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Over-recruitment in the aging brain as a function of task demands: evidence for a compensatory view

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Abstract

This study used functional magnetic resonance imaging (fMRI) to investigate the neural effects of increasing cognitive demands in normal aging and their role for performance. Simple and complex go/nogo tasks were used with two vs. eight colored letters as go stimuli, respectively. In both tasks, nogo 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 over-engaged a cohesive pattern of fronto-parietal regions with nogo stimuli under the specific combination of factors which progressively amplified task demands: high conflict nogo trials in the first phase of the complex task. This early neural over-recruitment was positively correlated with a lower error rate in the older group. Thus, the present data suggest that age-related extra-recruitment of neural resources can be beneficial for performance under taxing task conditions, such as when novel, weak and complex rules have to be acquired.

Keywords: Task complexity, normal aging, fronto-parietal network, PLS, go/nogo, fMRI.

Cognitive changes with aging are accompanied by modifications in brain functioning, as shown by neuroimaging evidence (e.g., Braver 2004; Grady 2008; Park et al. 2001). While some studies report an under-recruitment of brain regions with age (e.g. Rypma and D'Esposito 2000), different patterns of age-related neural over-recruitment 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 (Cabeza 2001, 2002; Hedden and Gabrieli 2004; Logan et al. 2002; Morcom et al. 2007; 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 (Hasher et al. 1999; Sweeney et al. 2001). Mirroring this age-specific inhibitory deficit in cognition (Hasher and Zacks 1988), brain imaging and electrophysiological evidence shows an increased neural activity (over-recruitment) associated with processing of interfering information in older adults (Nielson et al. 2002; Gazzaley et al. 2005; Gazzaley et al., 2008; Zysset et al. 2007; but see Grady et al. 1995).

Moreover, age-related differences in the capacity to circumvent interference from distracting non-target information are amplified by increasing task complexity (Viskontas et al. 2004; Gazzaley et al. 2007). 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 (Keys and White 2000; Verhaeghen et al. 2006), suggesting that a number of different mechanisms may underlie age-related decline in information processing. Again, at the neural level, age-related over-recruitment of brain regions often accompanies more complex and demanding task conditions, such as dual- vs. single-tasks (Smith et al. 2001), source vs. item memory retrieval (Morcom et al. 2007), or high vs. low selection demands in word generation tasks (Persson et al. 2004).

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

As briefly reviewed above, neural over-recruitment with aging has been associated to 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 over-recruitment in aging (i.e., when both cognitive conflict and task complexity are high), a factorial design crossing 2 complexity levels with 2 suppression levels was adopted. Specifically, two versions of a go/nogo 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 nogo stimuli) and to numbers of either color (low-conflict nogo stimuli). Go responses were prepotent for letters because they were twice more frequent than nogo 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), since 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 nogo decision, when appropriate.

Thus, we assumed that there was a need to suppress a prepotent go response in the presence of high-conflict nogo letters, while suppression was less required for low-conflict nogo stimuli, which were much faster to distinguish from go responses because they belonged to a different category (numbers vs. letters; see Vallesi et al., 2009c for Event-related Potential support to this assumption). In the more complex version, 4 vowels and 4 consonants replaced Os and Xs. A prediction was that neural over-recruitment would occur in older when task demands were maximal, that is, for the high-conflict nogo 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 the left lateral prefrontal cortex, since lesions in that region are associated with an increase in false alarms to non-target information in different domains and tasks (Stuss and Alexander 2007; Alexander et al. 2007; see also Bunge, 2004; Fletcher et al. 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 non-response (Vallesi et al., 2009a).

To partially anticipate the findings of the present study, older adults did engage an extensive set of fronto-parietal regions for the high-conflict nogo stimuli similarly to the young adults but, as expected, over-recruited these regions in the complex task, suggesting a relation between over-recruitment 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 and Nesselroade 1990), and age differences are substantially reduced after practice (Kramer et al. 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, and further divided the trials of the complex task into a first and a second run. The prediction was made that if over-recruitment 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 over-recruitment reflects adaptive plasticity to improve or maintain performance despite age-related neurodegenerative modifications (Buckner 2004; Cabeza et al. 1997; Grady et al. 1994; Gutchess et al. 2005; Reuter-Lorenz, 2002). 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 (Colcombe et al. 2005; Park et al. 2001; Rypma et al. 2007; Zarahn et al. 2007).

Our protocol provided the opportunity to test whether any neural over-recruitment 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 nogo condition of the complex task (where age-differences mostly occurred). The compensatory account would suggest that the older adults who showed more neural over-recruitment 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 over-recruited these regions more on the first run would also be the ones that show worse performance on this run (negative correlation).

Method

Participants. Fourteen young (8 females; mean age: 27 years, range: 20-34) and 14 older (9 females; mean age: 70 years, range: 60-80) 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 et al. 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 dollars. Part of the data of the young group (simple task) has already been reported elsewhere (Vallesi et al. 2009a).

