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Age-related differences in brain activation during working memory updating: An fMRI study

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Abstract

Recent neuroimaging studies have reported an age-related reduction in brain activations in response to working memory load in task-sensitive brain regions. The current fMRI study investigated the age-related differences in brain activations of the updating mechanism in working memory, which was not investigated in previous studies. With a hybrid block/event-related design, this study was able to examine changes in BOLD signals (i.e., neuromodulation) to increase in updating, a type of cognitive control that is understudied. Older adults were separated into young-old and old-old cohorts to examine whether, within healthy aging, the neuromodulation to cognitive control decreases with age. Our results show that younger adults activate left precentral gyrus and right cerebellum more during trials that require updating than trials that do not require updating. Although older adults showed reduced neuromodulation in these two regions, the old-old cohort failed to show any significant neuromodulation in response to updating. Moreover, older adults not only showed reduced suppressions of the default mode network (DMN) regions during the task, they also overactivated some of the DMN regions, esp. the old-old, when compared to the younger adults. Older adults also showed overactivations in a region (right precentral gyrus) that is contralateral to a task-sensitive region that was activated in the younger adults during updating. Brain-behavior correlations suggest that age-related overactivations of these DMN regions and the right precentral gyrus are maladaptive to their performance. Our results suggest that not only the neuromodulation in response to updating demands is diminished in healthy aging, older adults also show maladaptive increases in activations of task-irrelevant regions and reduced hemispheric specificity during updating. These effects are most pronounced in old-old cohort, compared to young-old, suggesting that age-related declines in neuromodulation during cognitive control is more pronounced in older cohorts within healthy aging.

Keywords

Working memory updating; Cognitive cost; Aging; fMRI; Neuromodulation

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CRediT authorship contribution statement

Shuo Qin: Data curation, Writing - original draft, Formal analysis, Visualization, Investigation. **Chandramallika Basak:** Conceptualization, Methodology, Supervision, Writing - review & editing, Visualization, Investigation, Funding acquisition, Resources, Software, Project administration.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.neuropsychologia.2020.107335>.

1. Introduction

Advancing age in adults is accompanied with impairments in cognitive control functions, especially in working memory (Basak and Verhaeghen, 2011a; Bopp and Verhaeghen, 2005, 2018; Cappelletti et al., 2010; Rose et al., 2009; Verhaeghen and Basak, 2005). Working memory is defined as the ability to rapidly maintain and update information necessary to perform a certain task (Baddeley, 1986). Correctly updating information in working memory is crucial in many real-world situations, from counting and organizing items in the kitchen pantry to remembering and adapting script lines in theatre acting. Failure in updating working memory thus may lead to potential health hazard (e.g. rotting food items forgotten in the cabinet) and public embarrassment (e.g. missing script lines with plot changes in live performance).

Working memory updating has been commonly assessed by the N-back task in the laboratory settings. N-back task is a typical continuous memory updating task, where N depicts the set-size, that is, the number of items participants have to hold in memory at any given time (Redick & Lindsey, 2013; Verhaeghen and Basak, 2005; Verhaeghen et al., 2006). Brain activations during the N-back task in younger adults have been observed in the dorsal lateral and ventral lateral prefrontal cortex as well as its surrounding frontal regions, such as the frontal pole (Owen et al., 2005). Moreover, in younger adults, increases in activations from these task-sensitive regions have also been reported with increasing working memory load, that is, N (Manoach et al., 1997). Such increase in BOLD activations in response to increasing memory load (increasing task difficulty) has been associated with better task performance in a lifespan sample (Kennedy et al., 2017). One term that cognitive neuroscientists use in reference to such changes in BOLD activation in response to task difficulty is “neuromodulation” (Braver and Barch, 2002; Grandjean et al., 2012; Hakun and Johnson, 2017; Kennedy et al., 2017).

The traditional N-back tasks measure the set-size effects by contrasting performance in 2- or 3-back task blocks with that from 0- or 1-back task blocks. Although such design is effective in measuring both working memory load effect as well as working memory updating effect, the latter has rarely been examined using the traditional N-back tasks. Updating effect can be measured from comparing performance in trials that pose a memory updating demand versus trials that do not. For example, during a 2-back task, participants are asked to compare the current digit to the digit two trials back (e.g., Verhaeghen and Basak, 2005). When the current digit is the same as the digit two trials back, participants then accept the digit as a match and move on; in such non-update trial, there is no memory updating demand. However, when the current digit is different from the digit two trials back, participants must first respond that the current digit is a mismatch, and then update and replace the previous digit in memory with the current digit. The update trials, therefore, place a higher cognitive demand on the participants and result in the “update cost” in reaction time, with update trials taking longer time to respond to than non-update trials (Verhaeghen and Basak, 2005). In terms of neural responses, memory updating should elicit differences in neural activations, or neuromodulations, between non-update and update trials. Such neuromodulation would then be specific to working memory updating.

The primary aim of the current fMRI study was to examine age-related differences in neuromodulation during working memory updating using a random 2-back task (Basak & O'Connell, 2016; Basak and Verhaeghen, 2011b). Traditional 2-back tasks have a predictable probe-cue expectancy; therefore, the participant is always matching the target digit to the probe item two trials back (i.e. not one or three trials back). In the random 2-back tasks, probe-cue expectancy is random (Oberauer, 2005; Basak and Verhaeghen, 2011b), where digits are presented in two different colors: yellow and pink. Participants are then asked to compare the current digit to the previous digit in the same color, while color switching is random. To perform the task, participants have to constantly hold two digits in their memory, one pink and one yellow. Since the probe-cue expectancy is unpredictable, greater cognitive demand is placed on the participants in these random N-back tasks when compared to the traditional, predictable, N-back tasks, evidenced by reaction times, in both younger and older adults (Basak & O'Connell, 2016; Basak and Verhaeghen, 2011a; Oberauer, 2005). Such unpredictable probe-cueing also simulates real-life scenarios where random event occur and older adults have difficulties in tracking such event. Therefore, this task may be sensitive in detecting early memory deficits in older adults.

For the current fMRI study, we hypothesized that younger adults would show activations during the task blocks in brain regions similar to brain regions observed for traditional 2-back tasks. However, younger adults would also show neuromodulation between update and non-update trials, such that update trials would elicit higher neural responses than non-update trials, thus identifying brain regions underlying the updating mechanism of working memory. Also, based on the past results regarding age-related differences in neuromodulation during tasks of working memory load, we hypothesized that the older adults would show reduced neuromodulation to memory updating. However, it is not known whether these age-deficits are monotonical, with old-old showing greater deficits than young-old, or are these age-deficits observed only in old-old when brain health is much compromised.

