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Executive functions and neurocognitive aging: dissociable patterns of brain activity

Gary R. Turner[a,b,*], R. Nathan Spreng[c]

[a] Heart and Stroke Foundation Centre for Stroke Recovery, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada
[b] Departments of Occupational and Rehabilitation Sciences, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada
[c] Department of Psychology, Harvard University, Cambridge, MA, USA

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Abstract

Studies of neurocognitive aging report altered patterns of brain activity in older versus younger adults performing executive function tasks. We review the extant literature, using activation likelihood estimation meta-analytic methods, to compare age-related differences in the pattern of brain activity across studies examining 2 categories of tasks associated with executive control processing: working memory and inhibition. In a direct contrast of young and older adult activations, older adults engaged bilateral regions of dorsolateral prefrontal cortex as well as supplementary motor cortex and left inferior parietal lobule during working memory. In contrast, age-related changes during inhibitory control were observed in right inferior frontal gyrus and presupplementary motor area. Additionally, when we examined task-related differences within each age group we observed the predicted pattern of differentiated neural response in the younger subjects: lateral prefrontal cortex activity associated with working memory versus right anterior insula/frontal opercular activity associated with inhibition. This separation was largely maintained in older subjects. These data provide the first quantitative meta-analytic evidence that age-related patterns of functional brain change during executive functioning depend on the specific control process being challenged.

Keywords: Aging; Neuroimaging; Activation likelihood estimation; Executive function; Working memory; Inhibition; Meta-analysis

1. Introduction

Neurocognitive changes in healthy aging have now been reported for almost 2 decades. Early work from Grady and colleagues (1994) first reported age-related differences in patterns of functional brain activity during a perceptual matching task using positron emission tomography. With the advent of functional magnetic resonance imaging, the number of investigations of neurocognitive aging has expanded exponentially and now include studies of numerous cognitive domains (see Spreng et al., 2010). Of these, executive functions have received the most attention. Functional brain imaging studies of executive control processes report robust differences in brain activity between older and younger subjects, particularly under conditions of high executive control demand (e.g., Grady et al., 1998; Jonides et al., 2000; Milham et al., 2002; Nielson et al., 2002; Postle et al., 1999; Reuter-Lorenz et al., 2000). These differences have been replicated across studies (see Park and Reuter-Lorenz, 2009; Reuter-Lorenz and Cappell, 2008 for reviews) and have generated several theoretical accounts of neurocognitive aging in the domain of executive functions.

The most commonly reported age-related pattern of brain activity during executive function tasks (e.g., working memory, inhibition, and task-switching) is increased recruitment of lateral aspects of the prefrontal cortex (PFC) bilaterally (Rypma and D'Esposito, 2000; Jonides et al., 2000; Townsend et al., 2006). These changes may reflect increased PFC modulation of processing operations in posterior cortices in response to noisier (i.e., reduced processing specificity) signaling in these regions (Persson et al.,

* Corresponding author at: Department of Psychology, York University (Room 244 BSB), 4700 Keele Street, Toronto, ON. Canada. M3J 1P3. Tel.: +1 416 736 5290; fax: +1 416 736 5814.
E-mail address: grturner@yorku.ca (G.R. Turner).

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2006). Increased lateral PFC activity may also reflect greater demands for executive control as cognitive operations become less automated with age, resulting in a general "posterior to anterior shift" (PASA) in functional brain activity (Davis et al., 2008) or as neural circuits become increasingly inefficient (compensation-related utilization of neural circuits hypothesis; CRUNCH; Reuter-Lorenz and Cappell, 2008). Recently, this increased demand for frontally-mediated control processes has been characterized as "neural scaffolding" (Park and Reuter-Lorenz, 2009). As age-related structural and functional brain changes, including cortical thinning, white matter changes, and reductions in hippocampal activation, lead to inefficient and/or noisy processing, demands for controlled processing operations are increased. In response, lateral prefrontal brain regions are recruited to provide a "neural scaffold" in support of new learning and sustained behavioral performance, particularly in the context of novel or complex tasks. A similar pattern has been observed in young adults as task challenge is increased requiring new strategy learning (Erickson et al., 2007a and see Hillary et al., 2006 for a review of functional brain changes in healthy young, aging, and neurological populations). While each of these theories argue that functional brain changes, particularly engagement of lateral PFC regions, occurs in normal aging they differ somewhat with respect to the mechanism underlying these changes. The work of Persson and colleagues (Persson et al., 2006) or the PASA account (Davis et al., 2008) suggest that lateral PFC recruitment may represent additional demands for frontally-mediated neuromodulation of posterior neural processing operations. In contrast, the CRUNCH (Reuter-Lorenz and Cappell, 2008) and neural scaffolding hypotheses (Park and Reuter-Lorenz, 2009) suggest that as brain circuits become less efficient with age, additional or alternate neural resources are engaged to compensate for degraded processing operations in both frontal and posterior brain regions. Further discussion of these mechanistic accounts is beyond the scope of the current study (but see Turner and D'Esposito, 2010, for a review). However, it is interesting to note that while each of these accounts converge around the notion of increased recruitment of lateral PFC to support controlled (i.e., executive) processing, to our knowledge, there has been no direct examination of how age-related changes are manifest for specific executive control processes.

It is now well understood that executive functions can be fractionated into dissociable processes both behaviorally (e.g., Miyake et al., 2000; Salthouse et al., 2003; Stuss et al., 1995) and neurally (e.g., Chikazoe, 2010; McNab et al., 2008; Wager and Smith, 2003). This raises the question of whether the age-related patterns of functional brain change described above are similarly dissociable depending upon the executive control process being challenged. The goal of the current report is to review the extant literature, using quantitative meta-analytic methods, to compare age-related differences in the pattern of brain activity between 2 executive processes that have been most frequently studied in the cognitive neuroscience literature: working memory and inhibition (Cabeza and Nyberg, 2000; Wager and Smith, 2003). Neurocognitive aging of task switching, the third executive control process identified by Miyake et al. (2000), remains an understudied domain of executive function and was not included in the current analysis (for exceptions, see: DiGirolamo et al., 2001; Esposito et al., 1999; Townsend et al., 2006). Specifically, we investigate whether age-related patterns of functional brain changes are similar across executive processes or whether changes with aging are specific to the executive process being challenged.

Working memory is a system for actively maintaining and manipulating information that is no longer present in the environment, yet must be organized and retained in the service of current and future goals (Wager and Smith, 2003). In younger subjects, working memory is associated with activation of lateral prefrontal cortical regions, typically left-lateralized (Smith and Jonides, 1998; Wager and Smith, 2003). In older adults, working memory tasks also engage PFC regions, however, neural response is greater and more bilateral at lower levels of task demand than in younger adults (Emery et al., 2008; Jonides et al., 2000; Reuter-Lorenz and Cappell, 2008). This pattern has been hypothesized to reflect poor modulation of prefrontal brain activity in response to increasing working memory demands (Reuter-Lorenz and Cappell, 2008; Schneider-Garces et al., 2010). Cappell and colleagues (Cappell et al., 2010) recently tested this hypothesis in a study of verbal working memory in older and younger adults under high and low load conditions. Consistent with their predictions, older adults overrecruited regions of right lateral PFC at lower working memory loads relative to younger subjects and underrecruited lateral prefrontal cortex regions bilaterally at higher memory loads. Thus age-related increases in lateral PFC during working memory may reflect reduced capacity to modulate this region in response to shifting executive control demands. Here we examine whether this account of age-related functional brain changes generalizes beyond working memory to other domains of executive function such as inhibitory control. To our knowledge this has not been investigated.

Inhibitory control is generally defined as intentional control over dominant, automatic, or prepotent responses and has also been widely studied using brain imaging methods (Chikazoe, 2010). As with working memory, the functional neural correlates of inhibitory control in younger adults have been well characterized for both cognitive and motor inhibition tasks (see Buchsbaum et al., 2005). Critical regions include ventral PFC (Chambers et al., 2009; Leung and Cai, 2007; Swann et al., 2009), presupplementary motor areas (Chen et al., 2009; Floden and Stuss, 2006; Li et al., 2006), as well as posterior parietal cortices, subthalamic nuclei, and cerebellar regions (see Chambers et al., 2009; Chikazoe, 2010 for recent reviews). However, the neural

correlates of inhibitory control processing in older adults are less well characterized. Several studies have now identified a highly overlapping pattern of brain regions between older and younger adults performing inhibition tasks (e.g., Jonides et al., 1998; Langenecker et al., 2004; Milham et al., 2002, but see Jonides et al., 2000). Others report greater age-related recruitment of dorsolateral aspects of PFC bilaterally as inhibitory control demands increase (e.g., Mathis et al., 2009; Wood et al., 2009), a pattern more consistent with the working memory literature. A recent study of age-related functional brain changes under variable inhibitory control demands argued that these changes reflected poor modulation of these regions resulting in greater functional brain response within lateral PFC (Prakash et al., 2009), a conclusion strikingly similar to that of Cappell and colleagues (Cappell et al., 2010) who investigated these age-related changes in the context of working memory.

While these latter findings suggest that patterns of age-related functional brain changes during executive function tasks may be generalizable across specific processes falling within the domain of executive functioning (or at least between working memory and inhibition), to our knowledge no study has directly tested this possibility in both younger and older adults. McNab and colleagues (McNab et al., 2008) recently compared brain activity during working memory and inhibition task performance in younger adults using within-subject contrasts. The 2 processes activated distinct functional brain networks, however, overlapping activity was observed in a small area of right inferior frontal gyrus. These results are consistent with previous reviews of working memory (e.g., Wager and Smith, 2003) and inhibitory control (e.g., Chambers et al., 2009; Simmonds et al., 2008) that suggest these 2 executive functions are implemented in discrete but overlapping brain networks in younger adults.

Numerous reports have now examined age-related functional brain changes associated with working memory and inhibition independently. However, we were unable to identify any reports that directly compared these 2 processes in younger and older adults in a single study. Here we review the findings of these previous single task reports to examine whether functional brain changes in older adults performing working memory and inhibitory control tasks are dissociable. We use the activation likelihood estimation (ALE) approach for neuroimaging data (Laird et al., 2005; Turkeltaub et al., 2002) as this meta-analytic method provides a quantitative estimate of the degree of overlap in functional activation patterns across multiple studies. Specifically, we investigated whether age-related neurocognitive changes overlapped for working memory and inhibitory control tasks. This would be evidence for a common pattern of age-related functional brain changes in executive functioning (i.e., greater bilateral activity in PFC in older adults for both task categories). Alternatively, if age-related brain changes differ between working memory and inhibition tasks, this would suggest that age-related functional brain changes in the domain of executive functioning are dependent on the specific executive process being taxed. We investigate this with several ALE analyses. First we present the quantitative review of studies examining age-related changes within each task by reporting reliable patterns of activation for working memory and inhibitory control within each age group. Next we directly contrast the task-related activation patterns for young and older subjects. Finally, we contrast task-related activation patterns within each age-group separately.

