI program 3dvolreg). Coregistration to a functional MNI template (EPI.nii) and spatial smoothing (8-mm Gaussian kernel) was performed in SPM5 (Friston et al., 1995). Group analyses were performed using Partial Least Square software (PLS; McIntosh, Bookstein, Haxby, & Grady, 1996). The anatomical scan was first coregistered to the functional run that occurred closest in time in AFNI during reconstruction (program siemenstoafni-beta2), and then coregistered to a structural MNI template (T1.nii) in SPM5.

Partial Least Square

We describe the conceptual details of the PLS analysis in the following paragraphs (but see McIntosh et al., 1996, for a more detailed explanation). PLS is a set of multivariate statistical analyses that assesses the relations between any set of independent measures, such as the experimental design, and a set of dependent measures, in our case, the whole brain hemodynamic response function (HRF). PLS carries out the computation of the optimal partial least squares fit to cross-block correlation between the independent and dependent measures.

We used task PLS, an analysis that identifies patterns of brain voxels whose signal change covaries with the experimental conditions. A trial was defined as a signal segment, beginning at the stimulus onset and lasting 7 lags, which represents the response of each voxel averaged across trials. Each lag corresponds to a TR (2 sec). The HRF for each trial was expressed as the intensity difference from trial onset, allowing investigation of changes in task-related activity at different lags along the whole temporal segment. No assumption was made about the shape of HRF. All task conditions were included in this analysis. Condition averages for each voxel and lag were expressed as a deviation from the grand mean of all conditions by lags. The deviation matrix undergoes singular value decomposition to extract a set of latent variables (LVs), which are defined as orthogonal pairs of singular vectors. These vector pairs reflect a symmetric relation between a cohesive pattern of brain activity (singular image) and a particular experimental effect represented as derived optimal contrast, or design scores. The numerical weights within the singular image are called saliences and can be positive or negative. The singular value for an LV is the covariance between the brain and the design scores. Each LV explains a progressively smaller percentage of the total covariance pattern, until all the covariance has been explained. For each LV, PLS yields also brain scores that indicate how strongly individual subjects express the patterns on the LV. These scores are calculated by multiplying the raw images by the singular image on a particular LV for each subject. Finally, when brain scores are computed for each time lag, a temporal brain score is obtained.

A permutation test is used to compute the overall significance for each LV (McIntosh et al., 1996). The data matrix rows are randomly reordered and a new set of LVs is calculated for each permutation. For the current experiment, 1000 permutations were used. If the singular value of each new LV exceeded the original value more than 99% of the times ($p = .01$), an LV as a whole was considered significant. To determine the reliability of the saliences identified by the LVs, all data were submitted to a bootstrap estimation of the standard errors by randomly resampling subjects with replacement 200 times. PLS is recalculated for each bootstrap sample to identify those saliences whose value remains stable regardless of the sample chosen. The ratio of the salience to the bootstrap standard error is approximately equivalent to a Z score (Efron & Tibshirani, 1986).

Clusters with at least 15 contiguous voxels with a salience-to-standard error ratio (bootstrap ratio, BSR) bigger than 5 (approximately corresponding to $p < .00001$) in each lag were considered as reliable. Coordinates of the voxel with the peak BSR within each cluster were obtained in MNI space and converted into Talairach coordinates to find the likely gyral locations using Matthew Brett's transformation (www.mrccbu.cam.ac.uk/Umaging/mnispace.html). Approximate Brodmann's areas were then identified using the Talairach Daemon (Lancaster et al., 2000).

A preliminary task PLS analysis including all the six conditions (3 go/no-go conditions × 2 tasks) and groups (younger and older) showed a complex pattern of results, but no difference in design scores for go stimuli in the two age groups and tasks was observed, as can be appreciated in Supplementary Figure S1. This pattern replicates previous results showing that most of the age-related fMRI differences in go/no-go tasks occur in no-go trials (Nielson et al., 2002). To focus on the most sensitive conditions (high- vs. low-conflict no-go) and also to avoid confounds derived from the differences between the go condition and the other two conditions (i.e., double frequency of occurrence, requirement of a motor response), we conducted a task PLS analysis (reported here) that did not include go conditions. This analysis showed a selective overrecruitment of brain regions in the older group during the complex task (see Results). Two subsequent PLS analyses were run to understand if the overrecruitment of brain regions involved in the processing of high-conflict no-go items in the complex task was modulated as a function of learning from Run 1 to Run 2 in the older group. A first analysis included both tasks (simple and complex). Because this analysis showed that critical age-related differences in practice effects occurred exclusively in the complex task, a second analysis focused on the complex task only (fully reported here).

As reported below, this analysis demonstrated an overrecruitment of an extensive set of brain regions in the older group with high-conflict no-go trials on the first run of the complex task. In PLS, the brain scores are an index of how strongly each individual contributed to a given LV. Hence, for both groups, the brain scores in this condition were correlated with the accuracy data on the same condition using a Pearson correlation analysis to get a hint on whether overrecruitment was actually beneficial or detrimental to the initial performance in the older group. The brain scores for the high-conflict no-go condition in the first run of the complex task were also correlated to the percentage of accuracy improvement in the second run (i.e., percent differences with respect to accuracy in the first run), in order to detect the nature of the relation between initial overrecruitment and later performance.

RESULTS

Accuracy and RT data are presented in Figure 1.