An common finding from most aging neuroimaging studies is the observation that older adults activate additional brain regions to the regions that are activated in younger adults during a cognitive task (Spreng et al., 2010). Such overactivations in older adults have been reported during tasks of episodic memory (Cabeza, 2002; de Chastelaine et al., 2011; Morcom et al., 2007), object discrimination (Grady et al., 1992; Park et al., 2004), executive functions (Eich et al., 2016; Nashiro, Qin, O'Connell and Basak, 2018; Steffener et al., 2014) and working memory (Alichniewicz et al., 2012; Bennett et al., 2013). Overactivations are typically reported in frontal brain regions (e.g., Davis et al., 2008; for reviews see, Park and Reuter-Lorenz, 2009; Reuter--Lorenz and Cappell, 2008; Reuter-Lorenz and Park, 2014) and in contralateral brain regions, in the opposite hemisphere, of where younger adults are activating for task (for a review see, Cabeza, 2002). Interpretations of overactivations in older adults typically depend on the relationship between these overactivations and task performance within the older adults, examined by brain-behavior correlations. Overactivations are interpreted as compensatory only when a significant, positive, brain-behavior relationship is reported (for a review, see Cabeza et al., 2018).

However, most neuroimaging studies examining age-related differences in brain activations during tasks of executive functions, including publication from our own lab, have failed to find positive relationship between overactivation and task performance in older adults (e.g., Nashiro, Qin, O'Connell and Basak, 2018; Prakash et al., 2012; Steffener et al., 2014). In fact, some studies have reported a negative relationship between these overactivations and task performance in older adults (e.g., Nashiro et al., 2018; Steffener et al., 2016). These overactivations, which are not positively correlated with task performance, have been interpreted as a reduced specificity in neural recruitment during tasks in older adults (neural dedifferentiation; Li et al., 2001; for a recent review, see Koen and Rugg, 2019). In particular, if these overactivations are associated with decreased task performance, they are then interpreted as maladaptive overactivations (Nashiro et al., 2018).

It is possible that some of these observed overactivations in older adults reflect age-related differences (i.e., cohort differences) in neural recruitment, either compensatory or maladaptive, and that these overactivations are only specific to the oldest cohort in healthy aging. This issue is understudied, however, it is important given the wide age-range used to represent healthy aging in fMRI studies (55 years–90 years). It is therefore important to understand whether differences in interpretation of the overactivations across different studies is not partially due to cohort differences between these studies. For example, it is plausible that in young-old there is either a nominal difference in neuromodulation to executive control or overactivations that are compensatory to task performance. However, old-old cohort may fail to neuromodulate to cognitive control and show maladaptive, reduced specificity in neural recruitment during tasks.

The second aim of the current fMRI paper was to examine overactivations in healthy older adults during the random 2-back task, typically assessed by old > young contrasts in task-related activations (e.g., Alichniewicz et al., 2012; Prakash et al., 2012). Results on overactivations during 2-back tasks have been mixed. Alichniewicz et al. (2012) contrasted activations between healthy older adults and younger adults during a 2-back task and observed increased activations in posterior cingulate gyrus and precuneus regions. Older adults (mean age = 60 years) performed equally well as the younger adults in the 2-back task, therefore suggesting that the increased activations in the cingulate gyrus and the precuneus may be compensatory (Alichniewicz et al., 2012). It is worth noting that the posterior cingulate cortex and precuneus are included in the default mode network (DMN) by some researchers (Buckner et al., 2008; Laird et al., 2011), and that the regions of the DMN are typically suppressed in younger adults during cognitive tasks (Buckner et al., 2008; Laird et al., 2011). Alichniewicz et al. (2012) did not perform further analyses on these brain regions; therefore, it was not clear whether increased activations from these DMN regions in older adults were reduced suppressions or increased activations, compared to the younger adults. Prakash et al. (2012) specifically measured activity in the default mode networks (DMN) in both younger and older adults during a 2-back task and found reduced DMN suppressions in the older adults during task when compared to the younger adults. However, these reduced DMN suppressions were related to worse task performance in older adults (Prakash et al., 2012), suggesting maladaptive brain activation patterns to older adults' performance.

One big difference between these two studies was the age of older participants in their sample. In the Alichniewicz et al. (2012) the mean age for older participants was 60, while in the Prakash et al. (2012) the mean age of older participants was 72. It was possible that age-related differences in activations (reduced suppressions or increased activations) in these DMN regions are compensatory to a younger cohort of the older adults (e.g., 60-year-old), but not to the older old (e.g., 70 years and beyond). Such differences in activations in brain regions of the same network could reflect a cohort difference between the 60-year-old and the 70-year-olds. On the other hand, these differences could reflect a continuation of the aging process in brain activations such that what was compensatory in the young-old could be maladaptive in the old-old due to further functional and structural degradation of other brain regions.

A unique characteristic of the current study is that we included two groups of older adults: young-old (age range: 55–67) and old-old (age range: 68–85). By having two cohorts of older adults – young-old and old-old – we can not only observe age-related differences in brain activations between younger and older adults (younger vs. old-old), we can also observe differences between the different stages of aging (young-old vs. old-old). We hypothesize that overactivations observed in young-old adults (young-old > old-old) may be compensatory. However, if overactivations are observed in old-old adults (old-old > young-old), then these overactivations may be maladaptive to task performance.

2. Methods

2.1. Participants

Twenty-seven right-handed younger adults ($M_{age} = 25.7$, $SD_{age} = 3.86$; $M_{education} = 16.69$, $SD_{education} = 1.99$; 17 female) and 54 right-handed healthy older adults ($M_{age} = 66.61$, $SD_{age} = 6.73$; $M_{education} = 15.76$, $SD_{education} = 2.06$; 28 female) were recruited from Dallas and its neighboring communities through fliers, online advertisement and local newspapers. We further separated older adults into two age-groups: 1. Young-Old ($N = 27$, $M_{age} = 61.22$, $SD_{age} = 3.38$; $M_{education} = 15.54$, $SD_{education} = 2.56$; 13 female) and 2. Old-Old ($N = 27$, $M_{age} = 72$, $SD_{age} = 4.54$; $M_{education} = 15.86$, $SD_{education} = 3.87$; 15 female). Participants were screened for any medical, neurological, or psychiatric illnesses. Other exclusion criteria included current or previous substance abuse, less than a high school education, left-handedness, depression (assessed by the Geriatric Depression Scale, Burke et al., 1991), psychiatric disorders, pregnancy, color blindness (assessed by the Ishihara Color Blindness test, Clark, 1924), and a Mini-Mental Status Examination (MMSE) score of less than 26 for older adults ($M_{MMSE} = 28.49$, $SD_{MMSE} = 1.39$). All participants were native or fluent English speakers and had normal or corrected 20/30 vision. All participants underwent training on a mock scanner to ensure their MRI compatibility. Participants signed an informed consent, approved both by the University of Texas at Dallas and the University of Texas Southwestern Medical Center Institutional Review Boards, and were paid \$45 for the 45 min MRI session and \$15 for the mock scanner session.