2. Methods

2.1. Selection of studies

Neuroimaging studies examining aging and executive function were selected using a systematic search process. Peer-reviewed articles, published in English between January 1982 and March 2010, were selected from the search results of 3 separate databases: MEDLINE, PsycInfo, and Science Citation Index. Searches were conducted using the following terms: (1) keyword: “age” or “aging” or “ageing” or “age-related” or “older adults” or “adult life-span”; and (2) keyword: “neuroimaging” or “cerebral blood flow” or “fMRI” or “functional magnetic resonance imaging” or “PET” or “positron emission tomography”; and (3) population: “human”. A second search specifically targeted executive function with the added search terms: “executive” or “working memory” or “inhibition”. As a result, 5156 unique reports were found.

Only studies that reported both healthy young and healthy older adult group results were included. Theoretical papers and reviews were excluded. Studies that reported combined group results and a region-of-interest analysis, reported only brain-behavior correlations, or did not report activation foci as 3-D coordinates in stereotaxic space were excluded because these studies could not be meaningfully analyzed with ALE. For studies that contained multiple nonindependent contrasts, in order to limit the contribution of any 1 set of participants to the pool of foci, we selected the contrast with the lowest level baseline (e.g., selection of incongruent vs. neutral over incongruent vs. congruent contrast for the Stroop task data reported by Mathis et al., 2010). We selected these lower level contrasts because functional brain activity is reduced in older relative to younger adults at higher levels of task challenge as performance limits are exceeded (e.g., Cappell et al., 2010). Inclusion of only high-level contrasts would confound age-related brain changes with potential ceiling effects on behavioral tasks (see below for discussion of performance-based differences in these data). Moreover, given the potential impact of contrast selection on the interpretation of the results of the review, we identify whether the selected contrast for each study contained a high (cognitive) or low (rest, simple motor) baseline. These are denoted with an “*”

Table 1
Details of studies included in the review

Study no.	First author	Year	*n*	Younger Age: Mean (SD)/range*	Foci	*n*	Older Age: mean (SD)/range*	Foci	Perf
Working Memory									
1	Cabeza	2004	20	22.6 (3.7)	15	20	70.3 (6.3)	23	=
2	Emery	2008	10	21.9 (2.6)	5	11	71.2 (6.2)	11	=
3	Freo	2005	13	27 (6)	12	13	65 (11)	15	≠
4	Grady	1998	13	25 (3)	10	16	66 (4)	14	=
5	Grossman	2002	13	22.6 (4.9)	6	11	63.5 (10.8)	7	=
6	Haut	2005	8	23.3 (1.6)	6	8	67.3 (10.4)	5	≠
7	Holtzer	2009	25	19–34	12	25	65–84	17	=
8	Johnson	2004	6	19.6	7	6	65.3	6	≠
9	Nagel	2009	30	25.6 (3)	9	30	64.1 (3)	11	=
10	Otsuka	2006	10	24.5 (20–29)	6	10	68.8 (65–71)	6	=
11	Park	2010	15	22.2 (2.4)	5	19	64.8 (2.8)	5	=
12	Paxton	2008a	21	22.8 (3.7)	11	20	73 (5.7)	24	=
13	Raye	2008	15	23 (18–26)	5	14	68 (61–81)	6	≠
14	Reuter-Lorenz	2000a	8	23.3 (21–30)	9	16	69.9 (65–75)	9	=
15	Reuter-Lorenz	2000b	10	21.2 (18–25)	6	10	67.4 (62–73)	10	≠
16	Ricciardi	2009	10	26.2 (1.4)	6	10	68.4 (4)	4	=
17	Rypma	2001	6	25.3 (22–29)	41	6	68.6 (62–73)	46	≠
18	Schneider-Garces	2009	12	23.8 (18–27)	1	30	70.9 (65–80)	7	≠
19	Smith	2001	12	22.9 (18–29)	14	12	66.6 (65–72)	11	≠
Inhibition									
1	Colcombe	2005	20	23.5 (19–25)	2	40	67.5 (52–87)	3	≠
2	Jonides	2000	12	19–30	1	12	61–72	0	≠
3	Lee	2006	12	29.8 (6.2)	0	9	65.2 (4.2)	9	=
4	Madden	2002	12	23 (2.13)	6	12	66.5 (4.96)	1	≠
5	Mathis	2009	12	26.8 (3.4)	4	12	62.8 (3)	7	=
6	Meinzer	2009	16	26.1 (3.7)	7	16	69.3 (5.6)	13	=
7	Mell	2009	14	26.48 (3.96)	8	14	67.82 (5.01)	8	=
8	Milham	2002	12	23 (21–27)	7	10	68 (60–75)	10	≠
9	Nielson	2004	14	29.7 (8.3)	10	14	71.1 (4.3)	24	≠
10	Paxton	2008b	16	21.56 (3.14)	3	16	72.38 (6.51)	31	≠
11	Prakash	2009	25	23.6 (18–35)	12	25	65.5 (58–75)	6	≠
12	Zhu	2010	22	20 (3)	8	22	74 (6)	9	=
13	Zysset	2007	23	26.6 (3.6)	25	24	57.1 (6.49)	32	=

Studies are listed in Appendix S1. Study numbers map to 'Contributing Studies' in Supplementary Tables S1–S3. A complete list of study references is included in Supplementary Appendix 1. Perf signifies whether performance was matched between younger and older adults on the behavioral task.
* Age data listed as mean (SD) or age-range based on format reported in original manuscript.

in the "contributing studies" columns in Supplementary Tables 1–3. For studies containing multiple independent samples, peak activation foci from each sample were included (e.g., Paxton et al., 2008). The reference lists of included reports were searched for additional studies that fit these criteria. A total of 30 reports fit our criteria; 2 studies reported 2 independent samples rendering 32 total experiments (Tables 1 and 2).

Next, these experiments were allocated to either the working memory ($n = 19$) or inhibition ($n = 13$) analysis. In cases where allocation to either category was unclear, we assigned the study based upon the author's characterization (e.g., Meinzer et al., 2009) or the standard characterization of the task paradigm in the literature (e.g., Mell et al., 2009).

2.2. *Creation of* ALE *maps*

The ALE method provides a voxel-based meta-analytic technique for functional neuroimaging data (Laird et al., 2005; Turkeltaub et al., 2002). The software (BrainMap GingerALE v1.1) computes statistically significant concordance in the pattern of brain activity across any number of independent experiments. Additionally, GingerALE can compute statistically significant differences in the pattern of brain activity between 2 sets of data from several independent experiments. Recently, a new version of GingerALE software was released (GingerALE 2.0) that models probability distributions at the experiment level instead of at the level of the foci, changing the analysis from fixed- to random-effects (Eickhoff et al., 2009). This version, however, does not yet compute differences between groups. ALE maps are derived based on foci of interest, which comprise statistically significant peak activation locations from published studies. Independent group analysis peak foci (working memory/inhibition task > control task in younger; working memory/inhibition task > control task in older) were extracted from 25 studies. We also included results from 7 studies that reported within- and between-group peak foci (i.e., combined younger/older, younger > older, and older > younger). Foci from the combined task effects were allocated to both groups and task by age interaction

Table 2
Details of studies included in the review

Study no.	Paradigm	Contrast
	Working memory	
1	Delayed word recognition	Delay trials vs. no-task baseline
2	Letter-number sequencing	Manipulation vs. maintenance or fixation trials
3	Delayed match to sample	Delay trials vs. fixation baseline
4	Delayed match to sample	Delay trials vs. sensorimotor baseline
5	Sentence comprehension	Pseudofont judgement baseline
6	Letter-number sequencing (WAIS)	Sequencing vs. span trials
7	Sternberg task (nonverbal)	Delay trials vs. no-task baseline
8	Refresh task	Refresh vs. repeat and read trials
9	Delayed spatial recognition	7-Item vs. 1-item set size trials
10	Reading span	Reading span vs. cued motor response baseline
11	Delayed recognition	Coordinate vs. control trials
12	Continuous performance task (AX-CPT)	Long delay vs. short delay trials
13	Refresh task	Refresh (3 items) vs. read trials
14	Delayed letter recognition	Delay trials vs. perceptual baseline
15	Delayed spatial recognition	Delay trials vs. perceptual baseline
16	Delayed match to sample	Delay trials vs. sensorimotor baseline
17	Sternberg task	6-Item vs. 1-item set size trials
18	Sternberg task	Linear trend analysis for set-size 2–4
19	Operation Span (problem-solving)	Math-problems vs. motor response baseline
	Inhibition	
1	Flanker task	Incongruent vs. no-task baseline
2	Delayed word recognition (recency manip)	Recent vs. nonrecent probes
3	Simon task (with response conflict)	Response incompatible vs. compatible trials
4	Visual search	Conjunction vs. guided search trials
5	Stroop task (incongruent vs. neutral)	Incongruent vs. neutral trials
6	Category fluency	Category fluency vs. word reading baseline trials
7	Probabilistic object reversal	Search- vs. learned-rule trials
8	Stroop task	Incongruent vs. neutral and congruent trials
9	Go-No Go task	Lure trials vs. no-task baseline
10	continuous performance task (AX-CPT)	BX (lure) probe epochs vs. fixation baseline
11	Stroop task	Incongruent vs. neutral trials
12	Flanker task	Incongruent vs. congruent trials
13	Stroop task	Incongruent vs. neutral trials

Studies are listed in Appendix S1.

foci (i.e., between-group effects) were allocated to each respective age group, consistent with previous methods (Spreng et al., 2010). Total foci for each meta-analysis were 186 for working memory-young; 237 for working memory-older; 93 for inhibition-younger, and 153 for inhibition-older. Eight separate ALE analyses were conducted in total, each yielding an ALE map and corresponding cluster report: (1–3) working memory in younger, older, and comparing younger with older; (4–6) inhibition in younger, older, and comparing younger with older; (7–8) working memory compared with inhibition in younger and older.