Experimental material and design. Stimuli were presented centrally against a grey background. Participants viewed the stimuli through a mirror placed on the head coil. Go/nogo 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 nogo stimuli were “blue O” and “red X” (*high-conflict nogo*), on the one side, and red and blue numbers 2 and 3 (*low-conflict nogo*), 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 nogo stimuli were blue vowels and red consonants (*high-conflict nogo*), or red and blue numbers 4, 5, 6 and 7 (*low-conflict nogo*). In both tasks, the association between colour and go-nogo letters was counterbalanced across subjects. Participants 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 nogo stimulus lasting for 300 ms. The deadline for the go response was 2 sec after stimulus onset. A blank screen followed the stimulus presentation. Inter-Stimulus-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 2 consecutive runs for each task. Each run had 64 *go* (50%), 32 *high-conflict nogo* (25%) and 32 *low-conflict nogo* (25%) stimuli. Although there was an equal number of go and nogo trials, when one only considers the conflicting go/nogo stimuli belonging to the same category (letters), nogo letters were half as frequent as the go letters, a typical manipulation in the go/nogo literature meant to produce prepotent go responding (e.g., Hester, Murphy, and 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 nogo stimulus appeared. Thus, the experiment consisted of a 2 task (simple vs. complex) by 3 condition (*go, high-conflict and low-conflict nogo*) by 2 run (first and second run) 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 2 tasks was counterbalanced across participants.

Analysis of the behavioural data. The familiarization trials and the first test trial were discarded from analyses. Moreover, the low-conflict nogo 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 nogo stimuli were analyzed separately by means of a 2x2x2 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.

Response Time (RT) analysis was limited to the go conditions only, because not enough commission errors occurred for the nogo conditions. A 2x2x2 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 pre-processing. Images were acquired on a 3T Siemens Magnetom Trio scanner with a matrix 12-channel head coil. Functional volumes were obtained using a whole head T2*-weighted echo-planar image (EPI) sequence (repetition time, TR: 2 s, echo time, TE: 30 ms, flip angle, FA: 70º, 28 oblique axial slices with interleaved acquisition, 3.1 x 3.1 x 5 mm voxel resolution, field of view, FOV: 20 cm, acquisition matrix, AM: 64 x 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 a MP-RAGE sequence (TR: 2 s, TE: 2.63 s, 160 oblique axial slices, with a 1 cubic mm voxel size, FOV = 25.6 cm, AM: 256 x 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 a MRI-compatible response pad. T2 Fluid Attenuated Inversion Recovery (FLAIR) sequences (TR: 9 s, TE: 96 ms, FA: 165º, FOV: 2.2 cm, AM: 256 x 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 pre-processing 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 body inter- and intra-run motion correction was then performed by co-registering volumes to a reference EPI volume (AFNI program 3dvolreg). Co-registration 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 et al. 1996). The anatomical scan was first co-registered to the functional run that occurred closest in time in AFNI during reconstruction (program siemenstoafni-beta2), and then co-registered to a structural MNI template (T1.nii) in SPM5.

PLS. 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 assess 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 co-varies with the experimental conditions. A trial was defined as a signal segment, beginning at the stimulus onset and lasting 7 lags, that 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 (SVD) 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 a 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 ($p = .01$), a 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 re-sampling 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 and 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 (http://www.mrccbu.cam.ac.uk/Umaging/mnispace.html). Approximate Brodmann areas were then identified using the Talairach Daemon (Lancaster et al. 2000).

A preliminary task-PLS analysis including all the 6 conditions (3 go/nogo conditions x 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/nogo tasks occur in nogo trials (Nielson et al. 2002). To focus on the most sensitive conditions (high- vs. low-conflict nogo) 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 over-recruitment of brain regions in the older group during the complex task (see Results). Two subsequent PLS analyses were run to understand if the over-recruitment of brain regions involved in the processing of high-conflict nogo 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). Since 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 over-recruitment of an extensive set of brain regions in the older group with high-conflict nogo 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 over-recruitment was actually beneficial or detrimental to the initial performance in the older group. The brain scores for the high-conflict nogo 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 over-recruitment and later performance.

Results

Performance results. Accuracy and RT data are presented in Figure 1.

------*Insert Figure 1 about here*------

Accuracy. Older participants tended to make significantly more commission errors (i.e., go responses) than young ones on the high-conflict nogo 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 2-way interaction indicated that commission errors to high-conflict nogo stimuli were especially frequent in the first run of the complex task [run x 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, while the difference between the two runs was much reduced in the simple task [run x task interaction: $F(1,26)=5.9$, $p < .05$]. This pattern was particularly pronounced in the older group [age x run x 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 3-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 nogo. 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 nogo in both tasks. Critically, it also showed a nogo condition by task complexity by age interaction. Older participants had greater (opposite) design scores for conflict and low-conflict nogo in the complex task than in the simple task, and than young participants in both tasks. The individual subjects' contribution to a LV is estimated with an overall measure called brain score (see method). The brain scores for each lag (i.e., temporal brain scores) were submitted to a mixed ANOVA with nogo 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 nogo condition by task by group three-way interaction showed a strong tendency in lag 3 [$F(1,26)=3.9$, $p = .059$] and was significant in lag 4 [$F(1,26)=4.4$, $p < .05$], while 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.