2.2. Imaging procedures

Scanning was performed with a Philips Achieva 3T MR scanner (Philips Medical Systems, Andover, MA, USA) with a 32-channel head coil. High-resolution anatomical images were acquired, using a transverse MPRAGE T1-weighted sequence with the following parameters (TR = 8.1 ms; TE = 3.7 ms; flip angle = 12°; acquisition matrix = 256 × 204; voxel size = 1 mm³; 160 slices). Functional images were acquired using an echo-planar sequence (TR = 1500 ms; TE = 30 ms; flip angle = 60°; acquisition matrix = 64 × 64; voxel size = 3.44 × 3.44 × 5 mm; 29 axial slices). We used a hybrid blocked and event-related design (for a review, see Peterson & Dubis, 2012). There were two runs, each run lasting for 6.5 min and consisted of a fixation block, followed by 6 alternating task and fixation blocks, each lasting for 30 s (see Fig. 1). There were 14 fixation blocks and 12 task blocks, resulting in a total of 240 trials (20 trials × 12 blocks). Functional images from the two runs were pre-processed independently and combined for higher-level group analyses.

2.3. Memory updating: the fMRI task

In this continuous working memory updating task, a single colored (pink or yellow) digit (1–9) was presented in the center of the screen, on a black background (Fig. 1). Participants were asked to judge if the current digit presented was the same (left hand button press) or different (right hand button press) from the last digit presented in the same color (for example, comparing a yellow digit to the last presented yellow digit). The current experiment focused on two types of trials during event-related analysis: 1) non-update trials, where the current digit had the same identity as the previous one of the same color, 2) update trials, where the current digit was different to the previous digit of the same color. These two types of trials were of same proportion (50%) and were randomly assigned in any block.

Each stimulus was presented for 1450 ms, followed by a fixation for a very short duration (50 ms), thus causing a visual separation between two subsequent stimuli. This short visual break allowed for detection of two consecutive same colored digits as two separate trials to respond to (e.g., yellow 3 followed by yellow 3). The average inter-stimulus interval (ITI) between two non-update trials was 2.93 ± 1.35 s, and average ITI between two update trials was 2.96 ± 1.38 s. Update and non-update trials were randomly presented in any task block, with ITI ranging between 1.5 and 6 s.

Prior to the fMRI session, all participants practiced the task multiple times until individual accuracy (percent correct) reached 80%.

2.4. Methods of analysis: behavioral data

Overall accuracy (percent correct) from the fMRI task were subjected to one-way analysis of variance (ANOVA) with age-group (young, young-old, old-old) as the between-subject variable. Reaction time (RT) was not included in the main analyses (See supplementary material).

Update cost was calculated based on the RTs of Update and Non-update trials [Update RT - Non-update RT]. Only RTs from accurate trials were included in the calculation of the update cost. Update cost was then subjected to one-way ANOVAs with age-group as the

between-subject variable. Sidak correction was applied to all post-hoc pair-wise comparisons if needed. Level of significance was set at 0.05.

2.5. Methods of analysis: fMRI data

2.5.1. Preprocessing—The first seven EPI volumes were not recorded to allow the signal to reach steady-state magnetization. Preprocessing were performed using FSL 5.0.4 (FMRIB's Software Library; www.fmrib.ox.ac.uk/fsl), which included motion correction with MCFLIRT (Jenkinson and Smith, 2001), removal of non-brain structures using BET (Smith, 2002), spatial smoothing of the data using a Gaussian kernel of 6 mm full-width at half-maximum, and high-pass temporal filtering equivalent to 100 s for block design analysis and event-related design analysis. The lengths of high-pass filter for block and event-related design were determined via the “estimate high-pass filter” function in FSL. We created a study-specific template by registering each participant's high-resolution structural image to 152 T1 Montreal Neurological Institute (MNI) using FLIRT, and subsequently smoothing and averaging these images into a composite image. We performed linear registration between the functional and structural images using affine boundary-based registration (Greve and Fischl, 2009). The structural images were then normalized to the study-specific template by linear registration (FLIRT tools from FSL; Jenkinson and Smith, 2001). The co-registered functional images were then combined, using distortion correction and registration (BBR), with the normalized structural images for group level analyses. The use of a hybrid block/event-related design in this study enabled us to perform block and event-related analyses of the same data set, as described below.

2.5.2. Whole brain analyses—Whole-brain analyses were conducted using FSL FEAT 6.00. Two analyses were conducted, a) block design analysis to investigate sustained activation during task blocks, and b) event-related analysis to investigate transient activation between update and non-update trials. Within each analysis, two contrasts were set up: 1) mean activation in younger adults and 2) older greater than younger activation contrasts.

2.5.2.1. Block design analyses.: For each run in every participant, stimulus-dependent changes in BOLD signal were modeled with two regressors (i.e., task and fixation blocks). The regressors were convolved with a double gamma hemodynamic response function, including the six head movement parameters as confounds. Temporal filtering was also applied. For the first-individual level analyses, the amplitude of the hemodynamic response was estimated to differentiate task blocks versus fixation blocks. The resulting images were then entered into a group analysis to obtain the average mean percent signal changes for the task > fixation and fixation > task contrast across all participants. A stringent cluster correction threshold was applied following recommendation from Woo and colleagues (Woo et al., 2014). Z (Gaussianised T/F) statistic images were thresholded at the whole-brain level using clusters determined by $z > 3.1$ and a cluster-corrected significance threshold of $p = .001$.