Prior to the analysis, coordinates reported in Montreal Neurological Institute (MNI) space were converted to Talairach coordinates using the Lancaster transformation (Laird et al., 2010; Lancaster et al., 2007). In the approach taken by ALE, localization probability distributions for the foci are modeled at the center of 3-D Gaussian functions, where the Gaussian distributions are summed across the experiments to generate a map of interstudy consistencies that estimate the likelihood of activation for each focus (the ALE statistic). The foci were modeled using a full-width half-maximum value (FWHM) of 8 mm^3. We then compared the summary of observations against a null distribution, determined through 5000 permutations of randomly-generated foci identical in number with those being tested. In order to determine reliable differences in brain activity between younger and older adults, we tested the null hypothesis that the 2 sets of foci were randomly distributed and the observed difference between them was 0. For all analyses, the false discovery rate (FDR) method was employed to correct for multiple comparisons at $p < 0.05$ and subjected to a cluster threshold of 250 mm^3 (Laird et al., 2005). Anatomical labels were applied to the clusters using the Talairach Daemon and visual inspection of the ALE maps that were imported into FSLview v3.1 (Smith et al., 2004). Coordinates are reported in Talairach space (Talairach and Tournoux, 1988). All ALE maps were transformed from a volume image to an average multifiducial surface map using Caret software (Van Essen, 2005) for presentation.

Next, we identified the study foci that contributed to each ALE cluster. This was performed using Analysis of Functional NeuroImages software (Cox and Hyde, 1997) by fitting a spherical region of interest (ROI) at each ALE cluster peak matched in size to the 8 mm FHWM kernel (input into the ALE analysis; see above). If any contributing study coordinate fell within the region of interest, it was considered to have contributed to the ALE result. All studies identified as contributing foci are reported in the "Contributing Studies" columns in Supplementary Tables 1–3.

3. Results

3.1. Within-task contrasts in young and older adults

3.1.1. Working memory

Studies of working memory showed reliable recruitment of lateral PFC, posterior parietal, and subcortical brain structures in younger adult subjects. Significant ALE clusters were evident in dorsal and ventral aspects of left lateral PFC, right dorsolateral PFC, bilateral parietal regions, visual association cortices, and subcortical nuclei including the thalamus and basal ganglia (Fig. 1A, and Supplementary Table S1 for a list

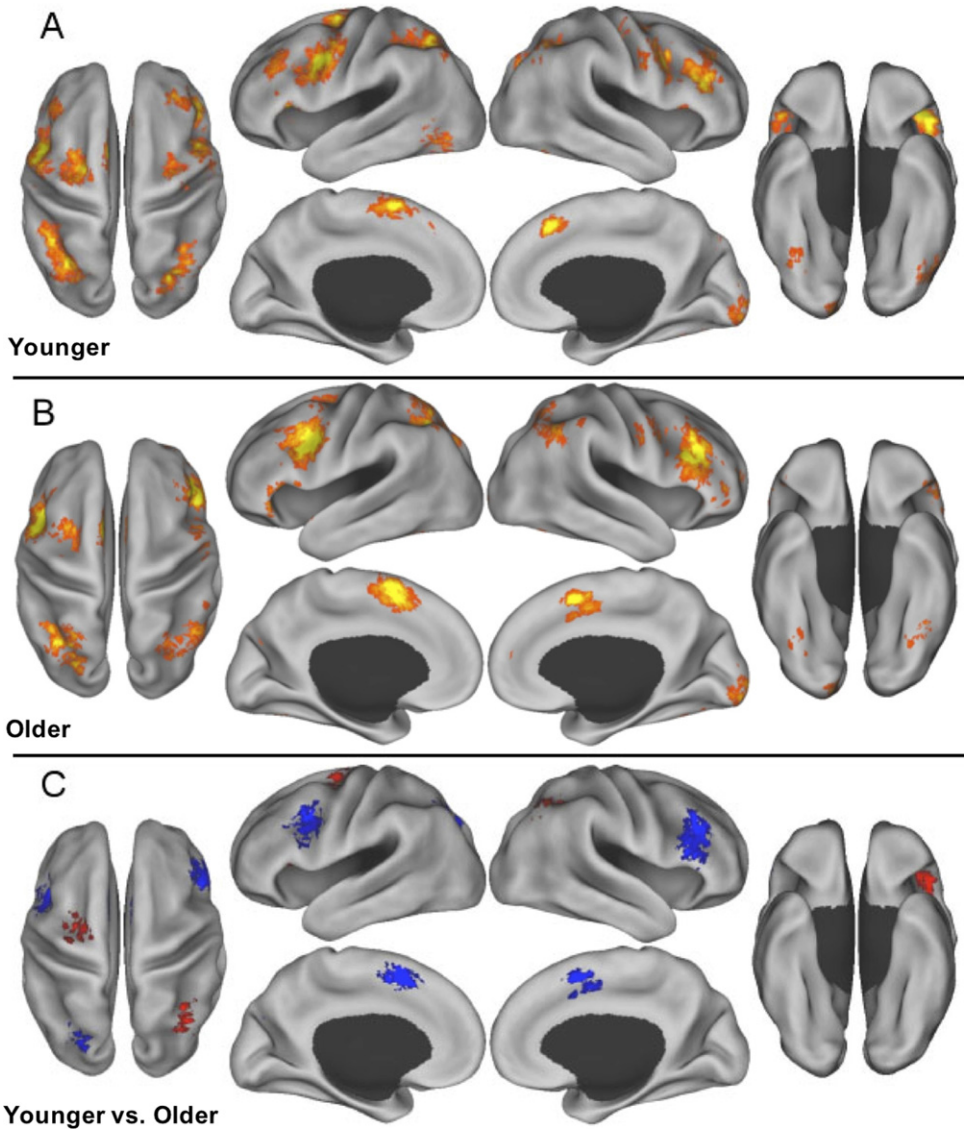

Fig. 1. Working memory. Reliable patterns of brain activity across all studies of working memory ($n = 19$). Clusters represent areas where activity was greater during working memory than baseline tasks. (A) Activation likelihood clusters for young adults. (B) Older adults. (C) Activation likelihood estimation (ALE) clusters displaying reliable differences between younger and older subjects on working memory tasks (red: younger adults > older adults; blue: older adults > younger adults). Activation likelihood clusters (FDR $p < 0.05$) are shown on an average multifiducial partially inflated surface map in Caret (Van Essen, 2005).

of the cluster maxima coordinates). This recruitment pattern was consistent for older adults with reliable ALE clusters in left ventrolateral PFC and dorsolateral PFC bilaterally. Older adults also showed recruitment of more anterior aspects of right dorsolateral prefrontal cortex (dorsolateral PFC) regions, posterior parietal, and ventral visual association cortices (Fig. 1B, Supplementary Table S1).

When we directly compared neural activity during working memory between older and younger adults across studies, significant differences in the pattern of neural response emerged (Fig. 1C, Table 3A). While both groups recruited regions of left lateral PFC, younger subjects recruited more posterior regions, including anterior insula/operculum and the frontal eye fields. In contrast, older adults showed significantly greater activation in dorsal and anterior regions at the junction of the middle and inferior frontal and precentral gyri. In the right hemisphere, this pattern was repeated: younger adults showed reliable activity in posterior regions of right dorsolateral PFC, as well in right frontal eye fields, while older subjects showed significantly greater activation in more anterior aspects of right dorsolateral PFC.

3.1.2. Inhibition

In younger adults significant clusters of activity were observed in left inferior frontal gyrus, supplementary motor area, and posterior parietal regions as well as in bilateral dorsolateral PFC and right anterior insula (Fig.

Table 3
Regions of activation demonstrating significant differences between young and older adults during working memory (A) and inhibition (B) task performance

Lat	Region	BA	Vol, mm^3	ALE, 10^{-2}	x	y	z
A. Working memory							
Younger > older							
R	IPS	40	352	2.63	32	−50	38
L	aIFO	13	328	2.10	−38	18	8
L	FEF	6	280	2.11	−24	−4	56
R	Frontal white matter		696	2.14	34	26	22
Older > younger							
R	MFG	46	1072	−3.34	46	26	24
B	SMA	32	848	−2.41	−6	8	46
L	IFG	9	664	−1.90	−46	8	32
L	IPS	7	408	−2.30	−24	−64	36
B. Inhibition							
Younger > older							
R	IOG	19	296	2.09	38	−76	0
Older > younger							
R	MFG/IFG	9/8/6	1000	−1.29	46	10	40
L	SFG	6	360	−1.91	−2	28	54

Key: aIFO, anterior insula/frontal operculum; ALE, activation likelihood estimation; B, bilateral; BA, Brodmann area; FEF, frontal eye field; IFG, inferior frontal gyrus; IOG, inferior occipital gyrus; IPS, intraparietal sulcus; L, left; Lat, laterality; MFG, middle frontal gyrus; R, right; SFG, superior frontal gyrus; SMA, supplementary motor area; Vol, volume; x, right/left coordinate; y, anterior/posterior coordinate; z, inferior/superior coordinate.

2A, Supplementary Table S2). Older adults engaged a similar set of brain regions as the younger subjects with significant clusters observed in the inferior frontal gyrus (bilaterally), supplementary motor area, dorsolateral PFC, and right anterior insula (Fig. 2B, Supplementary Table S2). In the direct contrast of activity patterns in young and older adults during inhibition tasks, significant differences emerged (Fig. 2C, Table 3B). Activity in an area of visual association cortex was significantly greater in younger subjects. In contrast, older adults showed more activity in the right inferior frontal gyrus, near the inferior frontal junction, and in the left medial superior frontal gyrus, presupplementary motor area region.

3.2. Between-task contrasts in young and older adults

In younger subjects, distinct ALE clusters were observed in lateral aspects of PFC, including left inferior frontal gyrus and right dorsolateral PFC, supplementary motor area, and superior parietal cortex (greater for working memory) as well as right posterior frontal cortex and anterior insula/operculum (greater for inhibitory control). Importantly, the spatial separation in the pattern of functional brain response across the 2 executive control processes observed in younger adults was maintained in the older subjects. This result is clearly displayed in Fig. 3 (and see Table 3) where task-related differences in activations for both groups are plotted on a single map. Activation patterns for working memory and inhibitory control studies are almost entirely nonoverlapping in the older subjects with the exception of a small area of overlap between the boundaries of 2 clusters in dorsalmedial PFC (Fig. 3, panel B and Supplementary Table 3).