----Insert Figures 2 and Table 1 about here-----

Clusters that showed greater activation for high-conflict than for low-conflict nogo conditions, especially in the older group and in the complex task, included bilaterally: inferior and middle frontal gyrus, inferior parietal lobule, posterior cerebellum; on the left: insula, precentral gyrus, fusiform gyrus, putamen; on the right: anterior cingulate, inferior temporal gyrus and precuneus. The only cluster that showed more activation for the opposite contrast, that is low-conflict vs. high-conflict nogo, mainly in the complex task and in the older group, was located on the rostral medial prefrontal region (Brodmann 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 nogo 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 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 nogo condition (high-conflict vs. low-conflict nogo).

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 nogo stimuli and negative saliences indicate voxels more activated in processing low-conflict nogo stimuli. Moreover, as the design scores show, the over-recruitment 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 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 nogo condition (high-conflict vs. low-conflict nogo) 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 3-way interaction between nogo 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 shown in Figure 3d.

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

----*Insert Figures 3 and Table 2 about here*----

In the older group only, there was a positive correlation between brain scores and accuracy in the high-conflict nogo condition during the first run of the complex task (r = .69, p = .007, see Figure 4), suggesting that over-recruitment 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 nogo condition during the second run (r = -.51, p = .06). This trend suggests that those older subjects that actually over-recruited 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 nogo 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 nogo condition in the second run of the complex task did not correlate significantly with performance in the second run in either age group.

----*Insert Figures 4 about here*----

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 nogo stimuli), complexity (simple vs. complex task) and novelty (first vs. second run).

Previous studies in the literature have already shown that conflict (Nielson et al. 2002; Gazzaley et al. 2005; Zysset et al. 2007), task complexity (Viskontas et al. 2004; Gazzaley et al. 2007) or novelty (Kramer et al. 1999; Erickson et al., 2007b) 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 nogo condition, while they made a number of commission errors for the high-conflict nogo stimuli, especially in the complex task. Both age-groups improved their performance to high-conflict nogo 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 nogo conditions, but given the nature of the go/nogo 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 nogo stimuli and deactivated for low-conflict nogo 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 and Poldrack, 2004; Hester et al., 2004; Rubia et al. 2001). Notwithstanding the specific role of each of these neural nodes (Stuss and Alexander, 2007), taken together they overlap with an extensive fronto-parietal network that is involved during most cognitive control tasks (Duncan & Owen, 2000; Fox et al., 2005; Kelly et al. 2006), and shows intrinsic functional connectivity even at rest (Vincent et al. 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 over-recruited these regions when conflicting-nogo stimuli were embedded in the complex task. These results corroborate previous fMRI studies of aging reporting over-recruitment of a similar fronto-parietal network during conditions requiring top-down control (Morcom et al. 2007; Grady 2008; Zysset et al. 2007). Thus, over-recruitment especially occurs in the older group with increasing task-demands (it mostly occurs for high-conflicting vs. low-conflict nogo stimuli and during the complex vs. simple task).

Since age-related difficulties are likely to emerge in non-routine situations, such as during the early phases of task performance (e.g., Kramer et al. 1999; Erickson et al., 2007b), 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, while 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, while those differences disappeared in the second run.

This study extends previous work by showing that the often reported non-selective over-recruitment of brain regions, including homologous fronto-parietal areas in both hemispheres (Cabeza 2002; Logan et al. 2002; Park et al. 2001; Reuter-Lorenz et al. 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 over-recruitment 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 nogo condition (ii) of the first run (iii) of the complex task. Moreover, this initial over-recruitment 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 sub-group.

Therefore, neural over-recruitment 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 nogo 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 nogo trials are those that mostly suffer from response conflict, and mostly activate partial go responses even on correct nogo 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, in press), as a more suitable dependent variable to correlate with brain activation on correct nogo 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., Rypma and D'Esposito, 2000; Vallesi et al 2009b), 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 towards a more reflective, deliberative cognitive style with age (Velanova et al. 2007). While 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 nogo 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. Since the task-PLS analysis, like 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 sub-part 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 1-7 days later in a subsequent ERP session with the same tasks (Vallesi et al. 2009c), any age x task complexity interaction disappeared both behaviorally and at the neural level 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, while 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 and colleagues (2002) showed that it is possible to reduce under-recruitment 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 over-recruitment 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 nogo trials, older adults deactivated more these regions during low-conflict nogo 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 nogo stimuli. On the other hand, age-specific increased activation for the low-conflict nogo stimuli was mainly present in the rostral medial prefrontal region (Brodmann 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 (Nobre et al. 1999; Petrides et al. 2002). 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 non-target information (cf. Gazzaley et al. 2005; Vallesi et al. 2009c; Vallesi, Hasher, & Stuss, 2010).