2.5.2.2. Event-related design analyses to identify “update-sensitive” regions.: For each run in every participant, stimulus-dependent changes in BOLD signal were modeled with three regressors: 1. non-update 2. update, and 3. error trials. ITI varied between 0.5 s and 6 s

for non-update and update trials. The regressors were convolved with a double gamma hemodynamic response function, including the six head movement parameters as confounds. Temporal filtering was applied, and temporal derivatives of each of the regressors were also included. To identify the effects of each regressors relative to fixation, the fixation blocks were implicitly modeled as “null event” epochs, similar to block design analysis (Mechelli et al., 2003). Such inclusion of trial-free period obtained a baseline level, from which event signals were compared to in an event-related fMRI paradigm with stochastic event distribution (Friston et al., 1999). The first two trials from each task block were removed from analysis to prevent a sharp increase in activation signal following a fixation block. The resulting images were then entered into a group analysis to obtain the average mean percent signal changes for the difference between update versus non-update trials, across all participants. Percent signal change necessary to detect a difference between the update and non-update trials was estimated to be about 1% by FSL (Smith et al., 2007), with 1.5s–6s ITI between the two types of trials. Z (Gaussianised T/F) statistic images were thresholded at the whole-brain level using clusters determined by $z > 3.1$ and a cluster-corrected significance threshold of $p = .001$.

2.5.3. Post-hoc region of interest (ROI) analyses—For task-sensitive ROIs defined in younger adults, mean percent signal changes averaged across all voxels were extracted from each participant, using the *featquery* function of FSL. Regional brain activation differences across the three age groups (young, young-old and old-old) were assessed by multiple analyses of variance (ANOVA) with age-group as the between-subject variable, and for event-related ROIs with task conditions (update and non-update) as within-subject variables. For ROIs defined by older greater than younger contrast, mean percent signal changes were extracted and plotted as bar plots, to visualize how activations in age-sensitive ROIs differ across age groups. Independent sample *T* tests between young-old and old-old adults activations from age-sensitive ROIs were conducted to examine whether increases in activation continued in the older age groups. For ROIs defined as updating sensitive regions (i.e., regions showing significant activation for update, compared to, non-update trials), correlation analyses were conducted across all participants regardless of age between neuromodulation (update minus non-update activations) and task performance (overall accuracy and update cost). Such correlations would suggest whether neuromodulation in these regions were directly related to working memory updating performance across all age groups.

For overactivation ROIs, brain-behavior correlation analyses were conducted across all participants. Positive relationships between activations from overactivations ROIs and task performance (higher accuracy or lower update cost) would suggest that such activations are beneficial (compensatory) to task performance. Negative relationships between activations and task performance (lower accuracy or higher update cost) would suggest that such activations are detrimental (maladaptive) to task performance. Alternatively, non-significant relationship between activations from these overactivations ROIs and task performance could indicate a reduction of neural specificity.

3. Results

Sidak correction was applied to any post-hoc pair-wise comparisons between the three age-groups (young, young-old, old-old), Alpha level of significance was set to 0.05.

3.1. Differences in behavioral outcomes between younger adults and older adults' groups

3.1.1. Accuracy—A one-way ANOVA, with age-group (young, young-old, old-old) as the between-subject variable and overall accuracy as the dependent variable, found a significant main effect of age-group on accuracy during the random 2-back task, $F(2,78) = 17.01$, $p < .01$, $\eta^2_{\text{partial}} = 0.30$ (Fig. 2a). Post-hoc pair-wise comparisons between the three age-groups showed that there were significant differences between the accuracies of younger adults and the two groups of older adults (young vs. young-old: $M_{\text{difference}} = 0.11$, $p < .01$; young vs. old-old: $M_{\text{difference}} = 0.12$, $p < .01$), but there was no difference between the two groups of older adults ($M_{\text{difference}} = 0.01$, $p = .92$).

3.1.2. Update cost—A one-way ANOVA, with age-group (young, young-old, old-old) as the between-subject variable and update cost as the dependent variable, found a significant main effect of age-group on update cost during the random 2-back task, $F(2,78) = 8.01$, $p < .01$, $\eta^2_{\text{partial}} = 0.25$ (Fig. 2b). Post-hoc pair-wise comparisons between the three age-groups showed that there were significant differences in the update costs of the two extreme age-groups, that is, younger adults and the old-old adults (young vs. old-old: $M_{\text{difference}} = -65.81$, $p < .01$). However, no differences were observed between the younger adults and the young-old adults (young vs. young-old: $M_{\text{difference}} = -33.2$, $p = .23$) or between the young-old and old-old adults ($M_{\text{difference}} = 45.21$, $p = .62$).

3.2. fMRI whole brain analyses and post-hoc ROI analyses results

3.2.1. Task-sensitive brain regions—A large frontal-parietal ROI that greatly overlapped with the frontal-parietal network (Laird et al., 2011; Supplementary material) showed higher mean percent signal change during the task blocks than the fixation blocks in younger adults (see Table 1, Fig. 3). Since the activity of this ROI was greater during the task blocks than during the fixation blocks, this ROI was labeled as a “task-positive” ROI. Four large ROIs, two of which closely mapped on to the default mode network (DMN; Laird et al., 2011; Supplementary material), showed negative mean percent signal changes during task blocks in younger adults (Table 1, Fig. 4). These ROIs were therefore labeled as “task-negative” ROIs. Event-related analysis of the data from the younger adults resulted in two significant “update-sensitive” regions (the Left Post-central gyrus and Right Cerebellum), where the mean percent signal change for the Update condition was greater than that for the Non-update condition (Table 1, Fig. 5).

Mean percent signal change from the task-positive and task-negative ROIs were averaged across all voxels and extracted for each participant. For the task-positive ROI (Fig. 3), there was no main effect of age-group, $F(2, 78) = 0.55$, $p = .58$, $\eta^2 = 0.01$, suggesting that activity from this cluster was similar across all three age-groups. Results from the four task-negative ROIs (Fig. 4) showed significant main effects of age-group on all four ROIs: Left Insula [$F(2, 78) = 0.55$, $p = .58$, $\eta^2 = 0.01$], Left Inferior Frontal Gyrus [$F(2, 78) = 0.55$, $p = .58$, η^2

= 0.01], Paracingulate Gyrus [$F(2, 78) = 0.55, p = .58, \eta^2 = 0.01$], and Precuneus [$F(2, 78) = 0.55, p = .58, \eta^2 = 0.01$]. Post-hoc comparisons between the three age groups indicated that older adults (both young-old and old-old) had reduced suppression of these task-negative regions compared to the younger adults: Left Insula (young-old vs. young: $M_{\text{difference}} = 0.14, p = .05$; old-old vs. young: $M_{\text{difference}} = 0.21, p = .01$), Left Inferior Frontal Gyrus (young-old vs. young: $M_{\text{difference}} = 0.39, p < .01$; old-old vs. young: $M_{\text{difference}} = 0.39, p < .01$), Paracingulate Gyrus (young-old vs. young: $M_{\text{difference}} = 0.25, p = .04$; old-old vs. young: $M_{\text{difference}} = 0.46, p < .01$), and Precuneus (young-old vs. young: $M_{\text{difference}} = 0.28, p < .01$; old-old vs. young: $M_{\text{difference}} = 0.37, p < .01$). There was no significant difference between the two older cohorts (young-old vs. old-old) in any of these task-negative regions (p 's > 0.1).