3.3. ALE *cluster composition*

3.3.1. *Performance differences*

Differences in behavioral performance between younger and older adults on the task may influence patterns of brain activity (e.g., Emery et al., 2008; Nagel et al., 2009). A meta-analytic review of performance-related differences across the cognitive domains of perception, memory encoding, memory retrieval, and executive function reported more reliable right frontal activity in poorer performing older adults and more reliable left frontal activity in performance-matched older adults (Spreng et al., 2010). While we do not have sufficient statistical power in the present report to examine performance differences directly, we identify whether performance was matched for each study (Table 1) and determine which of these studies contributed to each ALE cluster (Supplementary Tables S1–S3). We found that, for the working memory tasks, only studies reporting matched behavioral performance contributed to ALE clusters in left intraparietal sulcus, left precentral gyrus (young, Supplementary Table S1) and left inferior frontal gyrus, left frontal eye fields, right lingual gyrus, and cerebellum (older, Supplementary Table S1). Within the inhibition task category, 1 ALE cluster in right cerebellum showed a performance-driven pattern in younger subjects (Supplementary Table S2). For the direct contrasts of older and younger performance in these 2 categories (Table 3) only a single cluster in left superior frontal gyrus for the inhibition older > young contrast was driven exclusively by studies with matched-performance. The vast majority of ALE clusters reported here (92/104) were performance-heterogeneous, that is, studies contributing to the cluster had both matched and unmatched performance on the behavioral tasks. Criti-

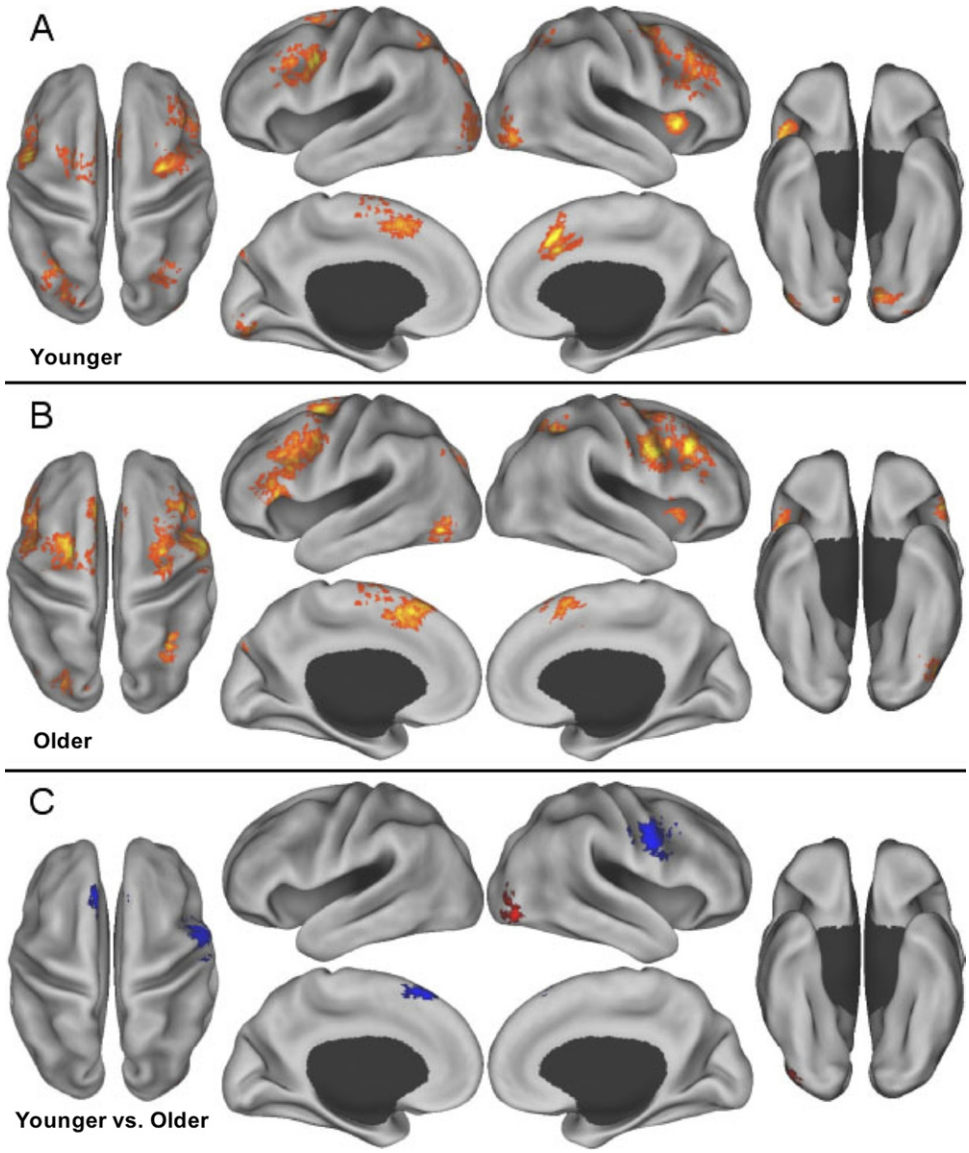

Fig. 2. Inhibition. Reliable patterns of brain activity for all studies of inhibitory control ($n = 13$). Clusters represent areas where activity was greater during inhibitory control than baseline tasks. (A) Activation likelihood clusters for young adults. (B) Older adults. (C) Activation likelihood estimation (ALE) clusters displaying reliable differences between younger and older subjects on inhibition tasks (red: younger adults > older adults; blue: older adults > younger adults).

cally, no cluster reported here emerged exclusively from studies where performance was not matched between younger and older subjects, suggesting that unequal performance between older and younger subjects was not a significant factor in these results.

3.3.2. Baseline (control) contrast differences

We further interrogated the clusters to determine whether the inclusion of both high and low cognitive demand baseline conditions impacted the ALE cluster results. As described above (see Methods), the majority of contrasts selected for this review involved low-demand control contrasts. Only 6 studies meeting criteria for the review had a "high" demand cognitive control condition (Emery et al., 2008; Grossman et al., 2002; Haut et al., 2005; Jonides et al., 2000; Paxton et al., 2008 [2 studies]). A maximum of 2 of these high demand contrasts contributed to any 1 ALE cluster and in every instance represented only a small minority of all contributing studies (Supplementary Tables S1–S3, "Contributing studies" columns). Heterogeneity in control conditions across the studies did not appear to affect our results.

4. Discussion

4.1. Age-related changes in working memory

As predicted, the ALE meta-analytic data demonstrated more reliable recruitment of dorsolateral PFC bilaterally

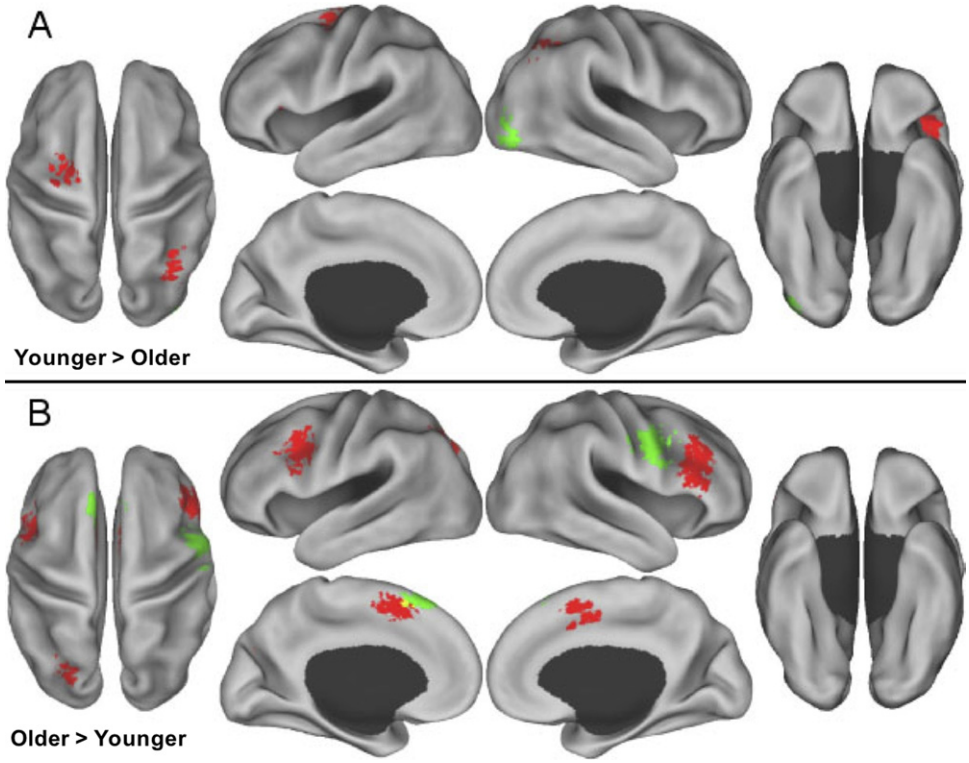

Fig. 3. Conjunction of working memory and inhibition maps. Activation likelihood estimation (ALE) clusters where brain activity differed significantly between younger and older subjects for the 2 executive control tasks: working memory (red) and inhibition (green). (A) Regions of greater activity for younger adults. (B) Regions greater activity for older adults. Region in yellow was reliably greater in the older group, compared with the young, in both working memory and inhibition.

(right greater than left) in older relative to younger adults during working memory, a finding consistent with previous reviews (Smith and Jonides, 1998; Wager and Smith, 2003). These results are also convergent with findings from individual studies that report greater and less lateralized recruitment of dorsolateral PFC in older relative to younger subjects, particularly at lower task demands (Reuter-Lorenz and Cappell, 2008; Reuter-Lorenz et al., 2000; Rypma and D'Esposito, 2000). Specific age-related increases in right dorsolateral PFC have also been associated with learning and acquisition of cognitive strategies in the context of increasing executive demands in older adults (Erickson et al., 2007b; Park and Reuter-Lorenz, 2009; and see Hillary et al., 2006 for a review of similar findings in neurological populations). There was also significantly greater reported activity across studies for older versus younger adults in the supplementary motor area. This region has been associated with increasing demand for error monitoring and cognitive control in working memory (Braver and Barch, 2006). Thus increased recruitment of this region may similarly reflect greater monitoring demands and greater frontal brain response relative to task demands in the older group.