The go/nogo procedure adopted here allowed us to investigate age-related changes in overcoming prepotent response tendencies. However, the use of nogo stimuli could make it unclear as to whether the brain regions that are over-activated in the older adults reflect a greater activation of inappropriate go-responses in the high-conflict nogo 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, since over-recruitment of the specific cognitive control regions reported here was more present in successful older individuals, if this over-recruitment 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 nogo conditions (Vallesi & Stuss, in press). 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 non-routine 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 frontopolar cortex (Sakai & Passingham, 2006) or in more extensive fronto-parietal networks (e.g., Dosenbach et al., 2008; Vallesi et al., 2009a). 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); non-routine motor learning (Jueptner et al., 1997); 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 over-recruitment occurs in aging with increasing task demands, as for instance by manipulating (possibly multi-componential) 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 (D'Esposito et al. 1999; Huettel et al. 2001). 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 over-recruitment usually reported in neuroimaging studies of aging may occur and on its possible functional significance. Compared to younger adults, older individuals engage more extensively 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, since it is strongly associated to the degree of success in avoiding commission errors.

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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 nogo conditions (conflict vs. irrelevant-nogo). R = right hemisphere. L = left hemisphere. BA = approximate Brodmann location. BSR = Bootstrap ratio in the PLS analysis.

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 Semi-Lunar 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

Table 2. Reliable clusters identified for LV1 in the task-PLS analysis concerning practice effects in the complex task. This analysis included the following experimental conditions: age group (young vs. older), run (first vs. second), and nogo condition (conflict vs. irrelevant-nogo). R = right hemisphere. L = left hemisphere. BA = approximate Brodmann location. BSR = Bootstrap ratio in the PLS analysis.

Positive saliences

			Talairach				
Lag	Cluster region	BA	x	y	z	Size	Bootstrap
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 Semi-Lunar Lobule	-	-44	-68	-40	18	6.3
4	R Middle Frontal Gyrus	9	36	9	33	31	6.1

Figure Captions

Figure 1. Behavioral data. (a) Percentage of errors (and standard errors of the mean) as a function of task, run, go/nogo 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.

Figure 2. Results of the first PLS analysis. (a) Design scores (arbitrary units) for the Latent Variable 1, according to age, task and nogo condition. (b) Temporal brain scores (arbitrary units and sign) indicating how the brain network in panel c generally responded to the task conditions. The symbols * and ** indicate a trend and a significant age x task x nogo 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 nogo 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-nogo in both tasks and groups). The bootstrap ratio map is superimposed on the average anatomical scans from all 28 participants.

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, nogo 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 nogo 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 x nogo condition x 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 nogo). The bootstrap ratio map is superimposed on the average anatomical scans from all 28 participants.

Figure 4. Correlation patterns between the individual brain scores for the high-conflict nogo 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.

Figure 1.