Mean percent signal changes for both update trials and non-update trials were extracted from all individuals in each age-group for the two update-sensitive ROIs (update $>$ non-update contrast): the Left Precentral gyrus and right Cerebellum, (Fig. 5). A repeated measures 2×3 ANOVA with condition (non-update, update) as a within-subject variable and age-group (young, young-old, old-old) as a between-subject variable, was conducted for each ROI. For Left Pre-central Gyrus (Fig. 5A), significant main effect of age-group was observed, $F(2, 78) = 3.63, p = .03, \eta^2 = 0.09$, together with significant age-group by condition interaction, $F(2, 78) = 17.07, p < .01, \eta^2 = 0.30$. Specifically, significant increases in activation during update trials (i.e., neuromodulation), compared to non-update trials, were observed in both younger adults ($M_{\text{difference}} = 0.46, p < .01$) and the young-old group ($M_{\text{difference}} = 0.13, p = .02$). However, such neuromodulation of left Precentral Gyrus was not observed for the oldest cohort, that is, the old-old age group ($M_{\text{difference}} = 0.03, p = .65$).

For Right Cerebellum, the 3×2 repeated measures ANOVA resulted in a significant main effect of age-group, $F(2, 78) = 3.83, p = .03, \eta^2 = 0.09$, as well as a significant condition by age-group interaction, $F(2, 78) = 5.35, p < .01, \eta^2 = 0.12$. Post-hoc comparisons showed that this significant interaction was driven by significant neuromodulations between non-update and update trials in younger adults ($M_{\text{difference}} = -0.23, p < .01$) and the young-old group ($M_{\text{difference}} = -0.12, p = .01$), but not in the old-old group ($M_{\text{difference}} = -0.04, p = .33$).

As expected, for both ROIs, there was also a significant main effect of condition [Left Post-central Gyrus: $F(1, 78) = 41.6, p < .01, \eta^2 = 0.35$; Cerebellum: $F(1, 78) = 28.6, p < .01, \eta^2 = 0.27$]. Although younger adults and young-old show significant increases in brain activation in response to updating, it is not clear if this neuromodulation to difficulty is reduced with age. Therefore, a MANOVA was performed with age-group as the between subject variable and neuromodulations (difference in mean percent signal change of update trials from non-update trials) from left pre-central gyrus and right cerebellum as the dependent variables. This MANOVA showed a significant main effects of age-group ($F(2, 78) = 19.7, p < .01, \eta^2 = 0.4$). Post-hoc pairwise comparison showed that neuromodulation is significantly decreased from younger adults to young-old cohort in left pre-central region ($M_{\text{difference}} = 0.33, p < .01$), but not in right cerebellum ($M_{\text{difference}} = 0.06, p = .13$).

Brain-behavior correlation analyses investigating the relationship between the extent of neuromodulation (Update - Non-update activations) and task performance (accuracy and update cost) in *all* participants showed that increased neuromodulations in both ROIs were significantly correlated with better task performance. For Left Precentral Gyrus, increased neuromodulation (update mean % sc – non-update mean % sc) was significantly correlated with increased accuracy ($r = .35, p < .01$) and with decreased update cost ($r = -0.37, p < .01$) for all participants. Similarly, for Right Cerebellum, increased neuromodulation was significantly correlated with increased accuracy ($r = 0.23, p = .05$) and decreased update cost ($r = -0.39, p < .01$) for all participants. These results suggest that, irrespective of age, greater extent of neuromodulation in the two update-sensitive regions (Left Precentral Gyrus and Right Cerebellum) was associated with better performance in the random 2-back task.

3.2.2. Overactivations in older adults (older > younger contrast)—In block design analysis (Older > Younger), older adults showed overactivations compared to younger adults in eight ROIs: 1) right superior frontal gyrus, 2) anterior cingulate gyrus, 3) left supramarginal gyrus, 4) right supramarginal gyrus, 5) left lateral occipital cortex, 6) right occipital fusiform, 7) bilateral precuneus, and 8) posterior cingulate gyrus (Table 2; Fig. 6). Mean percent signal change from these ROIs were extracted from all individuals in all three age-groups. Most of these regions were part of the DMN, which younger adults are expected to deactivate or suppress during the task blocks, when compared to the fixation blocks. Indeed, younger adults were suppressing seven of these eight ‘Overactivation’ regions, except the left supramarginal gyrus, where activation from younger adults was near zero. A multivariate analysis of variance (MANOVA), with age group (young, young-old, and old-old) as a between subject variable and activations from the 8 ROIs as dependent variables, showed significant main effect of age-group: $F(8, 72) = 8.32, p < .01$. Post-hoc pairwise comparison with Sidak correction showed that in two of these ROIs (the anterior and the posterior cingulate gyri) old-old adults showed significantly higher mean percent signal changes (representing either reduced suppressions or overactivations) than young-old adults (anterior: $M_{\text{difference}} = -0.35, p = .05$; posterior: $M_{\text{difference}} = -0.18, p = .05$).

Event-related analysis for age-related overactivations during updating (Update > Non-update; Older > Younger) resulted in a cluster that encompassed right post-central gyrus (Fig. 7). The analysis of this ROI indicates that the younger adults were activating the right pre-central gyrus only during the non-update trials, but suppressing it during the update trials. A univariate ANOVA with age-group as the between subject variable and activations from update trials as dependent variables showed significant main effect of age-group [$F(2, 78) = 17.71, p < .01$]. Post-hoc pairwise comparison showed that compared to younger adults both young-old ($M_{\text{difference}} = -0.47, p < .01$) and old-old adults ($M_{\text{difference}} = -0.63, p < .01$) had increased activation during update trials.

Since we did not observe any overactivations in the young-old group compared to the old-old group, it is possible that most of the observed overactivation ROIs in this study are representing maladaptive activations. To test if these age-related overactivations (Right Superior Frontal Gyrus, Posterior Cingulate/Postcentral, Bilateral Supramarginal Gyrus, Right Occipital Fusiform Gyrus and Right Pre-central Gyrus) or reduced suppressions (Left Anterior Cingulate Gyrus, left Lateral Occipital Gyrus, and Precuneus) are truly

maladaptive, we conducted brain-behavior regression analyses with activations from these 9 ROIs as independent predictors and task performance (accuracy and update cost) as dependent variables. To reduce the number of comparisons, as well as to control for type 1 error, mean percent signal changes from these 9 ROIs were averaged to investigate the overall relationship between overactivation and task performance. Regression results show that overall overactivations in these ROIs are associated with worse accuracy ($\beta = -.3$, $p < .01$) as well as higher update cost ($\beta = 0.26$, $p = .02$). These results indicate that increased activation or reduced suppression of these regions are maladaptive to task performance.