4.2. Age-related changes in inhibition

When we examined patterns of activity in young and older adults during inhibition tasks a different pattern emerged. Older adults showed greater activity in the right inferior frontal gyrus, near the inferior frontal junction and in the left medial superior frontal gyrus, presupplementary motor area region. These results are consistent with previous ALE meta-analytic reviews of inhibitory control tasks in younger adults which reported inferior frontal and anterior insula activity during simple inhibitory control tasks (Buchsbaum et al., 2005; Simmonds et al., 2008). Similar findings were reported in 2 recent qualitative reviews (Chambers et al., 2009; Chikazoe, 2010). Thus, in contrast to the working memory results, these data suggest that age-related changes during inhibitory control are best characterized as enhanced activation of the young adult network. This "young-plus" pattern has now been reported in several studies (e.g., Langenecker et al., 2004; Zhu et al., 2010; Zysset et al., 2007).

4.3. Contrasting age-related changes in working memory and inhibition

Critically, when we directly contrasted patterns of activity between working memory and inhibition tasks in each age group, the spatial separation in the pattern of functional brain response across the 2 executive control processes, predicted in younger adults, was largely maintained in the older subjects (Fig. 3). This evidence of differentiated patterns of functional brain change between working memory

and inhibitory control is consistent with a process-specific account of executive functions and neurocognitive aging. To our knowledge this is the first quantitative review to demonstrate that age-related functional brain changes on tasks purported to tap dissociable executive control processes remain differentiated in older adulthood.

It is important to note that age-related functional brain changes may manifest as alterations in both spatial distribution as well as magnitude of activation. However, ALE methods are currently limited to assessing differences in activation magnitude between groups. As greater spatial distribution may not affect peak activations within the individual activation studies, ALE methods would be insensitive to these changes and potentially mask common patterns of age-related change between the working memory and inhibition tasks. While we cannot address this issue directly, it follows that if functional brain activity was more spatially distributed for older adults, we would expect a wider distribution of peak activations for the older groups across studies—and larger ALE activation clusters. This was not the case. The summed cluster volumes of reliably active voxels across the working memory and inhibition contrasts (Supplementary Tables S1 and S2) for young and older adults were virtually identical (younger: 22,520; older: 22,040). Thus there is no evidence that differences in the spatial distribution of brain activity would alter our conclusion that age-related neurocognitive changes within the domain of executive functioning are process-specific.

4.4. Executive functions and neurocognitive aging: a process-specific account

Recent theories suggest that greater functional recruitment of lateral PFC may be a common compensatory mechanism supporting executive functioning in older adults (Park and Reuter-Lorenz, 2009; Reuter-Lorenz and Cappell, 2008). Yet, to our knowledge, no studies have directly compared age-related functional brain changes on tasks tapping different executive control processes. By using quantitative meta-analysis to review studies that have examined age-related functional brain changes in working memory and inhibitory control, we have provided the first evidence that age-related neurocognitive changes are dissociable within the domain of executive functioning. These data are consistent with a recent review of neurocognitive aging (Spreng et al., 2010). In this review, which was the first quantitative meta-analytic review of neurocognitive aging across cognitive domains, Spreng and colleagues observed that healthy aging was associated with increased recruitment of frontal brain regions across cognitive domains, particularly during executive control tasks. Their conclusions from this meta-analytic review were consistent with earlier qualitative reviews of the neurocognitive aging literature (e.g., Grady, 2008; Hillary et al., 2006; Park and Reuter-Lorenz, 2009; Reuter-Lorenz and Cappell, 2008) suggesting that enhanced PFC recruitment reflects greater engagement of strategic control processes, mediated by dorsolateral prefrontal cortex, in older adults or a decline in the efficiency of processing operations, requiring greater functional brain response to maintain similar levels of executive control performance. While these explanations suggest that age-related functional brain changes may be domain-general, and therefore unaffected by the specific executive control process engaged, this had not been directly investigated.

Here we extend the conclusions of these earlier reviews (e.g., Grady, 2008; Hillary et al., 2006; Park and Reuter-Lorenz, 2009; Reuter-Lorenz and Cappell, 2008; Spreng et al., 2010) by examining age-related changes specifically within the domain of executive functioning. Our data suggest that age-related functional brain changes are dependent upon the specific executive control process being challenged. Thus, while increased recruitment of dorsolateral PFC in older adults characterizes executive function changes in the context of working memory, this pattern does not appear to generalize to inhibition. In contrast, we report that older adult performance on inhibitory control tasks do not involve over- or underrecruitment of dorsolateral PFC regions, but rather engages a "young plus" pattern of enhanced activity in brain regions commonly recruited in younger subjects.

Previous accounts of neurocognitive aging: PASA (Davis et al., 2008), CRUNCH (Reuter-Lorenz and Cappell, 2008), and neural scaffolding (Park and Reuter-Lorenz, 2009) propose that increased frontal activation is associated with increased demand for executive control as cognitive processing becomes less automated (Davis et al., 2008) or slower (Salthouse, 1996) or as neural processing becomes noisier (e.g., Persson et al., 2006) or circuits become less efficient (e.g., Cappell et al., 2010). Increased demand for executive control is typically associated with greater bilateral activation of dorsolateral PFC relative to more lateralized processing in younger adults. We observed this pattern in our working memory but not in our inhibition contrasts, suggesting that these age-related neurocognitive changes depend upon the specific executive process being engaged. In a qualitative meta-analytic review, Rajah et al., 2008 and D'Esposito (2005) examined commonalities in patterns of age-related change in the recruitment of specific areas within PFC during performance of mnemonic tasks engaging executive control (i.e., working and episodic memory tasks). Consistent with our findings, they reported age-related increases in recruitment of dorsolateral PFC for the working memory studies. They also reported a similar, albeit more variable, pattern for the episodic memory studies. However, a review of their data (Table 3) suggests that even within the relatively narrow context of executive control of memory, there are process-specific differences in the patterns of age-related functional brain change.

As reviews of the neurocognitive aging literature are equivocal regarding process-specificity, within-subject investigations of older adult performance on tasks tapping 2 or more dissociable processes (similar to the study in

younger adults from McNab et al. [2008]) will be necessary to determine whether patterns of age-related functional brain change associated with executive functioning vary across specific control processes. However, 1 recent quantitative meta-analysis investigating functional brain changes during inhibitory control processing under variable working memory demands in younger adults (Simmonds et al., 2008) may be particularly informative on this question. In their review, the authors report that simple inhibitory control tasks activate right inferior frontal gyrus and presupplementary motor area as well as posterior brain regions. When working memory demands were increased on these inhibition tasks, brain activity extended into dorsolateral PFC regions. Thus, while "pure" inhibitory control demands activated a process-specific brain network, increased working memory demand was associated with greater recruitment of dorsolateral PFC regions. In the context of neurocognitive aging, these data suggest that age-related recruitment of dorsolateral PFC may reflect differential reliance on working memory strategies in older relative to younger adults rather than a generalized response to increased executive function demands per se. Thus dissociating working memory demands from other executive control processes engaged during executive function tasks will represent an important line of future research.

Cognitive neuroscience methods have been instrumental in the fractionation of executive control functioning into component processes with overlapping but unique neural signatures. Here we present the first quantitative meta-analytic review of the cognitive neuroscience literature to examine process-specific changes in executive control functioning in older adults. Our results suggest that patterns of age-related functional brain change depend upon the specific executive control process being challenged (e.g., working memory or inhibition). These data argue for targeted investigations of how individual executive control processes are implemented in the aging brain.

Disclosure statement

The authors report no conflict of interests in the conduct of this research.

Appendix: A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.neurobiolaging.2011.06.005.

References

Braver, T.S., Barch, D.M., 2006. Extracting core components of cognitive control. Trends Cogn. Sci. 10, 529–532.

Buchsbaum, B.R., Greer, S., Chang, W.L., Berman, K.F., 2005. Meta-analysis of neuroimaging studies of the Wisconsin card-sorting task and component processes. Hum. Brain Mapp. 25, 35–45.

Cabeza, R., Daselaar, S.M., Dolcos, F., Prince, S.E., Budde, M., Nyberg, L., 2004. Task-independent and task-specific age effects on brain activity during working memory, visual attention and episodic retrieval. Cereb. Cortex 14, 364–375.

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

Cappell, K.A., Gmeindl, L., Reuter-Lorenz, P.A., 2010. Age differences in prefontal recruitment during verbal working memory maintenance depend on memory load. Cortex 46, 462–473.

Chambers, C.D., Garavan, H., Bellgrove, M.A., 2009. Insights into the neural basis of response inhibition from cognitive and clinical neuroscience. Neurosci. Biobehav. Rev. 33, 631–646.

Chen, C.Y., Muggleton, N.G., Tzeng, O.J., Hung, D.L., Juan, C.H., 2009. Control of prepotent responses by the superior medial frontal cortex. Neuroimage 44, 537–545.

Chikazoe, J., 2010. Localizing performance of go/no-go tasks to prefrontal cortical subregions. Curr. Opin. Psychiatry 23, 267–272.

Colcombe, S.J., Kramer, A.F., Erickson, K.I., Scalf, P., 2005. The implications of cortical recruitment and brain morphology for individual differences in inhibitory function in aging humans. Psychol. Aging 20, 363–375.

Cox, R.W., Hyde, J.S., 1997. Software tools for analysis and visualization of fMRI data. NMR Biomed. 10, 171–178.

Davis, S.W., Dennis, N.A., Daselaar, S.M., Fleck, M.S., Cabeza, R., 2008. Que PASA? The posterior-anterior shift in aging. Cereb. Cortex 18, 1201–1209.

DiGirolamo, G.J., Kramer, A.F., Barad, V., Cepeda, N.J., Weissman, D.H., Milham, M.P., Wszalek, T.M., Cohen, N.J., Banich, M.T., Webb, A., Belopolsky, A.V., McAuley, E., 2001. General and task-specific frontal lobe recruitment in older adults during executive processes: a fMRI investigation of task-switching. Neuroreport 12, 2065–2071.

Eickhoff, S.B., Laird, A.R., Grefkes, C., Wang, L.E., Zilles, K., Fox, P.T., 2009. Coordinate-based activation likelihood estimation meta-analysis of neuroimaging data: a random-effects approach based on empirical estimates of spatial uncertainty. Hum. Brain Mapp. um30, 2907–2926.

Emery, L., Heaven, T.J., Paxton, J.L., Braver, T.S., 2008. Age-related changes in neural activity during performance matched working memory manipulation. Neuroimage 42, 1577–1586.

Erickson, K.I., Colcombe, S.J., Wadhwa, R., Bherer, L., Peterson, M.S., Scalf, P.E., Kim, J.S., Alvarado, M., Kramer, A.F., 2007a. Training-induced functional activation changes in dual-task processing: an FMRI study. Cereb. Cortex 17, 192–204.