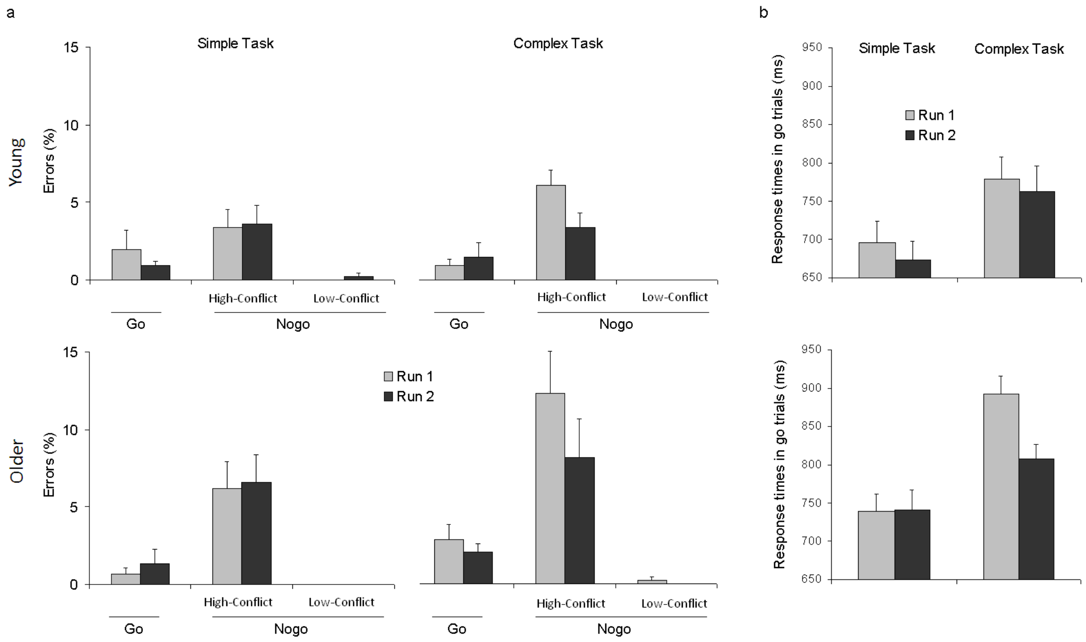

a
Simple Task
Complex Task
Young
Errors (%)
15
10
5
0
Go
High-Conflict
Low-Conflict
Nogo
Older
Run 1
Run 2
b
Response times in go trials (ms)
950
900
850
800
750
700
650
Simple Task
Complex Task
Run 1
Run 2

Figure 2

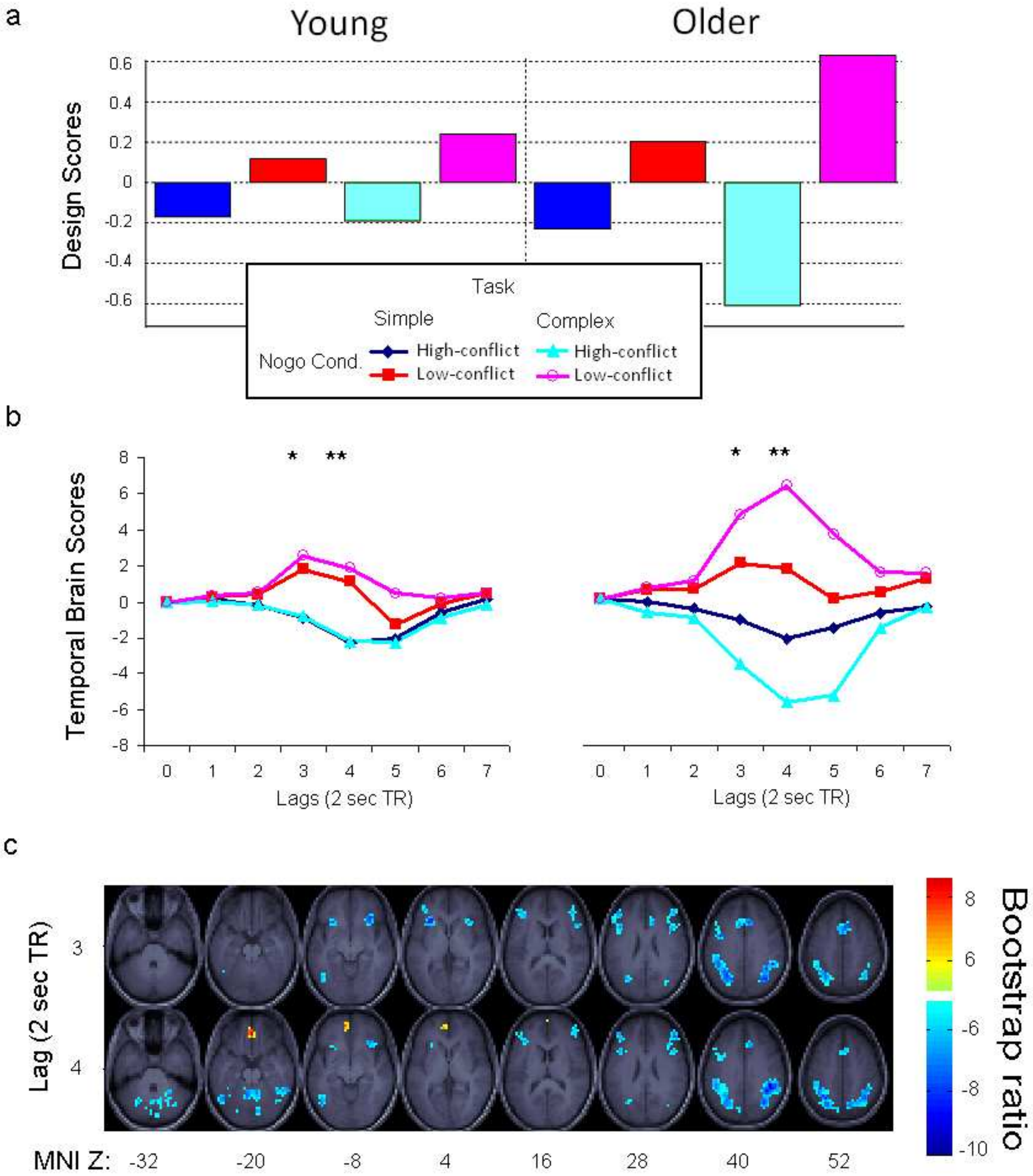

a
Young
Older
Design Scores
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
Task
Simple
Complex
Nogo Cond.
High-conflict
Low-conflict
High-conflict
Low-conflict
b
Temporal Brain Scores
8
6
4
2
0
-2
-4
-6
-8
*
**
*
**
0 1 2 3 4 5 6 7
Lags (2 sec TR)
0 1 2 3 4 5 6 7
Lags (2 sec TR)
c
Lag (2 sec TR)
3
4
MNI Z: -32 -20 -8 4 16 28 40 52
Bootstrap ratio
8
6
-6
-8
-10