In addition, individual brain-behavior correlations between activations from these 9 ROIs and task performance (that is, accuracy and update cost) were also conducted to explore the relationship between overactivations and performance in each ROI. These brain-behavior correlations are reported in Table 3. We found a consistent pattern of negative relationship between brain activations from these regions and task performance, such that increased activations in these regions were associated with worse accuracy and higher update cost. As expected, no compensatory overactivations (positive relationship) was observed.

4. Discussion

The main aim of the current fMRI study was to examine age-related differences in brain activations during a continuous working memory updating task, that is, the random 2-back task. Such random N-back tasks have been used in behavioral studies (Oberauer, 2005; Basak and Verhaeghen, 2011a), and, for N greater than or equal to 2, showed slower RTs than the traditional, predictable N-back tasks in both older (Basak & O'Connell, 2016) and younger adults (Basak and Verhaeghen, 2011a; Verhaeghen and Basak, 2005). Although past studies have investigated age-related differences in brain activations during the N-back tasks (Buckner et al., 2008; Kennedy et al., 2017; Prakash et al., 2012), none have investigated the neural mechanism involved in the updating process while performing these tasks. Such an investigation is timely and significant given the importance of updating as one of the three cognitive control processes (Miyake et al., 2000) and its relationship with complex cognition, such as reasoning (Friedman and Miyake, 2017). In continuous memory updating paradigms, updating is severely affected by aging (Verhaeghen and Basak, 2005; Verhaeghen et al., 2006; Basak and Zelinski, 2013; Basak & O'Connell, 2016), however its neural underpinnings and any age-related differences associated with these neural responses are understudied. By using the random 2-back task in the current study, we investigated the updating mechanism involved during unpredictable probe-cueing in working memory. This unpredictability underlies many real-world scenarios where the memory probes occur in random temporal order. Therefore, it is important to study brain activations to better understand how we update unpredictably cued information in working memory, and how aging influences this cognitive control mechanism.

In the current study, brain regions sensitive to neuromodulation between randomly cued non-update and update items (that is, the task-sensitive regions) were first defined in the younger adults. A large fronto-parietal cluster in young showed significant task-sensitive activations. These results are similar to those from previous block design fMRI studies on standard N-back task, where significant activations have been observed in the bilateral dorsolateral and

ventrolateral prefrontal cortices, as well as in the lateral parietal regions (for a meta-analysis, see Owen et al., 2005). In addition to the task-sensitive activations in the large fronto-parietal cluster, we also observed suppressions of four brain regions, including regions of the DMN, during the task. These four large regions of suppressions were precuneus, paracingulate gyrus, insula and inferior frontal gyrus. These results are in line with past fMRI studies on N-back tasks, where suppressions of similar DMN regions, especially the precuneus and paracingulate gyrus, have been reported in younger adults (Buckner et al., 2008; Prakash et al., 2012). Although the insula and the inferior frontal gyrus are not typically considered to be a part of the DMN, suppressions of these two regions have been in cognitively challenging tasks, including tasks of executive functions (Harrison et al., 2011; Prakash et al., 2012).

In addition to these activations and suppressions in response to the task blocks in the current study, younger adults also showed significant neuromodulation to the updating process (that is, increased activation during update, compared to non-update, trials) of working memory in the left pre-central gyrus and in the right cerebellum. These two regions are considered to be responsible for motor coordination, and executive functions related to psychomotor responses. In particular, activations in the pre-central gyrus and cerebellar regions have been observed during tasks of executive functions in younger adults (Visual working memory: Lacourse et al., 2005; Auditory working memory: Oullier et al., 2005; Dual tasking: Wu et al., 2013), suggesting that these regions respond to greater demands of cognitive control across a wide variety of tasks. Only two neuroimaging studies have specifically examined the updating process in past (Murty et al., 2011; Podell et al., 2012). However, they did not use continuous memory updating paradigm that is used in the current study. Both studies used a cued updating paradigm where participants were cued to either update or remember target digits presented on screen as independent events in an event-related design. Results from these two studies also reported neuromodulation in pre-central gyrus and cerebellum (Murty et al., 2011; Podell et al., 2012). Our results, therefore, generalizes these findings of neuromodulation in the pre-central gyrus and cerebellum in working memory updating to the continuous memory updating paradigms, such as the random N-back task.

It is important to note that both updating sensitive regions are motor coordination regions. Both the current paradigm and the cued working memory updating paradigm used by Murty et al. (2011) did not counterbalance the hand press responses, such that memory updating judgement for both paradigms are confounded with hand press responses. The right hand in both paradigms was always associated with the working memory updating judgement—“different” in the current paradigm and “correctly updated” in the 2011 cued updating paradigm. It is, therefore, possible that the brain regions showing neuromodulation to working memory updating in both paradigms are confounded with brain regions controlling motor responses of the right hand, specifically the left pre-central gyrus.

However, if activations from the left pre-central gyrus were solely due to right hand motor response, then we would expect to observed opposite activation pattern (non-update > update) in the homologous brain region in the opposite hemisphere, that is, the right pre-central gyrus. But no such activation was observed for non-update > update contrast. Our results therefore suggest that activations from the left precentral gyri are related to working

memory updating, although some of these activations could be partially, but not completely, attributed to execution of the hand press responses.

Age-related differences in neuromodulation were of particular interest to the current study. Many fMRI studies investigating age-related differences in working memory have reported that successful neuromodulation with increasing working memory load was related to better task performance in both younger and older adults (Bennett et al., 2013; Kennedy et al., 2017; Mattay et al., 2006; Schneider-Garces et al., 2010). Our results show that the young-old (age range: 55–67) had similar neuromodulations in the two update-sensitive brain regions (esp. the right cerebellum) when compared to the younger adults. However, the old-old adults (age range: 68–85) failed to show neuromodulation in either region. Importantly, brain-behavior correlations between neuromodulations of the update-sensitive region (left pre-central gyrus, right cerebellum) and task performance (updating cost, accuracy) shows that participants with increased neuromodulation also had better task performance. The current results, therefore, suggest that older adults who could maintain neuromodulation in left pre-central gyrus and right cerebellum like younger adults also performed like younger adults, and that this maintenance ability diminished in older adults, esp. old-old.