Erickson, K.I., Colcombe, S.J., Wadhwa, R., Bherer, L., Peterson, M.S., Scalf, P.E., Kim, J.S., Alvarado, M., Kramer, A.F., 2007b. Training-induced plasticity in older adults: effects of training on hemispheric asymmetry. Neurobiol. Aging 28, 272–283.

Esposito, G., Kirkby, B.S., Van Horn, J.D., Ellmore, T.M., Berman, K.F., 1999. Context-dependent, neural system-specific neurophysiological concomitants of ageing: mapping PET correlates during cognitive activation. Brain 122, 963–979.

Floden, D., Stuss, D.T., 2006. Inhibitory control is slowed in patients with right superior medial frontal damage. J. Cogn. Neurosci. 18, 1843–1849.

Freo, U., Ricciardi, E., Pietrini, P., Schapiro, M.B., Rapoport, S.I., Furey, M.L., 2005. Pharmacological modulation of prefrontal cortical activity during a working memory task in young and older humans: a PET study with physostigmine. Am. J. Psychiatry 162, 2061–2070.

Grady, C.L., 2008. Cognitive neuroscience of aging. Ann. N. Y. Acad. Sci. 1124, 127–144.

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

Grady, C.L., McIntosh, A.R., Bookstein, F., Horwitz, B., Rapoport, S.I., Haxby, J.V., 1998. Age-related changes in regional cerebral blood flow during working memory for faces. Neuroimage 8, 409–425.

Grossman, M., Cooke, A., DeVita, C., Alsop, D., Detre, J., Chen, W., Gee, J., 2002. Age-related changes in working memory during sentence comprehension: an fMRI study. Neuroimage 15, 302–317.

Haut, M.W., Kuwabara, H., Moran, M.T., Leach, S., Arias, R., Knight, D., 2005. The effect of education on age-related functional activation during working memory. Aging Neuropsychol. Cogn. 12, 216–229.

Hillary, F.G., Genova, H.M., Chiaravalloti, N.D., Rypma, B., DeLuca, J., 2006. Prefrontal modulation of working memory performance in brain injury and disease. Hum. Brain Mapp. 27, 837–847.

Holtzer, R., Rakitin, B.C., Steffener, J., Flynn, J., Kumar, A., Stern, Y., 2009. Age effects on load-dependent brain activations in working memory for novel material. Brain Res. 1249, 148–161.

Johnson, M.K., Mitchell, K.J., Raye, C.L., Greene, E.J., 2004. An age-related deficit in prefrontal cortical function associated with refreshing information. Psychol. Sci. 13, 127–132.

Jonides, J., Marshuetz, C., Smith, E.E., Reuter-Lorenz, P.A., Koeppe, R.A., Hartley, A., 2000. Age differences in behavior and PET activation reveal differences in interference resolution in verbal working memory. J. Cogn. Neurosci. 12, 188–196.

Jonides, J., Smith, E.E., Marshuetz, C., Koeppe, R.A., Reuter-Lorenz, P.A., 1998. Inhibition in verbal working memory revealed by brain activation. Proc. Natl. Acad. Sci. U. S. A. 95, 8410–8413.

Laird, A.R., Fox, P.M., Price, C.J., Glahn, D.C., Uecker, A.M., Lancaster, J.L., Turkeltaub, P.E., Kochunov, P., Fox, P.T., 2005. ALE meta-analysis: controlling the false discovery rate and performing statistical contrasts. Hum. Brain Mapp. 25, 155–164.

Laird, A.R., Robinson, J.L., McMillan, K.M., Tordesillas-Gutiérrez, D., Moran, S.T., Gonzales, S.M., Ray, K.L., Franklin, C., Glahn, D.C., Fox, P.T., Lancaster, J.L., 2010. Comparison of the disparity between Talairach and MNI coordinates in functional neuroimaging data: Validation of the Lancaster transform. Neuroimage 51, 677–683.

Lancaster, J.L., Tordesillas-Gutiérrez, D., Martinez, M., Salinas, F., Evans, A., Zilles, K., Mazziotta, J.C., Fox, P.T., 2007. Bias between MNI and Talairach coordinates analyzed using the ICBM-152 brain template. Hum. Brain Mapp. 28, 1194–1205.

Langenecker, S.A., Nielson, K.A., Rao, S.M., 2004. fMRI of healthy older adults during Stroop interference. Neuroimage 21, 192–200.

Lee, T.M., Zhang, J.X., Chan, C.C., Yuen, K.S., Chu, L.W., Cheung, R.T., Chan, Y.S., Fox, P.T., Gao, J.H., 2006. Age-related differences in response regulation as revealed by functional MRI. Brain Res. 1076, 171–176.

Leung, H.C., Cai, W., 2007. Common and differential ventrolateral prefrontal activity during inhibition of hand and eye movements. J. Neurosci. 27, 9893–9900.

Li, C.S., Huang, C., Constable, R.T., Sinha, R., 2006. Imaging response inhibition in a stop-signal task: neural correlates independent of signal monitoring and post-response processing. J. Neurosci. 26, 186–192.

Madden, D.J., Turkington, T.G., Provenzale, J.M., Denny, L.L., Langley, L.K., Hawk, T.C., Coleman, R.E., 2002. Aging and attentional guidance during visual search: functional neuroanatomy by positron emission tomography. Psychol. Aging 17, 24–43.

Mathis, A., Schunck, T., Erb, G., Namer, I.J., Luthringer, R., 2009. The effect of aging on the inhibitory function in middle-aged subjects: a functional MRI study coupled with a color-matched Stroop task. Int. J. Geriatr. Psychiatry 24, 1062–1071.

McNab, F., Leroux, G., Strand, F., Thorell, L., Bergman, S., Klingberg, T., 2008. Common and unique components of inhibition and working memory: An fMRI, within-subjects investigation. Neuropsychologia 46, 2668–2882.

Meinzer, M., Flaisch, T., Wilser, L., Eulitz, C., Rockstroh, B., Conway, T., Gonzalez-Rothi, L., Crosson, B., 2009. Neural signatures of semantic and phonemic fluency in young and old adults. J. Cogn. Neurosci. 21, 2007–2018.

Mell, T., Wartenburger, I., Marschner, A., Villringer, A., Reischies, F.M., Heekeren, H.R., 2009. Altered function of ventral striatum during reward-based decision making in old age. Front. Hum. Neurosci. 3, 34.

Milham, M.P., Erickson, K.I., Banich, M.T., Kramer, A.F., Webb, A., Wszalek, T., Cohen, N.J., 2002. Attentional control in the aging brain: insights from an fMRI study of the stroop task. Brain Cogn. 49, 277–296.

Miyake, A., Friedman, N.P., Emerson, M.J., Witzki, A.H., Howerter, A., Wager, T.D., 2000. The unity and diversity of executive functions and their contributions to complex "Frontal Lobe" tasks: a latent variable analysis. Cogn. Psychol. 41, 49–100.

Nagel, I.E., Preuschhof, C., Li, S.C., Nyberg, L., Bäckman, L., Lindenberger, U., Heekeren, H.R., 2009. Performance level modulates adult age differences in brain activation during spatial working memory. Proc. Natl. Acad. Sci. U. S. A. 106, 22552–22557.

Nielson, K.A., Langenecker, S.A., Garavan, H., 2002. Differences in the functional neuroanatomy of inhibitory control across the adult life span. Psychol. Aging 17, 56–71.

Nielson, K.A., Langenecker, S.A., Ross, T.J., Garavan, H., Rao, S.M., Stein, E.A., 2004. Comparability of functional MRI response in young and old during inhibition. Neuroreport 15, 129–133.

Otsuka, Y., Osaka, N., Morishita, M., Kondo, H., Osaka, M., 2006. Decreased activation of anterior cingulate cortex in the working memory of the elderly. Neuroreport 17, 1479–1482.

Park, D.C., Polk, T.A., Hebrank, A.C., Jenkins, L.J., 2010. Age differences in default mode activity on easy and difficult spatial judgment tasks. Front. Hum. Neurosci. 3, 75.

Park, D.C., Reuter-Lorenz, P., 2009. The adaptive brain: aging and neurocognitive scaffolding. Annu. Rev. Psychol. 60, 173–196.

Paxton, J.L., Barch, D.M., Racine, C.A., Braver, T.S., 2008. Cognitive control, goal maintenance, and prefrontal function in healthy aging. Cereb. Cortex 18, 1010–1028.

Persson, J., Nyberg, L., Lind, J., Larsson, A., Nilsson, L.G., Ingvar, M., Buckner, R.L., 2006. Structure-function correlates of cognitive decline in aging. Cereb. Cortex 16, 907–915.

Postle, B.R., Berger, J.S., D'Esposito, M., 1999. Functional neuroanatomical double dissociation of mnemonic and executive control processes contributing to working memory performance. Proc. Natl. Acad. Sci. U. S. A. 96, 12959–12964.

Prakash, R.S., Erickson, K.I., Colcombe, S.J., Kim, J.S., Voss, M.W., Kramer, A.F., 2009. Age-related differences in the involvement of the prefrontal cortex in attentional control. Brain Cogn. 71, 328–335.

Rajah, M.N., D'Esposito, M., 2005. Region-specific changes in prefrontal function with age: a review of PET and fMRI studies on working and episodic memory. Brain. 128, 1964–1983.

Raye, C.L., Mitchell, K.J., Reeder, J.A., Greene, E.J., Johnson, M.K., 2008. Refreshing one of several active representations: behavioral and functional magnetic resonance imaging differences between young and older adults. J. Cogn. Neurosci. 20, 852–862.

Reuter-Lorenz, P., Cappell, K.A., 2008. Neurocognitive Aging and the Compensation Hypothesis. Curr. Directions Psychol. Sci. 17, 177–182.

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

Ricciardi, E., Pietrini, P., Schapiro, M.B., Rapoport, S.I., Furey, M.L., 2009. Cholinergic modulation of visual working memory during aging: a parametric PET study. Brain Res. Bull. 79, 322–332.

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

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

Salthouse, T.A., 1996. The processing-speed theory of adult age differences in cognition. Psychological Review 103 (3), 403–428.

Salthouse, T.A., Atkinson, T.M., Berish, D.E., 2003. Executive functioning as a potential mediator of age-related cognitive decline in normal adults. J. Exp. Psychol. Gen. 132, 566–594.