Figure 3

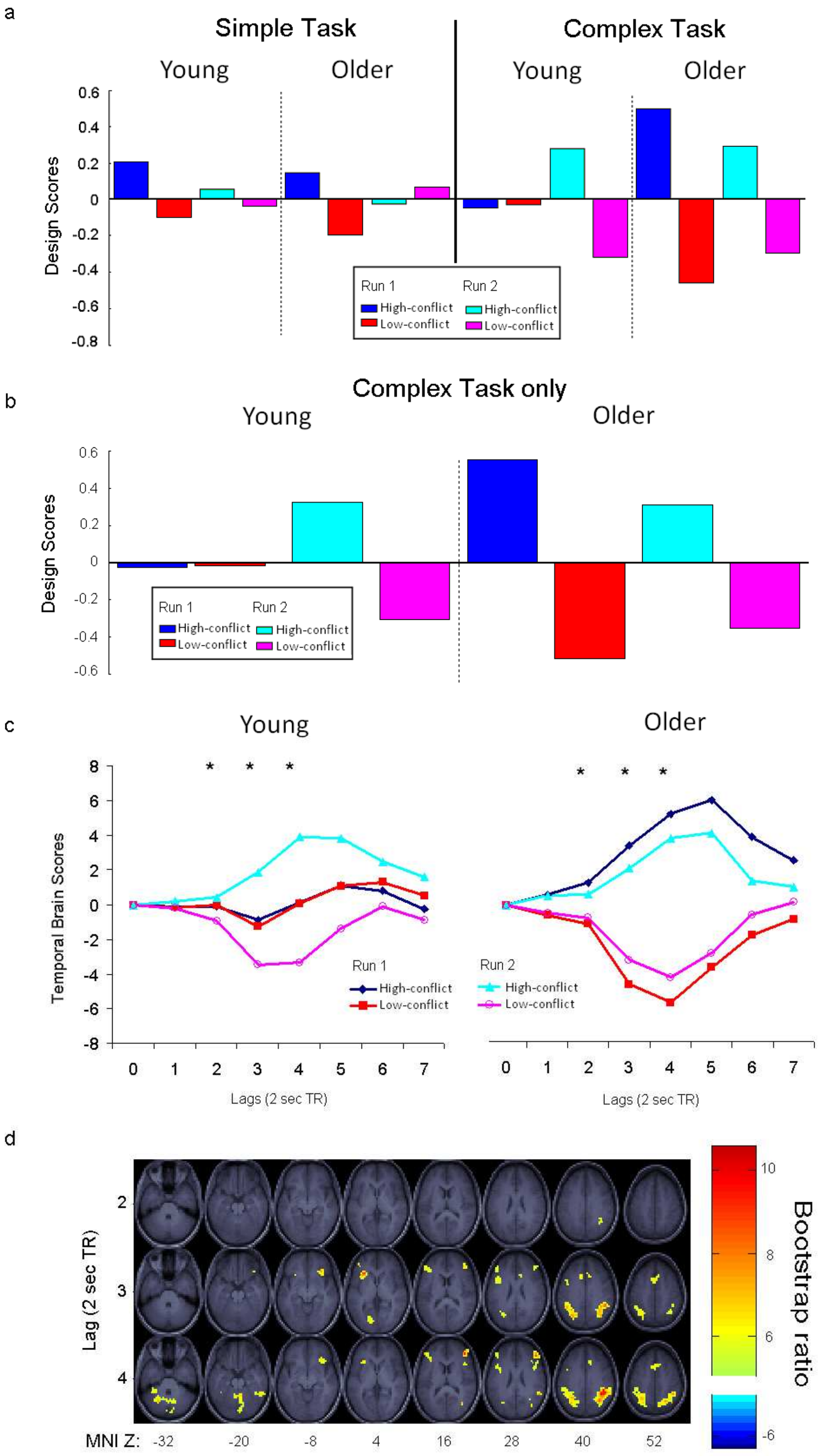
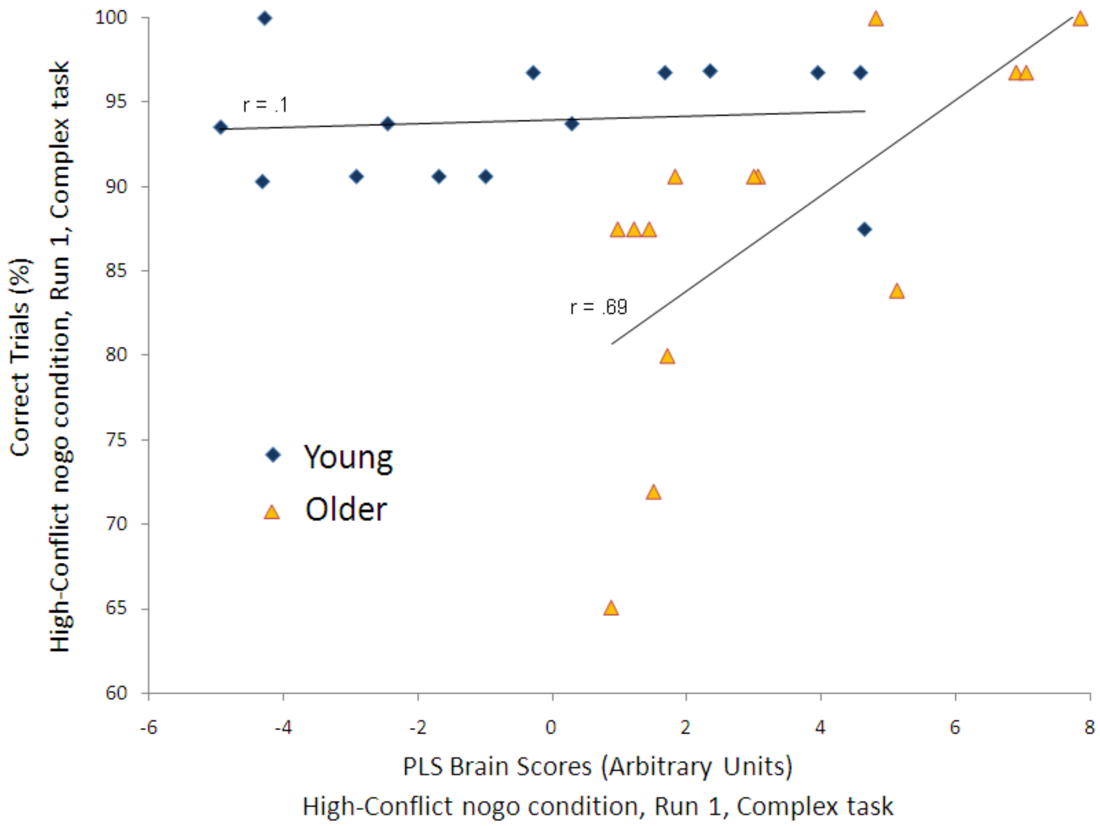