Although older adults showed brain activations similar to younger adults in the task-sensitive fronto-parietal cluster, older adults showed significantly worse performance than younger adults. There are two possibilities of such poorer performance in older adults. First possibility is that older adults may show reduced suppression of task-irrelevant regions, particularly the DMN regions, that are well suppressed in younger adults during the task. The second possibility arises from older adults overactivations of additional brain regions during the task that are typically not recruited in young. Overactivations during tasks of executive functions have been reported in frontal brain regions (e.g., Davis et al., 2008; for a reviews see, Park and Reuter-Lorenz, 2009; Reuter-Lorenz and Cappell, 2008; Reuter-Lorenz and Park, 2014), and brain regions contralateral to where younger adults were activating (for a review see, Cabeza, 2002). These overactivations have been argued to be either compensatory to older adults' performance, indicated by positive brain-behavior correlations (Basak et al., 2018; Cabeza et al., 2002; Cabeza and Dennis, 2012; Davis et al., 2008), or are maladaptive and detrimental to performance, indicated by negative brain-behavior correlation (Nashiro et al., 2018; Prakash et al., 2012; Steffener et al., 2014). If maladaptive overactivations are observed in older adults, activations of such task-irrelevant regions may add detrimental noise to the memory system and contribute to worsened updating. We therefore tested these two possibilities.

The first possibility was tested by investigating age-related differences in four task-negative brain regions, which included regions of the DMN. In these four regions, younger adults had shown significant suppression during the task. Older adults, however, showed significantly less suppression during the task when compared to the younger adults. Age-related reductions in DMN suppression during task has been associated with worse task performance in executive functions (Rieck et al., 2017) and working memory (Kennedy et al., 2017; Prakash et al., 2012). These results therefore support our first possibility, that is, deficits in effectively suppressing the DMN during the random 2-back task may contribute to worse accuracy and increased updating costs in the older adults.

The second possibility of maladaptive overactivations was tested by examining activation patterns where older adults, compared to young, showed greater activations during the task blocks (task > fixation contrast) as well as during updating within the task blocks (update > non-update contrast). During the task blocks, eight regions of overactivations were observed. These regions were suppressed by younger adults, while older adults, especially the old-old, showed either reduced suppression or, in some regions, increased activation during the task blocks. During the update trials, older adults showed increased activation in right pre-central gyrus, a region that was not activated in young. Moreover, this overactivated brain region is contralateral to the left precentral gyrus – a region that was activated in younger adults during update trials. The Hemispheric Asymmetry Reduction in Older Adults (HAROLD) model of aging suggests that activations from frontal brain regions tend to be less lateralized in older adults, and overactivations, contralateral to where younger adults activate, could be either compensatory or maladaptive due to reduced hemispheric specificity (Cabeza, 2002).

Therefore, to determine if these overactivations, esp. the contralateral overaction of right pre-central gyrus, as well as the reduced suppressions in older adults from these brain regions (8 from task blocks and 1 from update trials) were maladaptive or compensatory to task performance, we conducted brain-behavior correlation analyses. In the current study, increased activations in most (8 out of 9) of these age-sensitive overactivated brain regions were associated with worse task performance across all participants, irrespective of their age.

The eight brain regions, where older adults showed increased activations compared to younger adults during the task blocks, were mostly suppressed by younger adults for task. Importantly, some of the regions, such as the precuneus, the anterior and posterior cingulate cortices were commonly considered parts of the DMN in younger adults and were usually suppressed during tasks of executive functions (Buckner et al., 2008; Laird et al., 2011). Brain-behavior correlations from these regions suggest that deficits in effective suppression of the DMN regions as well as task-irrelevant regions contribute to deficits in working memory updating performance in older adults. Reduced suppressions in the DMN regions in older adults, particularly, the posterior cingulate gyrus and precuneus, have been previously reported in N-back tasks, but these overactivations have been either interpreted as compensatory (Alichniewicz et al., 2012) or maladaptive (Prakash et al., 2012). Among other differences, the two studies varied in their age cohorts, such that mean age of older adults was younger in the Alichniewicz et al. study (60 years) than Prakash et al. study (72 years). The current study was aimed to resolve this conflict by considering younger and older cohort of older adults, and comparing them to younger adults. We found evidence only for maladaptive overactivations, not compensation, in the random 2-back paradigm. Furthermore, the old-old cohort showed even less suppression of DMN regions compared to young-old adults, suggesting an increase in the maladaptive activation patterns in the DMN with age, within the older cohort.

Event-related analysis found one region of overactivation in the older adults during the update trials – the right pre-central gyrus. The right pre-central gyrus is contralateral to where younger adults activate during the update trials (that is, the left pre-central gyrus). Overactivation from this region, therefore, could be examined as reduced hemispheric

lateralization with aging according to the HAROLD model (Cabeza, 2002). The HAROLD model suggests that if overactivation, contralateral to where younger adults activate for task, was directly associated with task performance then it should be considered compensatory. Otherwise, contralateral overactivations in older adults should be interpreted reduced hemispheric specificity that may be maladaptive to task performance. Furthermore, for brain regions responsible of motor control, especially the left and right pre-central gyrus, older adults have been found to show reduced response asymmetry, compared to younger adults (Bernard and Seidler, 2012; Graziadio et al., 2015; Mattay et al., 2002; Vallesi et al., 2010). When responding with their right hands, younger adults tend to show exclusively left motor region activations whereas older adults would show bilateral motor region activations (Mattay et al., 2002). Such reduced motor region asymmetry has been suggested as contributing to the age-related decline in inhibition across hemispheres—also a case of reduced functions specificity (Bernard and Seidler, 2012). The current results, however, showed that increased activation from this motor region during update trials was negatively associated with overall accuracy, suggesting that reduced motor asymmetry during updating likely reflected reduced hemispheric specificity that was detrimental to task performance in older adults.