Accuracy

Older participants tended to make significantly more commission errors (i.e., go responses) than young ones on the high-conflict no-go trials [age main effect: $F(1, 26) = 4.1$, $p = .053$]. These types of errors were more frequent for both groups in the first run than in the second one [run main effect: $F(1, 26) = 7.9$, $p < .01$], and in the complex task than in the simple one [task main effect: $F(1, 26) = 5.5$, $p < .05$]. A significant two-way interaction indicated that commission errors to high-conflict no-go stimuli were especially frequent in the first run of the complex task [Run × Task interaction: $F(1, 26) = 8.6$, $p < .01$]. The ANOVA concerning accuracy on go stimuli did not reveal any significant effect.

Response Times

Older subjects tended to be slower than young ones [age main effect: $F(1, 26) = 4$, $p = .056$]. RTs were longer in the complex than in the simple task [task main effect: $F(1, 26) = 121.8$, $p < .001$], and in the first than in the second run [run main effect: $F(1, 26) = 17.8$, $p < .001$]. RTs were much longer in the first run of the complex task than in the second one, whereas the difference between the two runs was much reduced in the simple task [Run × Task interaction: $F(1, 26) = 5.9$, $p < .05$]. This pattern was particularly pronounced in the older group [Age × Run × Task interaction: $F(1, 26) = 8.9$, $p < .01$]. When the raw data for each subject were transformed to percent change scores (i.e., mean RT in each condition divided by the overall mean RT and then multiplied by 100), this critical three-way interaction was still significant [$F(1, 26) = 6.9$, $p = .01$], thus showing that it was not an artifact of general slowing.

fMRI Data

PLS Results: High-conflict and Low-conflict No-go

This analysis yielded one significant LV only (observed singular value = 29.6, explained cross-block covariance = 44.4%, $p < .001$). The design scores for this LV are shown in Figure 2A.

This LV showed a contrast between high-conflict and low-conflict no-go in both tasks. Critically, it also showed a No-go condition × Task complexity × Age interaction. Older participants had greater (opposite) design scores for conflict and low-conflict no-go in the complex task than in the simple task, and than young participants in both tasks. The individual subjects' contribution to an LV is estimated with an overall measure called brain score (see Methods). The brain scores for each lag (i.e., temporal brain scores) were submitted to a mixed ANOVA with no-go condition (high-conflict vs. low-conflict) and task (simple vs. complex) as the within-subject factors, and age (young vs. older) as the between-subjects factor. The No-go condition × Task × group three-way interaction showed a strong tendency in lag 3 [$F(1, 26) = 3.9$, $p = .059$] and was significant in lag 4 [$F(1, 26) = 4.4$, $p < .05$], whereas it was far from significance in the other lags (see Figure 2B). Therefore, clusters with reliable saliences for lags 3 and 4 are listed in Table 1 and shown in Figure 2C.

Clusters that showed greater activation for high-conflict than for low-conflict no-go conditions, especially in the older group and in the complex task, included bilaterally the inferior and middle frontal gyrus, inferior parietal lobule, posterior cerebellum; on the left, the insula, precentral gyrus, fusiform gyrus, putamen; and on the right, the anterior