a
Simple Task
Complex Task
Young
Older
Young
Older
Design Scores
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
Run 1
Run 2
High-conflict
Low-conflict
High-conflict
Low-conflict
b
Complex Task only
Young
Older
Design Scores
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
Run 1
Run 2
High-conflict
Low-conflict
High-conflict
Low-conflict
c
Young
Older
Temporal Brain Scores
8
6
4
2
0
-2
-4
-6
-8
* * *
* * *
Run 1
High-conflict
Low-conflict
Run 2
High-conflict
Low-conflict
0 1 2 3 4 5 6 7
Lags (2 sec TR)
0 1 2 3 4 5 6 7
Lags (2 sec TR)
d
Lag (2 sec TR)
2
3
4
MNI Z: -32 -20 -8 4 16 28 40 52
10
8
6
-6
Bootstrap ratio

Figure 4


Correct Trials (%)
High-Conflict nogo condition, Run 1, Complex task
100
95
90
85
80
75
70
65
60
-6
-4
-2
0
2
4
6
8
r = .1
r = .69
Young
Older
PLS Brain Scores (Arbitrary Units)
High-Conflict nogo condition, Run 1, Complex task

Supplementary task-PLS analysis: high-conflict and low-conflict nogo in simple vs. complex task, in the young group only.

A Partial Least Square analysis was run in order to understand if learning effects could be detected for the complex task also in the young subjects, when they were considered on their own and not in comparison with the older group. This analysis included 2 nogo conditions (high-conflict and low-conflict), 2 tasks (simple and complex) and 2 runs (run 1 and run 2). Permutation and bootstrap tests were performed using the same parameters as in the other PLS analyses reported in the text of the main article. Like in those analyses, 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 mni2tal.m script (http://www.mrccbu.cam.ac.uk/Umaging/mnispace.html). The Talairach Daemon was used to find the likely Brodmann areas (Lancaster et al. 2000).