Schneider-Garces, N.J., Gordon, B.A., Brumback-Peltz, C.R., Shin, E., Lee, Y., Sutton, B.P., Maclin, E.L., Gratton, G., Fabiani, M., 2009. Span, CRUNCH, and beyond: working memory capacity and the aging brain. J. Cogn. Neurosci. 22, 655–669.

Simmonds, D.J., Pekar, J.J., Mostofsky, S.H., 2008. Meta-analysis of Go/No-go tasks demonstrating that fMRI activation associated with response inhibition is task-dependent. Neuropsychologia 46, 224–232.

Smith, E.E., Geva, A., Jonides, J., Miller, A., Reuter-Lorenz, P., Koeppe, R.A., 2001. The neural basis of task-switching in working memory: effects of performance and aging. Proc. Natl. Acad. Sci. U. S. A. 98, 2095–2100.

Smith, E.E., Jonides, J., 1998. Neuroimaging analyses of human working memory. Proc. Natl. Acad. Sci. U. S. A. 95, 12061–12068.

Smith, S.M., Jenkinson, M., Woolrich, M.W., Beckmann, C.F., Behrens, T.E., Johansen-Berg, H., Bannister, P.R., De Luca, M., Drobnjak, I., Flitney, D.E., Niazy, R.K., Saunders, J., Vickers, J., Zhang, Y., De Stefano, N., Brady, J.M., Matthews, P.M., 2004. Advances in functional and structural MR image analysis and implementation as FSL. Neuroimage 23 Suppl 1, S208–S219.

Spreng, R.N., Wojtowicz, M., Grady, C.L., 2010. Reliable differences in brain activity between young and old adults: A quantitative meta-analysis across multiple cognitive domains. Neurosci. Biobehav. Rev. 34, 1178–1194.

Stuss, D.T., Shallice, T., Alexander, M.P., Picton, T.W., 1995. A multidisciplinary approach to anterior attentional functions. Ann. N. Y. Acad. Sci. 769, 191–211.

Swann, N., Tandon, N., Canolty, R., Ellmore, T.M., McEvoy, L.K., Dreyer, S., Disano, M., Aron, A.R., 2009. Intracranial EEG reveals a time- and frequency-specific role for the right inferior frontal gyrus and primary motor cortex in stopping initiated responses. J. Neurosci. 29, 12675–12685.

Talairach, J., Tournoux, P., 1988. Co-Planar Stereotaxic Atlas of the Human Brain, Rayport, M. (Trans.). Thieme Medical Publishers, New York.

Townsend, J., Adamo, M., Haist, F., 2006. Changing channels: an fMRI study of aging and cross-modal attention shifts. Neuroimage 31, 1682–1692.

Turkeltaub, P.E., Eden, G.F., Jones, K.M., Zeffiro, T.A., 2002. Meta-analysis of the functional neuroanatomy of single-word reading: method and validation. Neuroimage 16, 765–780.

Turner, G.R., D'Esposito, M., 2010. Functional neuroimaging in aging, in: Knoefel, J., Albert, M.L. (Eds.), Clinical Neurology of Aging, third ed. Oxford University Press, Oxford.

Van Essen, D.C., 2005. A population-average, landmark- and surface-based (PALS) atlas of human cerebral cortex. Neuroimage 28, 635–662.

Wager, T.D., Smith, E.E., 2003. Neuroimaging studies of working memory: a meta-analysis. Cogn. Affect. Behav. Neurosci. 3, 255–274.

Wood, G., Ischebeck, A., Koppelstaetter, F., Gotwald, T., Kaufmann, L., 2009. Developmental trajectories of magnitude processing and interference control: an FMRI study. Cereb. Cortex 19, 2755–2765.

Zhu, D.C., Zacks, R.T., Slade, J.M., 2010. Brain activation during interference resolution in young and older adults: an fMRI study. Neuroimage 50, 810–817.

Zysset, S., Schroeter, M.L., Neumann, J., Yves von Cramon, D., 2007. Stroop interference, hemodynamic response and aging: An event-related fMRI study. Neurobiol. in press.

Supplemental Table 1

Working Memory

Lat	Region	BA	Vol (mm^3)	ALE (10^-2)	x	y	z	Studies contributing to each cluster									
Younger																	
R	MFG	9/46	2008	2.73	34	24	22	5*°	**8°**	10°	14°	**15*°**	**17°**				
L	MFG/IFG/PCG	9/6	1768	3.16	-42	2	28	1	**6**	7	**8**	10	12	**15***	16*	**17**	
L	IPS/SPL	7	1456	2.11	-30	-56	44	**3**	**6**	7	10	11	**15***	16*	**18**		
R	IPS	40/7	1080	2.69	32	-50	38	**3°**	4°	7	**15*°**	16*					
L	IFG	13	1008	2.95	-38	20	10	1°	**8°**	10°	12°	**17**					
L	FEF	6	864	2.53	-24	-4	54	2*	4°	7°	16*°	**17°**	**18°**				
B	SMA	6	744	2.66	-4	4	54	1	**3**	12							
R	PCG	9	728	2.81	42	4	32	**3**	5	10	**15***	**18**					
L	IPS/SPL	40	696	2.13	-40	-38	38	1	4	7	16*						
B	preSMA	8	560	2.73	2	26	42	**6**	10	11							
L	FG/MOG	19/37	360	1.46	-42	-68	-10	1	7	**8**	10						
R	FEF	6	344	1.73	28	-8	46	**3**	4	**18**							
L	MFG	9	312	2.16	-42	30	32	11	**17**								
R	LG	17	296	2.03	12	-92	-2	1	5								
L	PCG	4/6	296	1.71	-52	-4	42	9*	10	12							
R	Putamen		528	2.36	18	10	6	5	10	**13**	14						
L	Thalamus		488	2.20	-10	-20	10	1	10	**15***							
L	Caudate		368	1.87	-18	6	16	10	**13**								
R	Cerebellum		688	2.46	32	-56	-20	1	5	7	**8**						
Older																	
L	IFG/PCG	9/6	2408	3.52	-36	6	28	1°	4°	5°	**6°**	7°	**8**	9*°	10°	**19**	
R	MFG/PCG	9/46	1960	3.47	46	26	24	1°	2*°	**3°**	5°	**8**	10°	16*°	**17°**	**18°**	**19°**
B	SMA	6/32	1920	3.23	4	8	44	1°	**3°**	7°	10°	**15*°**	**17°**	**18°**	**19°**		
L	IPS/SPL	40/7	960	2.55	-34	-52	40	1	4	**6**	10	11	**15***	16*			
L	IPS	7	632	2.45	-24	-62	34	4°	7°	10°	**17°**						
L	IFG	47	592	2.66	-48	22	-4	9*	10	11	12	16*					
R	LG	17	440	2.21	14	-92	-2	1	5	10							
L	FG		424	1.39	-40	-50	-16	1	**3**	4	**8**	16*					
R	aIPL	40	416	1.88	48	-48	40	1	4	10	**15***						
R	IPS	7	400	1.93	30	-58	48	**3**	4	**6**	7						
R	RLPFC	10	384	2.02	22	46	10	5	**8**	10	14	**15***					
L	FEF	6	360	1.93	-28	2	52	1	7	16*							
R	MFG	46	312	2.48	36	38	2	5	**8**								
R	PCG	6	312	1.81	42	2	34	10	**15***	**17**							
L	Putamen		304	2.14	-24	6	-2	12	**13**								
R	Cerebellum		664	2.68	30	-56	-20	1	5	7	16*						

Table S1: Regions of activation for working memory tasks. Study #s listed under Contributing Studies refer to Table 1 (Working Memory). Bold indicates unequal performance between Younger and Older; '*' indicates a 'high' cognitive demand baseline (control) condition, see Methods for details. '°' signifies studies contributing to difference clusters in Table 3. Abbreviations: Lat, laterality; L, left; R, right; B, bilateral; X, right/left coordinate; Y, anterior/posterior coordinate; Z, inferior/superior coordinate; Vol, volume. Brain regions: aIPL, anterior inferior parietal lobule; aIFO, anterior insula/frontal operculum; FEF, frontal eye field; FG, Fusiform Gyrus; IFG, inferior frontal gyrus; IPS, intra-parietal sulcus; LG, lingual gyrus; MFG, Middle frontal gyrus; MOG, middle occipital gyrus; PCG, precentral gyrus; RLPFC, rostro-lateral prefrontal cortex; SMA, supplementary motor area; SPL, superior parietal lobule; STG, superior temporal gyrus.

Supplemental Table 2

Inhibition

Lat	Region	BA	Vol (mm^3)	ALE (10^-2)	x	y	z	Studies contributing to each cluster					
Younger													
B	SMA	6/32	1272	1.95	-6	12	46	3	**4**	**8**	**11**		
R	MFG	9/46	936	1.71	38	26	30	3	5	**8**	**9**	**10**	12
R	MFG/PCG	6	768	1.99	30	0	46	3	5	6	**9**		
L	IFG	9	672	2.25	-42	2	30	**10**	**11**	13			
R	al/fO	13	656	2.61	40	14	4	13	**14**				
L	IPS	19	512	1.87	-26	-70	34	5	**9**	13			
L	MOG	18	488	2.12	-30	-82	0	3	**8**	**9**			
R	IOG	19	384	2.10	38	-76	0	3°	5°	**9°**			
L	FEF	6	368	1.39	-22	2	52	3	7*	**9**	**11**		
L	IPS/SPL	7	360	1.93	-32	-56	44	3	7*	**10**			
L	MFG	9	328	1.81	-44	16	30	3	**4**				
R	IPS/SPL	7	312	1.43	30	-60	46	**9**	**10**				
L	Cerebellum (Declive)		560	1.80	-10	-80	-12	3	**8**	13			
R	Cerebellum (Declive)		312	2.02	10	-76	-18	3	13				
Older													
L	MFG/PCG	9/46	1568	2.14	-44	18	26	3	5	6	**10**	**11**	13
L	SFG/MFG	6	1528	2.67	-4	14	44	3°	5°	7*°	**10**	**11**	
R	MFG/IFG/PCG	9/8/6	1496	2.35	54	8	36	3°	5°	6°	7*°	**9°**	12°
R	MFG	9	1016	2.90	40	22	32	**2**	3	4	7*	**10**	
L	FEF	6	1016	2.58	-24	0	50	3	5	7*	9	**11**	
R	FEF	6	704	1.90	30	-4	56	**2**	3	5	7*	**9**	
L	IFG	45/46	512	2.23	-46	24	12	3	**10**				
L	IPS	19	504	1.78	-26	-68	30	7*	**10**	**11**	13		
L	IOG	19	440	1.69	-44	-68	-6	3	**9**				
R	Anterior insula		400	1.81	40	14	2	3	**8**	**11**			
R	IPS/SPL	40	368	2.32	32	-46	44	**2**	3				

Table S2: Regions of activation for younger and older adults for inhibition tasks. Study #s listed under Contributing Studies refer to Table 1 (Inhibition). Abbreviations: IOG, inferior occipital gyrus; SFG, superior frontal gyrus. Other details as in Table S1.