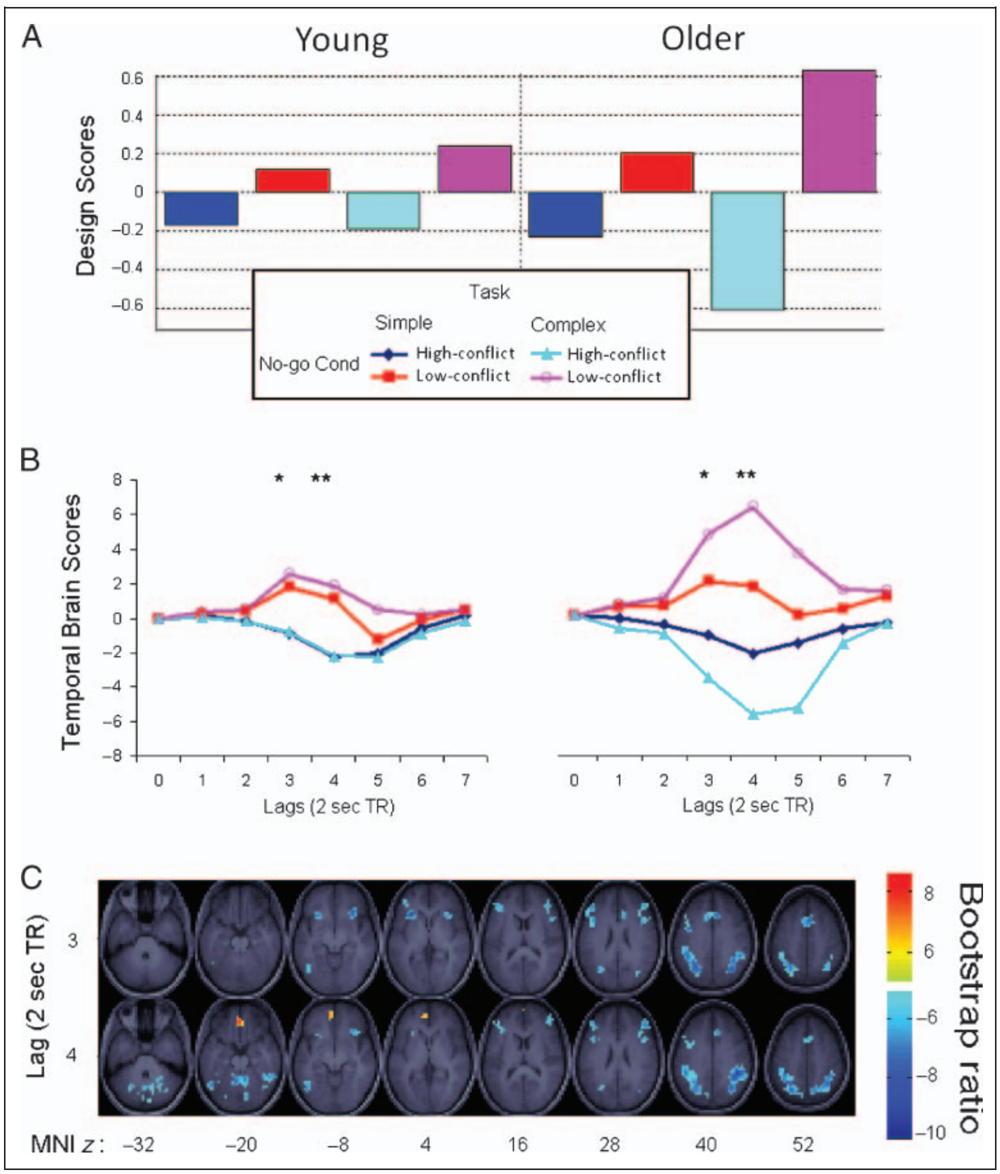

Figure 2. Results of the first PLS analysis. (A) Design scores (arbitrary units) for the Latent Variable 1, according to age, task, and no-go condition. (B) Temporal brain scores (arbitrary units and sign) indicating how the brain network in (C) generally responded to the task conditions. The symbols * and ** indicate a trend and a significant Age × Task × No-go condition interaction in lags 3 and 4, respectively. (C) Brain clusters (number of voxels ≥ 15, bootstrap ratio ≥ 5), where design and temporal scores shown in Panels A and B were mainly expressed. Time from stimulus onset is indicated on the *y*-axis of the singular image and is expressed in lags (1 lag = 2 sec repetition time). The *x*-axis shows the *z*-coordinate of the axial slice in MNI space. Cold colors indicate clusters with negative bootstrap ratios, which were differentially more activated for experimental conditions with negative design scores in Panel A and negative temporal scores in Panel B (i.e., high-conflict no-go in both tasks and groups). Warm colors indicate clusters with positive bootstrap ratios, which were differentially more activated for experimental conditions with positive design scores in Panel A and positive temporal scores in Panel B (i.e., irrelevant no-go in both tasks and groups). The bootstrap ratio map is superimposed on the average anatomical scans from all 28 participants.

Table 1. Reliable Clusters Identified for LV1 in the First Task-PLS Analysis Including Both Age Groups (Young vs. Older), Tasks (Simple vs. Complex), and No-go Conditions (Conflict vs. Irrelevant No-go)

Negative Saliences							
			Talairach				
Lag	*Cluster Region*	*BA*	*x*	*y*	*z*	*Size*	*BSR*
3	R Claustrum	–	28	23	−1.2	68	−10
3	L Inferior Parietal Lobule	40	−48	−33	42	273	−9.9
3	L Insula	13	−28	19	−4.3	60	−9.9
3	L Precentral Gyrus	6	−40	1.7	33	169	−8.9
3	R Precuneus	19	32	−64	36	194	−8.8
3	R Middle Frontal Gyrus	46	48	36	20	39	−8.2
3	R Cingulate Gyrus	32	8	21	39	119	−7.3
3	L Fusiform Gyrus	37	−48	−59	−11	31	−7.1
3	R Inferior Frontal Gyrus	9	40	9	25	23	−6.1
4	L Inferior Parietal Lobule	40	−32	−52	43	350	−10
4	R Inferior Parietal Lobule	40	32	−44	43	297	−9.7
4	R Uvula	–	16	−75	−33	286	−9.4
4	L Middle Frontal Gyrus	46	−44	36	20	127	−9.2
4	L Inferior Semilunar Lobule	–	−32	−72	−37	104	−8.4
4	R Middle Frontal Gyrus	46	51	36	20	96	−8.1
4	R Cingulate Gyrus	32	8	25	39	38	−7.9
4	R Inferior Temporal Gyrus	20	63	−47	−14	30	−7.7
4	L Fusiform Gyrus	37	−51	−59	−14	43	−7.4
4	R Inferior Frontal Gyrus	47	32	27	−8.1	34	−7.2
4	L Putamen (Lentiform Nucleus)	–	−24	3.9	−0.2	25	−6.7
4	L Fusiform Gyrus	37	−40	−44	−18	28	−6.6

Positive Salience							
			Talairach				
Lag	*Cluster Region*	*BA*	*x*	*y*	*z*	*Size*	*Bootstrap*
4	Bilateral Medial Frontal Gyrus	11	0	38	−19	63	8.4

R = right hemisphere; L = left hemisphere; BA = approximate Brodmann's area; BSR = bootstrap ratio in the PLS analysis.

cingulate, inferior temporal gyrus and precuneus. The only cluster that showed more activation for the opposite contrast, that is, low-conflict versus high-conflict no-go, mainly in the complex task and in the older group, was located on the rostral medial prefrontal region (Brodmann's area 11).