This analysis yielded two significant Latent Variables (LV). The first LV (observed singular value = 30.5, explained cross-block covariance = 27.8%, $p < .01$) showed a set of brain regions that decreased their activation during high-conflict nogo conditions from run 1 to run 2 in the simple task and increased their activation in the same condition from run 1 to run 2 in the complex task, basically resembling the pattern of design scores observed in the young group in the PLS analysis reported in the main article (see Figure 3a, Young subjects' panels). Critically, the second LV (observed singular value = 26.2, explained cross-block covariance = 20.6%, $p = .052$) extracted a set of brain regions that tended to decrease their activation during high-conflict nogo conditions from run 1 to run 2 in the complex task (see Figure S2a). The clusters involved in this LV are shown in Figure S2b and the voxels with the peak bootstrap ratios within each cluster are reported in Table S1.

Table S1. Reliable clusters identified for LV2 in the supplementary task-PLS analysis including the young group only, with tasks (simple vs. complex), and nogo conditions (high- vs. low-conflict nogo) as the experimental conditions. R = right hemisphere. L = left hemisphere. BA = approximate Brodmann area. BSR = Bootstrap ratio in the PLS analysis.

Positive saliences

			Talairach				
Lag	Cluster region	BA	x	y	z	Size	BSR
3	L Inferior Frontal Gyrus	9	-44	9	25	35	7.2
3	L Superior Parietal Lobule	7	-36	-56	47	41	6.9
3	R Inferior Frontal Gyrus	47	32	23	-5	17	6.6
3	L Anterior Cingulate Gyrus	32	-8	18	43	16	5.5
3	L Insula	13	-28	19	-4	15	5.2
4	R Inferior Parietal Lobule	40	44	-37	39	18	6.1
4	L Superior Parietal Lobule	7	-32	-60	51	22	5.9

Supplementary Figures

Figure S1. Design scores (arbitrary units) for the Latent Variable 1 (explained cross-block covariance = 30.4%, $p < .0001$) of the overall PLS analysis. This initial analysis included all the conditions from the 3 (go, high-conflict nogo, low-conflict nogo) x 2 groups (young, older) experimental design. Note that the design scores for the go conditions do not vary between the two age-groups.

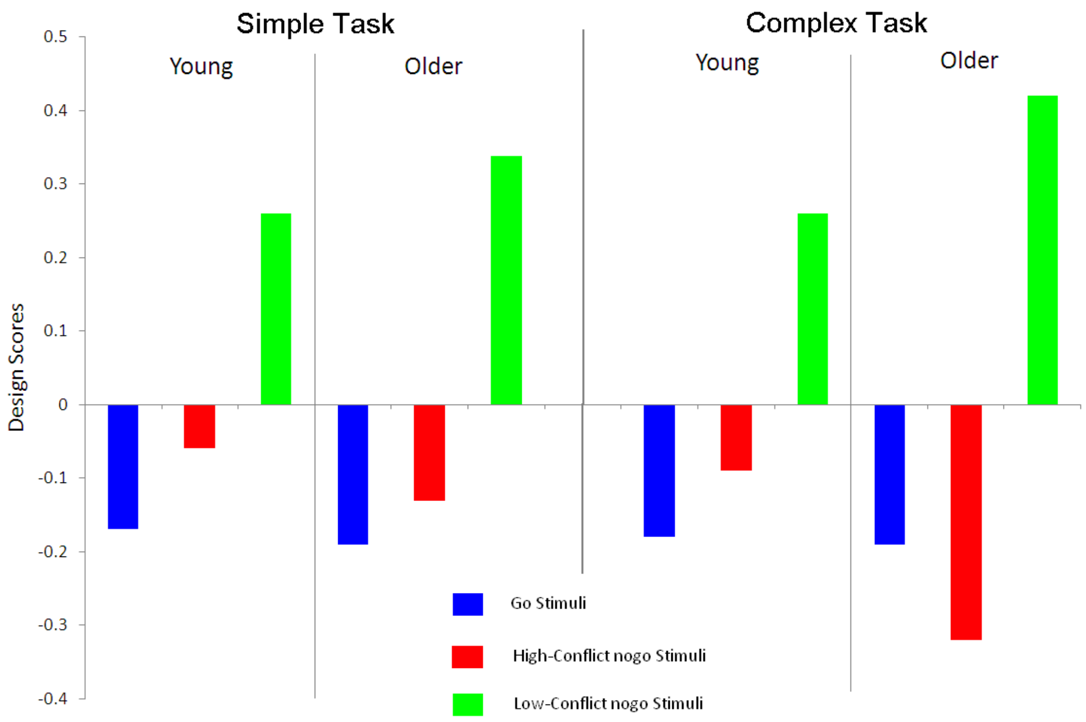


Figure S2. Results of the supplementary PLS analysis. (a) Design scores (arbitrary units) for the Latent Variable 2, according to task, run and nogo condition. (b) Brain clusters (number of voxels ≥ 15, bootstrap ratio ≥ 5) where design shown in panel a were mainly expressed. Main clusters from lag 3 only are shown (third Repetition Time: 4-6 sec). 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 design scores in panel a. The bootstrap ratio map is superimposed on a representative subject's anatomical scan.