5. Conclusion

To our knowledge, the current study was the first to examine neuromodulation (brain activation differences) between non-update and update trials, and age-related differences in such neuromodulations within a random N-back task. Our results suggest that working memory deficits in older adults can be detected by comparing performance between update and non-update trials within a 2-back task. In addition to performance deficits, older adults also showed decreased neuromodulations to working memory updating process in the task-sensitive regions. These deficits in older adults were specific to updating, and not confounded by deficits in working memory capacity in older adults. With the unpredictable probe-cue expectancy, our task design closely simulated real-life scenarios in which memory updating are usually randomly cued for. Therefore, future studies could consider detecting age-related deficits in other working memory updating paradigms with a constant set-size using random probe-cueing, thus disentangling neural underpinnings of updating deficits from the age-specific deficits of working memory capacity. In the current study, older adults showed either reduced suppressions or increased activations of DMN regions, which were effectively suppressed by younger adults during the random 2-back task (block design analysis). For memory updating (event-related analysis), overactivation of a frontal region, the right pre-central gyrus, was observed in older adults during the update trials. This region is contralateral a region that is activated in younger adults during the update trials. Importantly, brain-behavior correlations suggest that increased activation of all but one DMN region during the task and of the right pre-central gyrus was associated with decreased performance. Therefore, these overactivations were found to be maladaptive to older adults' working memory performance, possibly due to reduced hemispheric specificity with age. Age-related differences were also found within the older cohort, with the old-old showing further reduced suppression of the DMN regions and increased overactivation in the right pre-central gyrus compared to the young-old. These results suggest that age-related

differences in brain activations were result of a continuous process that extended beyond the normal “older adults” criterion of 60 years of age.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.

Memory update task paradigm. A hybrid blocked and event-related design was used, which consisted of six blocks of task interspersed by seven fixation blocks. Participants were asked to compare the current digit to the previous digit in the same color. Brain activations associated with two trial types were analyzed: non-update, and update. Average ITI between two update trials was 2.96 s, and average ITI between two non-update trials was 2.93 s. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Fig. 2. Accuracy (percent correct) Performance differences across the three age groups in a) Accuracy (percent correct) and b) Update Cost (=Update RT – Non-update RT). * indicates significance at $p < .05$. Error bars are standard error.

Fig. 3.

Task-positive clusters identified by block design analyses in younger adults, and cluster corrected at $z = 3.1$, $p < .001$. There was no age difference in activation of the task-positive cluster. Error bars are standard error.

Fig. 4.

Task negative clusters identified by block design analyses in younger adults, and cluster corrected at $z = 3.1$, $p < .001$. There was a significant difference in suppressing the task negative regions between younger and older adults. * indicates significance at $p < .05$. Error bars are standard error.

Fig. 5.

Task-sensitive clusters identified by event-related design analyses in younger adults and cluster corrected at $z = 3.1$, $p < .001$. The resulting two update-sensitive regions (from update > non-update contrast) are shown in A (left Pre-central) and B (right Cerebellum) panels, where Update trials (U) elicited higher brain activation compared to Non-update (NU) trials in younger adults and young-old adults. * indicates significant neuromodulation within each age group at $p < .05$. Error bars are standard error.

Fig. 6.

The eight “overactivation” regions resulting from older > younger contrast. In these regions, older adults showed increased activations and reduced suppressions during the task blocks when compared to younger adults. In posterior cingulate gyrus/post-central gyrus, the old-old showed significantly increased activations compared to the young-old. In the left anterior cingulate gyrus, the old-old showed significantly reduced suppressions compared to the young-old. * indicates significance at $\alpha = 0.05$, Sidak corrected. Error bars are standard error. Overall, all ROIs suggest increased activations or reduced suppressions of DMN regions with increase in age.

Fig. 7.

Right pre-central gyrus where older adults showed increased neuromodulation (update > non-update; older > younger) compared to younger adults. The significant interaction effect was driven by younger adults suppressing this region during the update trials. Older adults activated this region for update trials as well as for non-update trials. * indicates significant age-related increases in brain activations during update trials at $p < .05$. Error bars are standard error.

Table 1

Regions of task-related brain activations, identified in younger adults.

Design	Contrast	H	Region	MNI			Cluster Index	Voxel Size			
				x	y	z					
Block											
	Task > Fixation	L	Frontal Pole	32	54	18	12.7	1	109566		
		L	Supramarginal Gyrus	-54	-44	18	12.8	1			
		R	Inferior Frontal Gyrus	52	10	18	12.9	1			
		L	Precuneus	-8	-60	20	9.69	1		19045	
	Fixation > Task	L	Paracingulate Gyrus	0	56	12	8.56	2	8093		
		L	Frontal Orbital Cortex	-34	34	-12	7.15	3			1567
		L	Insula Cortex	-40	-14	0	7.03	4			
Event-related											
Update > Non-Update	L	Pre-central Gyrus	-36	-30	70	7.44	1	4486			
	R	Cerebellum	22	-54	-24	6.38	2	571			

Note. Three peak voxels are hereby reported for the frontal-parietal cluster to give a representative view of varied regions included in the large cluster. $Z > 3.1$, $p < .001$.

Table 2
Regions of overactivation regions in older adults, identified through OA > YA contrast.

Design	Contrast	H	Region	MNI			Cluster Index	Voxel Size	
				x	y	z			
Block	Task > Fixation	R	Posterior Cingulate Gyrus	10	-14	46	5.49	1	6203
		R	Precuneus	34	-44	-10	7.02	2	3022
		R	Fusiform	-30	-44	-8	5.94	3	2268
		L	Lateral Occipital Cortex	-36	-84	32	5.58	4	1025
		R	Supramarginal Gyrus	54	-16	8	4.62	5	810
		L	Anterior Cingulate Gyrus	-4	36	6	4.89	6	779
		L	Supramarginal Gyrus	-62	-30	32	5.23	7	480
		R	Superior Frontal Gyrus	6	24	62	5.53	8	430
		R	Pre-central Gyrus	56	-20	58	5.92	1	1882
		Event-related	Update > Non-update						

Note. $Z > 3.1, p < .001$.

Table 3

Relationships between brain activations from regions identified in the OA > YA contrast (age-related overactivation) and task performance (accuracy and update cost) across all participants.

Overactivation ROIs	Accuracy	Update Cost (ms)
Average Overactivations	$\beta = -.3, p < .01$	$\beta = .26, p = .02$
R. Posterior Cingulate Gyrus	$r = -.21; p = .06$	$r = -.23; p = .04$
Precuneus	$r = -.24; p = .03$	$r = -.23; p = .03$
R. Occipital Fusiform Gyrus	$r = -.27; p = .02$	$r = -.29; p < .01$
L. Lateral Occipital Cortex	$r = -.24; p = .04$	$r = -.23; p = .04$
R. Supramarginal Gyrus	$r = -.17; p = .1$	$r = -.19; p = .08$
L. Anterior Cingulate Gyrus	$r = -.27; p = .02$	$r = -.19; p = .09$
L. Supramarginal Gyrus	$r = -.23; p = .04$	$r = -.23; p = .04$
R. Superior Frontal Gyrus	$r = -.22; p = .05$	$r = -.12; p = .1$
R. Pre-central Gyrus	$r = -.29; p < .01$	$r = -.18; p = .1$