PLS Results: Practice Effects

A first analysis of practice effects from Run 1 to Run 2 included both tasks. As the design scores suggest (Figure 3A), LV1 (observed singular value = 41.2, explained cross-block covariance = 25%, $p < .0001$) expressed a complex interaction between task complexity, run, condition, and age. In the simple task, design scores for high-conflict and low-conflict no-go diminished from Run 1 to Run 2, without substantial difference between the two age groups. On the other hand, marked age differences emerged in the complex task. To better understand this interaction, and to focus on the conditions in which learning occurred, in terms of accuracy in both groups and in terms of speed especially in the older adults, we focused

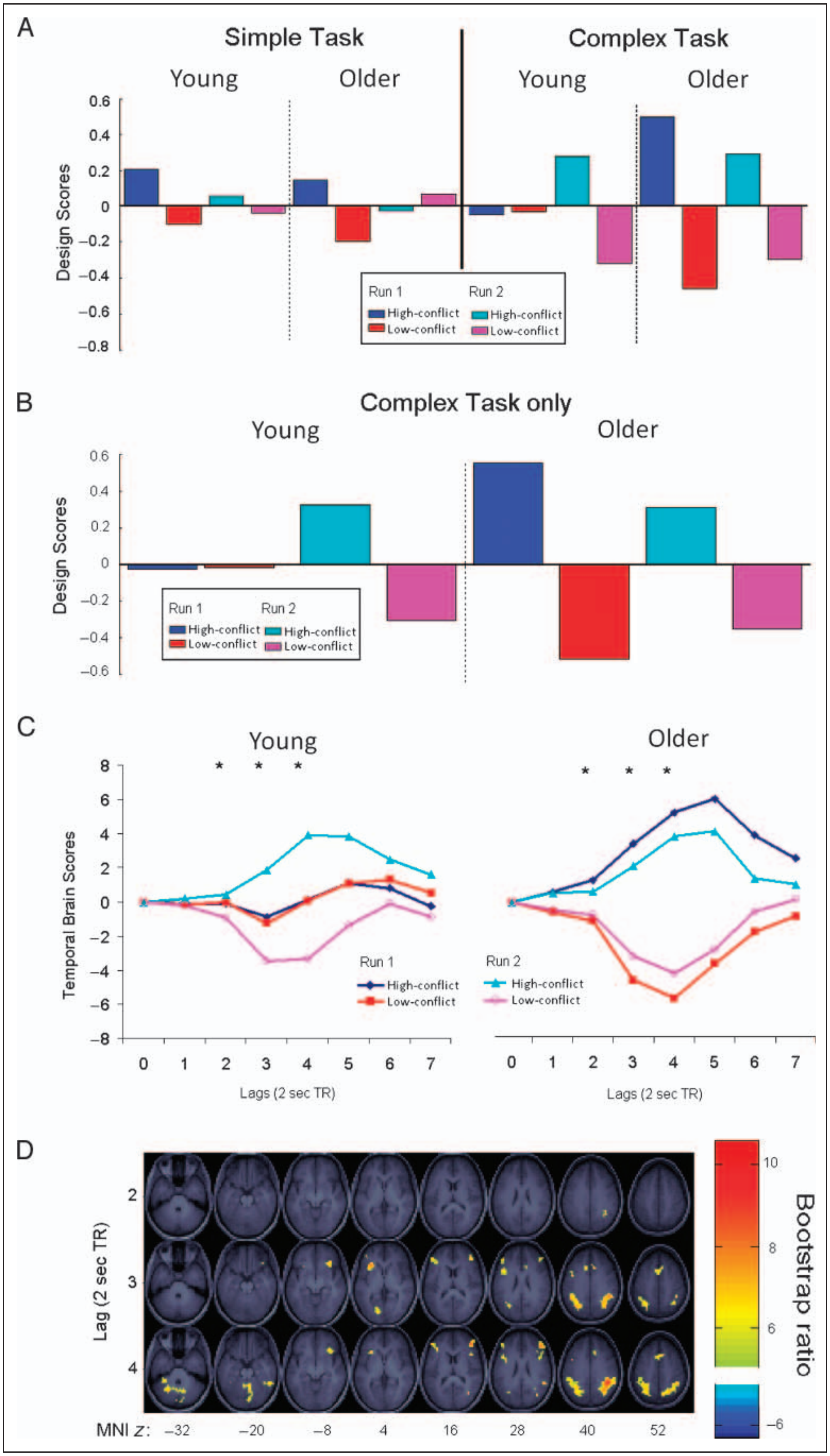

Figure 3. Results of the PLS analyses on practice effects between Run 1 and Run 2. (A) Design scores for the Latent Variable 1 of the PLS analysis including task, no-go condition, run, and age. (B) Design scores for the Latent Variable 1 of the PLS analysis focusing on practice effects in the complex task only. Experimental conditions included no-go condition, run, and age. (C) Temporal brain scores for the Latent Variable 1 of the PLS analysis focusing on practice effects in the complex task only. The symbol * indicates significant Age × No-go condition × Run interaction in lags 2, 3, and 4. (D) Brain clusters (number of voxels ≥ 15, bootstrap ratio ≥ 5), where design and temporal scores shown in B and C were mainly expressed. Time from stimulus onset is indicated on the *y*-axis of the singular image and is expressed in lags (1 lag = 2 sec repetition time). The *x*-axis shows the *z*-coordinate of the axial slice in MNI space. Warm colors indicate clusters with positive bootstrap ratios, which were differentially more activated for experimental conditions with positive (vs. negative) design scores in Panel B and temporal scores in Panel C (i.e., high-conflict no-go). The bootstrap ratio map is superimposed on the average anatomical scans from all 28 participants.

on the complex task only in a subsequent task-PLS analysis that we report below. This analysis included the following conditions: age (young vs. older), run (first vs. second), and no-go condition (high-conflict vs. low-conflict no-go).

The first LV only was significant (observed singular value = 38.9, LV1 explained cross-block covariance = 42.4%, $p < .0001$). The design scores are reported in Figure 3B. Positive saliences indicate brain voxels differentially more activated in processing high-conflict no-go stimuli and negative saliences indicate voxels more activated in processing low-conflict no-go stimuli. Moreover, as the design scores show, the overrecruitment of brain regions present in the first run of the complex task in older subjects diminished in the second run. On the other hand, young subjects used the same network as older subjects in the second run only. Hence, age-related differences were observed in the learning phase of the complex task (Run 1), and disappeared once the task has been practiced for one run.

We also examined the brain scores in each of the 7 lags (temporal brain scores; Figure 3C), by means of mixed ANOVAs with no-go condition (high-conflict vs. low-conflict no-go) and run (first vs. second) as the within-subject factors, and age (young vs. older) as the between-subjects factor. The effect of interest of these ANOVAs would be a three-way interaction between no-go condition, run, and age. This interaction was significant for lags 2–4 [$F(1, 26)$ range = 4.8–8.2, all ps $< .05$], and showed a weak trend for lag 5 ($p = .1$). Clusters with reliable saliences in lags 2–4 are reported in Table 2 and are shown in Figure 3D.

Table 2. Reliable Clusters Identified for LV1 in the Task-PLS Analysis Concerning Practice Effects in the Complex Task

			Talairach				
Lag	*Cluster Region*	*BA*	*x*	*y*	*z*	*Size*	*Bootstrap*
Positive Saliences							
2	R Inferior Parietal Lobule	40	36	−48	43	23	6.3
3	R Inferior Parietal Lobule	40	48	−41	43	174	9.4
3	L Insula	13/45	−28	23	3	50	9.0
3	L Inferior Parietal Lobule	40	−32	−52	43	214	8.5
3	R Middle Frontal Gyrus	46	48	36	20	38	8.0
3	R Inferior Frontal Gyrus	47	32	27	−5	51	7.7
3	L Inferior Frontal Gyrus	9	−44	9	29	50	7.2
3	L Middle Frontal Gyrus	46	−44	36	17	59	7.0
3	Medial Frontal Gyrus	6	0	14	44	59	6.9
3	L Cuneus	17	−16	−77	8	17	6.1
4	R Inferior Parietal Lobule	40	36	−45	39	340	10.4
4	R Inferior Frontal Gyrus	46	44	39	13	79	9.5
4	L Middle Frontal Gyrus	46	−44	36	17	39	8.9
4	L Inferior Parietal Lobule	40	−32	−52	43	304	8.9
4	L Inferior Frontal Gyrus	9	−44	9	29	42	8.0
4	R Medial Frontal Gyrus	8	8	18	43	53	7.7
4	L Fusiform Gyrus	20	−40	−40	−18	23	7.5
4	L Insula	13	−32	23	−1	19	7.3
4	L Culmen	–	−24	−63	−24	208	7.1
4	R Inferior Frontal Gyrus	47	32	27	−8	36	6.5
4	R Inferior Temporal Gyrus	20	51	−47	−14	19	6.4
4	L Inferior Semilunar Lobule	–	−44	−68	−40	18	6.3
4	R Middle Frontal Gyrus	9	36	9	33	31	6.1

This analysis included the following experimental conditions: age group (young vs. older), run (first vs. second), and no-go condition (conflict vs. irrelevant no-go). R = right hemisphere; L = left hemisphere; BA = approximate Brodmann's area; BSR = bootstrap ratio in the PLS analysis.

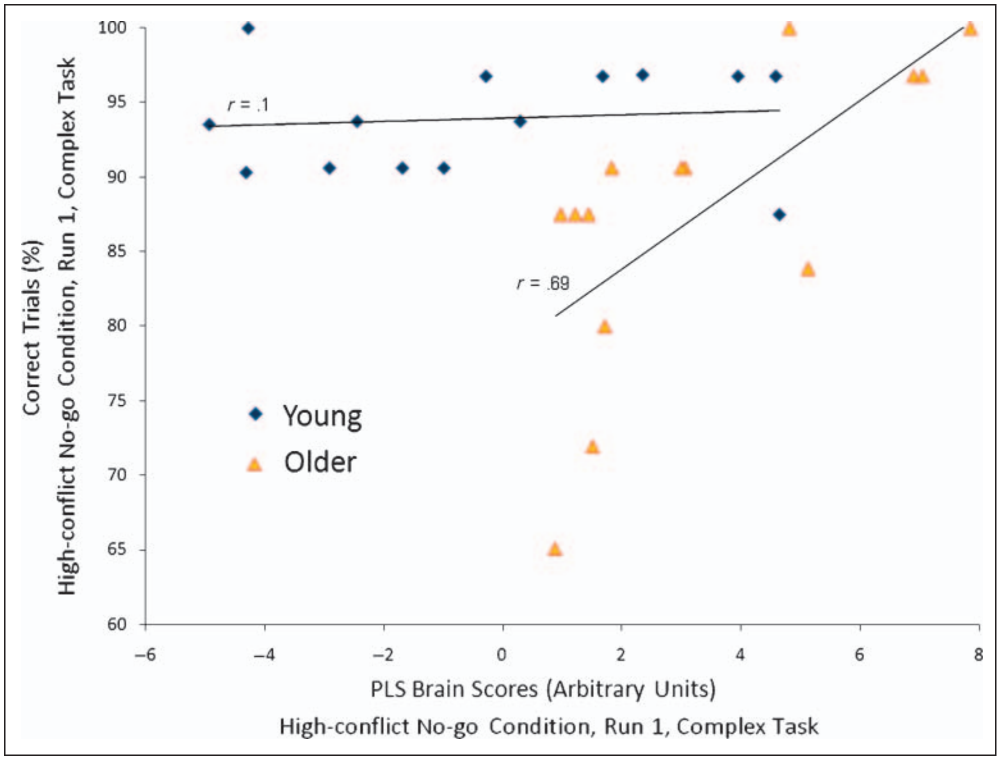

Figure 4. Correlation patterns between the individual brain scores for the high-conflict no-go condition in the first run of the complex task (as obtained in the last partial least square analysis) and percentage of correct trials in the same task condition for both the young and older groups.

Clusters that showed greater activation for high-conflict no-go than for low-conflict no-go conditions (positive saliences), especially in the older adults and in the first run of the complex task, included bilaterally, the inferior and middle frontal gyrus, inferior parietal lobule, and posterior cerebellum; on the left, the insula, fusiform gyrus, cuneus, and cerebellum; and on the right, the superior medial frontal gyrus. No cluster with negative saliences (i.e., low-conflict no-go > high-conflict no-go) survived the chosen threshold.

In the older group only, there was a positive correlation between brain scores and accuracy in the high-conflict no-go condition during the first run of the complex task ($r = .69$, $p = .007$; see Figure 4), suggesting that overrecruitment of these regions was actually beneficial to the older individuals' performance. There was a trend for a negative correlation between brain scores in this condition and the percentage of accuracy improvement in the same high-conflict no-go condition during the second run ($r = -.51$, $p = .06$). This trend suggests that those older subjects that actually overrecruited the network most for this condition on the first run did not improve much on the second run, probably because they were already performing at their best on the first run. On the other hand, young subjects did not show any significant correlation between brain scores in the high-conflict no-go condition of the first run and performance on this condition during the first run or improvement during the second run (for both, $p > .37$), although ceiling effects may play a role in this case. Finally, the brain scores for the high-conflict no-go condition in the second run of the complex task did not correlate significantly with performance in the second run in either age group.

DISCUSSION

The present study investigated age-related differences in the recruitment of brain regions as a function of progressively increasing task demands. To this aim, three features were systematically manipulated: cognitive conflict (high-conflict vs. low-conflict no-go stimuli), complexity (simple vs. complex task), and novelty (first vs. second run).

Previous studies in the literature have already shown that conflict (Zysset et al., 2007; Gazzaley et al., 2005; Nielson et al., 2002), task complexity (Gazzaley et al., 2007; Viskontas et al., 2004), or novelty (Erickson et al., 2007b; Kramer et al., 1999) may affect performance and brain activation in older adults. The current study extends these previous findings by combining, in a single experimental design, manipulations concerning these three task components. As it will appear from the following discussion, this design was successful in showing that this combination of factors is important for observing age-related differences in brain activation.

At the behavioral level, participants in both age groups performed at ceiling in the low-conflict no-go condition, whereas they made a number of commission errors for the high-conflict no-go stimuli, especially in the complex task. Both age groups improved their performance to high-conflict no-go stimuli from the first to the second run of the complex task. Analyses on RTs to go stimuli showed that beneficial practice effects in speeding up the task execution especially occurred in the older group for the complex task. We speculate that this speeding up was similar in go and high-conflict no-go conditions, but given the nature of the go/no-go task, we did not have a measure of speed for the latter.

In the following sections, we will describe the cumulative effects of the factors influencing age-related changes in the functional brain activity (i.e., conflict, complexity and novelty). First, we will consider the effect of cognitive conflict. A cohesive set of brain regions, including bilateral fronto-parietal regions and superior medial prefrontal cortex, was similarly activated in both age groups for high-conflict no-go stimuli and was deactivated for low-conflict no-go stimuli in the simpler task. Some of these regions, such as right lateral prefrontal cortex, have been related to inhibitory processes (e.g., Aron, Robbins, & Poldrack, 2004; Hester et al., 2004; Rubia et al., 2001). Notwithstanding the specific role of each of these neural nodes (Stuss & Alexander, 2007), taken together they overlap with an extensive fronto-parietal network that is involved during most cognitive control tasks (Kelly, Hester, Foxe, Shpaner, & Garavan, 2006; Fox et al., 2005; Duncan & Owen, 2000), and shows intrinsic functional connectivity even at rest (Vincent, Kahn, Snyder, Raichle, & Buckner, 2008).

However, marked age-specific modulation in the activation of these regions emerged as the task difficulty increased, as reflected in the interaction with task complexity. Older participants overrecruited these regions when conflicting no-go stimuli were embedded in the complex task. These results corroborate previous fMRI studies of aging reporting overrecruitment of a similar fronto-parietal network during conditions requiring top–down control (Grady, 2008; Morcom et al., 2007; Zysset et al., 2007). Thus, overrecruitment especially occurs in the older group with increasing task demands (it mostly occurs for high-conflict vs. low-conflict no-go stimuli and during the complex vs. simple task).

Because age-related difficulties are likely to emerge in nonroutine situations, such as during the early phases of task performance (e.g., Erickson et al., 2007b; Kramer et al., 1999), the early and late runs of the complex task were directly compared in a follow-up task-PLS analysis. This analysis showed a set of brain regions similar to those extracted in the previous analysis, and further characterized their *modus operandi* by revealing opposite effects of practice for the two age groups. Older participants showed a pronounced cohesive activation of these regions in the first run, whereas activation was reduced in the second run. In contrast, in the young group, this set of regions did not show a consistent activation in the first run, but its overall activation appeared in the second run only. As a result, pronounced age-dependent differences were present in the pattern of brain activation in the first run, whereas those differences disappeared in the second run.

This study extends previous work by showing that the often reported nonselective overrecruitment of brain regions, including homologous fronto-parietal areas in both hemispheres (Cabeza, 2002; Logan et al., 2002; Park et al., 2001; Reuter-Lorenz, Stanczak, & Miller, 1999), mostly occurs in aging with increasing task demands. More specifically, older adults need more neural resources than younger controls to initially set up the criteria for overcoming prepotent responding under complex task rules. Our next question was whether using these extra neural resources was, in fact, beneficial or detrimental for older adults' performance. Important insights on this issue came from brain–behavior correlation analyses. Correlation analyses indeed showed that neural overrecruitment mostly occurs in those older individuals who were more successful in dealing with increasing task demands, that is, those individuals who made less commission errors (i) in the conflicting no-go condition (ii) of the first run (iii) of the complex task. Moreover, this initial overrecruitment tended to occur much less in the older adults whose performance improved during the second run only, suggesting a less efficient capacity to initially set up the task criteria in this subgroup.

Therefore, neural overrecruitment is beneficial for initial task performance in aging, favoring compensatory accounts over inefficiency ones (see Grady, 2008, for a review). More generally, these findings underscore the importance of looking at the between-subjects variability in the use of spared neural resources to determine the functional neuroanatomy that distinguish the older adults who age gracefully from those who do not (Buckner, 2004; Cabeza, Anderson, Locantore, & McIntosh, 2002).

A possible limit of the brain–behavior correlation analysis used in the present study is that it correlates errors with a measure of brain activation on correct conflicting no-go trials. Accuracy was the only behavioral measure available for this condition in the present study, and it is conceivable that the same subjects that produce most commission errors on no-go trials are those that mostly suffer from response conflict, and mostly activate partial go responses even on correct no-go trials, although we did not have any measure to support this assertion in the present study. Future studies should employ a measure of partial response activation, such as electromyographic recording on the peripheral muscle used for the go responses or electroencephalographic correlates of response preparation (see Vallesi & Stuss, 2010), as a more suitable dependent variable to correlate with brain activation on correct no-go trials.

An apparently surprising result is that, in the first run of the complex task, young adults did not activate the fronto-parietal network engaged in a cohesive manner by older participants and, to a minor extent, by both groups in the first run of the simple task (Figure 3A). A similar pattern has already been described in young adults when learning occurs specifically under highly demanding task conditions (Erickson et al., 2007a; Sakai, Ramnani, & Passingham, 2002), suggesting a link between this increasing activity and the emergence of a strategy that is gradually set up in young adults. At any rate, this opposite pattern of results shows that the relation between functional brain activity and performance may change with age up to the point of overturning in different age groups (e.g., Vallesi, McIntosh, Shallice, & Stuss, 2009; Rypma & D'Esposito, 2000), an issue that certainly deserves further investigation.

Possible differences in the strategy used by the two age groups should be considered. The fact that older subjects use the regions belonging to the control network in the learning stages of task performance (cf. Chein & Schneider, 2005) more than young controls (and reduce the need to use it after practice) may reflect a strategic shift toward a more reflective, deliberative cognitive style with age (Velanova, Lustig, Jacoby, & Buckner, 2007). Although the older adults as a group seem to use this control network to reach a high performance level as soon as they begin to face a complex task, young individuals might start to use this network later on, probably to compensate for fatigue and distraction arising as the task goes on, selectively in the high-conflict no-go trials of the more difficult task, in which they need to keep their focus on a task that does not become automatic with practice due to its complexity (see Kelly et al., 2006, for similar results).

However, it is not plausible that young people do not use brain resources at the beginning of the complex task, as it would appear if one only considers the analyses reported here. Because the task-PLS analysis, like the principal component analysis, emphasizes the latent variables that explain most of the variance in the data, it is possible that it does not detect more subtle age-specific dynamics when both groups were considered together. To overcome this potential pitfall, additional analyses (reported in the Supplementary Material) focused on the brain activity in young adults while they perform the complex task. Results of these analyses suggest that, in the young group, only a subpart of this extensive network is consistently sensitive to practice effects (see Table S1 and Supplementary Figure S2).

Notwithstanding the fact that different and, not necessarily, mutually exclusive accounts may explain the practice-related divergence between brain activations in the two age groups, the present results underscore the importance of training in reducing age differences both at the behavioral and at the neural level, especially with high task demands. This can explain why, when participants (partially overlapping with those tested here) were retested 1 to 7 days later in a subsequent ERP session with the same tasks (Vallesi, Stuss, et al., 2009), any Age × Task complexity interaction disappeared both behaviorally and neurally as shown by the ERP data.

These findings corroborate and extend the existing literature. In a recent fMRI study (Erickson et al., 2007b), younger and older adults performed two visual tasks (color and letter detection) either separately or simultaneously. Participants then underwent extensive training on the tasks over several weeks. Older adults showed a decrease in dorsal prefrontal activity after training, whereas younger subjects showed an opposite pattern. The present study extends these results by showing that age-related differential effects of practice do not occur with extensive training only (Erickson et al., 2007b) because even a modest amount of practice during a single experimental session is enough to dramatically reduce age differences in functional neural activity (see also Kramer et al., 1999, for similar behavioral evidence).

A seminal neuroimaging study by Logan et al. (2002) showed that it is possible to reduce underrecruitment of certain brain regions when older adults are provided with explicit instructions on effective strategies to perform a given task. Complementing these results, the present data show that also overrecruitment associated with age, which was present in that study independently of the instructions provided (Logan et al., 2002), can decrease with practice, even without exogenous instructions. These findings suggest that the aging brain is capable of functional flexibility to a larger extent than was previously believed.

As a flip side of the extra engagement of fronto-parietal regions in high-conflict no-go trials, older adults deactivated these regions more during low-conflict no-go trials. A possible explanation is that these areas are constantly engaged in the task in the older group and phasically decrease their activation only after the onset of low-conflict no-go stimuli. On the other hand, age-specific increased activation for the low-conflict no-go stimuli was mainly present in the rostral medial prefrontal region (Brodmann's area 11). Previous studies have shown that this region is selectively engaged whenever stimuli markedly deviate from previous ones, either in location or identity, even when they do not require any overt decision (Petrides, Alivisatos, & Frey, 2002; Nobre, Coull, Frith, & Mesulam, 1999). The present data suggest that older adults engage this region more extensively for deviations from the context (particularly within a novel and complex task) and, more generally, that they are less able than young adults in suppressing processing of nontarget information (cf. Vallesi, Hasher, & Stuss, in press; Vallesi, Stuss, et al., 2009; Gazzaley et al., 2005).

The go/no-go procedure adopted here allowed us to investigate age-related changes in overcoming prepotent response tendencies. However, the use of no-go stimuli could make it unclear as to whether the brain regions that are overactivated in the older adults reflect a greater activation of inappropriate "go" responses in the high-conflict no-go condition (failure in response suppression), engagement of control processes necessary to suppress these inappropriate responses, or both. The activated areas were distinct from those activated for go conditions when the latter were also included in the PLS analyses (not reported here), thus making the second alternative relatively more plausible. Furthermore, because overrecruitment of the specific cognitive control regions reported here was more present in successful older individuals, if this overrecruitment is related to the need to suppress partial activation of wrong go responses, it could have a compensatory role. We have tested with a more appropriate ERP methodology whether age-related partial motor activations can be detected even in the absence of errors for different no-go conditions (Vallesi & Stuss, 2010). The results of this study showed that this can be the case especially in those older individuals who show faster go responses, further confirming a compensatory view.

Overall, the current study suggest that older adults need more neural resources to implement task setting, a putative executive function necessary to establish complex and nonroutine task rules that compete with prepotent stimulus–response contingencies (see the first latent variable of the PLS analysis). Many neuropsychological and neuroimaging studies have postulated the existence of task setting, whether they localize it in left lateral prefrontal cortex (e.g., Alexander et al., 2007), in fronto-polar cortex (Sakai & Passingham, 2006), or in more extensive fronto-parietal networks (e.g., Vallesi, McIntosh, Alexander, et al., 2009; Dosenbach et al., 2008). Other authors have used different terms to express the same construct according to the domain of investigation, such as "sculpting the response space" (Fletcher et al., 2000), cognitive association formation (e.g., Kim, Vallesi, Picton, & Tulving, 2009), nonroutine motor learning (Jueptner et al., 1997), and strategy production (Shallice, 2004). However, task setting should be investigated more extensively in future research, also from the cognitive point of view, before this unitary construct can be confidently adopted as an alternative and more parsimonious account to the explanation that neural overrecruitment occurs in aging with increasing task demands, as for instance, by manipulating (possibly multicomponential) factors such as the need for suppression, task complexity, and novelty.

Changes in the coupling between neural activity and hemodynamic response may occur with age (Huettel, Singerman, & McCarthy, 2001; D'Esposito, Zarahn, Aguirre, & Rypma, 1999). Nonetheless, these changes mainly pertain to a decreased signal-to-noise ratio in older adults, an effect that would bring results somewhat opposite of those observed here. Moreover, any intrinsic difference in the hemodynamic response per se as a function of age could not explain the condition-specific effects observed here.

In conclusion, the present study sheds light on the conditions in which the neural overrecruitment usually reported in neuroimaging studies of aging may occur and on its possible functional significance. Compared to younger adults, older individuals engage more extensively in a cohesive set of fronto-parietal regions to successfully overcome a prepotent and inappropriate response, but only if the task is complex and novel. The initial engagement of these regions has a compensatory role in aging, as it is strongly associated to the degree of success in avoiding commission errors.

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