Supplemental Table 3

A. Working Memory > Inhibition

Lat	Region	BA	Vol (mm^3)	ALE (10^-2)	x	y	z	Studies contributing to each cluster								
Younger								*Working Memory*								
R	MFG	9/46	1656	2.21	28	32	30	5	**8**	10	14	**15***	**17**			
R	IPS	7/40	872	2.29	28	-60	34	**3**	4	7	**15***	16*				
L	IFG	45	600	2.57	-40	20	10	1	**8**	10	12					
L	IPS	40	560	1.73	-40	-42	46	1	**4**	7	16*					
L	SFG	6	504	2.51	-4	6	54	1	**3**	12						
R	PCG	9	408	2.28	42	4	32	**3**	10	**15***	**18**					
R	MFG	8	368	2.63	2	26	42	**6**	10	11						
L	PCG	4	296	1.71	-52	-4	42	9*	10	12						
R	LG	17	288	2.03	12	-92	-2	1	5							
L	MTG	22/21	272	1.26	-58	-52	8	9*	10	11						
L	FEF	6	256	2.10	-26	-4	56	2*	4	7	16*	**17**	**18**			
R	Putamen		512	2.36	18	10	6	5	10	**13**	14					
L	Thalamus		432	2.17	-10	-20	10	1	10	**15***						
L	Caudate		344	1.85	-18	6	16	10	**13**							
R	Cerebellum (Culmen)		640	2.46	32	-56	-20	1	5	7	**8**					
Older																
B	SMA	6/32	1272	2.68	-4	6	54	1	**3**	7	10	**17**	**18**	**19**		
R	MFG	9/46	1184	2.05	34	26	28	1	**3**	5	**8**	10	**16***	**17**	**18**	**19**
L	IFG	9	1040	2.29	-48	6	30	1	4	5	7	**8**	9*	10	**19**	
R	LG	17	440	2.21	14	-92	-2	1	**5**	10						
L	FG	37	392	1.39	-40	-50	-16	1	**3**	4	**8**	16*				
L	IPS	7	352	2.06	-24	-62	36	4	7	10	**17**					
R	SPL	7	344	1.93	30	-58	48	**3**	4	**6**	7					
R	RLPFC	10	272	1.97	22	46	10	**8**	14	**15***						
R	Frontal white matter		320	2.47	36	36	2	5	**8**							
R	Cerebellum (Culmen)		656	2.68	30	-56	-20	1	5	7	16*					

B. Inhibition > Working Memory

Lat	Region	BA	Vol (mm^3)	ALE (10^-2)	x	y	z	Studies contributing to each cluster								
Younger								*Inhibition*								
R	al/fO	13	344	-2.55	40	14	4	3	5	**10**	13					
R	FEF	6	304	-1.81	30	0	44	3	5	6	**9**					
R	MFG	9	288	-1.58	38	24	32	3	5	**8**	**10**					
L	Cerebellum (Declive)		376	-1.80	-10	-80	-12	**3**	**8**	13						
Older																
R	MFG/PCG	9/6	496	-2.35	54	8	36	3	5	6	7*	12				
R	al/fO		328	-1.81	40	14	2	3	**11**							
L	MFG	6	296	-2.07	-2	16	44	3	5	**10**	**11**					
R	IPS	7	272	-2.31	30	-46	42	**2**	3							
L	SFG	6	264	-1.91	-2	28	54	3	5	7*						

Table S3: Differences between working memory (A) and inhibition (B) for younger and older adults. Abbreviations: MTG, middle temporal gyrus. Other details as in Table S1 & S2.

Appendix S1

Meta-analysis studies listed alphabetically.

1. Cabeza, R., Daselaar, S. M., Dolcos, F., Prince, S. E., Budde, M., & Nyberg, L. (2004). Task-independent and task-specific age effects on brain activity during working memory, visual attention and episodic retrieval. *Cereb Cortex, 14*(4), 364-375.

2. Emery, L., Heaven, T. J., Paxton, J. L., & Braver, T. S. (2008). Age-related changes in neural activity during performance matched working memory manipulation. *Neuroimage, 42*(4), 1577-1586.

3. Freo, U., Ricciardi, E., Pietrini, P., Schapiro, M. B., Rapoport, S. I., & Furey, M. L. (2005). Pharmacological modulation of prefrontal cortical activity during a working memory task in young and older humans: a PET study with physostigmine. *Am J Psychiatry, 162*(11), 2061-2070.

4. Grady, C. L., McIntosh, A. R., Bookstein, F., Horwitz, B., Rapoport, S. I., & Haxby, J. V. (1998). Age-related changes in regional cerebral blood flow during working memory for faces. *Neuroimage, 8*(4), 409-425.

5. Grossman, M., Cooke, A., DeVita, C., Alsop, D., Detre, J., Chen, W., et al. (2002). Age-related changes in working memory during sentence comprehension: an fMRI study. *Neuroimage, 15*(2), 302-317.

6. Haut, M. W., Kuwabara, H., Moran, M. T., Leach, S., Arias, R., & Knight, D. (2005). The effect of education on age-related functional activation during working memory. *Aging, Neuropsychology and Cognition, 12*, 216-229.

7. Holtzer, R., Rakitin, B. C., Steffener, J., Flynn, J., Kumar, A., & Stern, Y. (2009). Age effects on load-dependent brain activations in working memory for novel material. *Brain Res, 1249*, 148-161.

8. Johnson, M. K., Mitchell, K. J., Raye, C. L., & Greene, E. J. (2004). An age-related deficit in prefrontal cortical function associated with refreshing information. *Psychological Science, 13*(2), 127-132.

9. Nagel, I. E., Preuschhof, C., Li, S. C., Nyberg, L., Backman, L., Lindenberger, U., et al. (2009). Performance level modulates adult age differences in brain activation during spatial working memory. *Proc Natl Acad Sci U S A, 106*(52), 22552-22557.

10. Otsuka, Y., Osaka, N., Morishita, M., Kondo, H., & Osaka, M. (2006). Decreased activation of anterior cingulate cortex in the working memory of the elderly. *Neuroreport, 17*(14), 1479-1482.

11. Park, D. C., Polk, T. A., Hebrank, A. C., & Jenkins, L. J. (2010). Age differences in default mode activity on easy and difficult spatial judgment tasks. *Front Hum Neurosci, 3*, 75.

12. Paxton, J. L., Barch, D. M., Racine, C. A., & Braver, T. S. (2008a). Cognitive control, goal maintenance, and prefrontal function in healthy aging. *Cereb Cortex, 18*(5), 1010-1028.

13. Raye, C. L., Mitchell, K. J., Reeder, J. A., Greene, E. J., & Johnson, M. K. (2008). Refreshing one of several active representations: behavioral and functional magnetic resonance imaging differences between young and older adults. *J Cogn Neurosci, 20*(5), 852-862.

14. Reuter-Lorenz, P. A., Jonides, J., Smith, E. E., Hartley, A., Miller, A., Marshuetz, C., et al. (2000a). Age differences in the frontal lateralization of verbal and spatial working memory revealed by PET. *J Cogn Neurosci, 12*(1), 174-187.

15. Reuter-Lorenz, P. A., Jonides, J., Smith, E. E., Hartley, A., Miller, A., Marshuetz, C., et al. (2000b). Age differences in the frontal lateralization of verbal and spatial working memory revealed by PET. *J Cogn Neurosci, 12*(1), 174-187.

16. Ricciardi, E., Pietrini, P., Schapiro, M. B., Rapoport, S. I., & Furey, M. L. (2009). Cholinergic modulation of visual working memory during aging: a parametric PET study. *Brain Res Bull, 79*(5), 322-332.

17. Rypma, B., Prabhakaran, V., Desmond, J. E., & Gabrieli, J. D. (2001). Age differences in prefrontal cortical activity in working memory. *Psychol Aging, 16*(3), 371-384.

18. Schneider-Garces, N. J., Gordon, B. A., Brumback-Peltz, C. R., Shin, E., Lee, Y., Sutton, B. P., et al. (2010). Span, CRUNCH, and beyond: working memory capacity and the aging brain. *J Cogn Neurosci, 22*(4), 655-669.

19. Smith, E. E., Geva, A., Jonides, J., Miller, A., Reuter-Lorenz, P., & Koeppe, R. A. (2001). The neural basis of task-switching in working memory: effects of performance and aging. *Proc Natl Acad Sci U S A, 98*(4), 2095-2100.

20. Colcombe, S. J., Kramer, A. F., Erickson, K. I., & Scalf, P. (2005). The implications of cortical recruitment and brain morphology for individual differences in inhibitory function in aging humans. *Psychol Aging, 20*(3), 363-375.

21. Jonides, J., Marshuetz, C., Smith, E. E., Reuter-Lorenz, P. A., Koeppe, R. A., & Hartley, A. (2000). Age differences in behavior and PET activation reveal differences

in interference resolution in verbal working memory. *J Cogn Neurosci, 12*(1), 188-196.

22. Lee, T. M., Zhang, J. X., Chan, C. C., Yuen, K. S., Chu, L. W., Cheung, R. T., et al. (2006). Age-related differences in response regulation as revealed by functional MRI. *Brain Res, 1076*(1), 171-176.

23. Madden, D. J., Turkington, T. G., Provenzale, J. M., Denny, L. L., Langley, L. K., Hawk, T. C., et al. (2002). Aging and attentional guidance during visual search: functional neuroanatomy by positron emission tomography. *Psychol Aging, 17*(1), 24-43.

24. Mathis, A., Schunk, T., Gilles, E., Izzie, J. N., & Luthringer, R. (2009). The effect of aging on the inhibitory function in middle-aged subjects: a functional MRI study coupled with a color-matched Stroop task. *International Jounral of Geriatric Psychiatry, 24*, 1062-1071.

25. Meinzer, M., Flaisch, T., Wilser, L., Eulitz, C., Rockstroh, B., Conway, T., et al. (2009). Neural signatures of semantic and phonemic fluency in young and old adults. *J Cogn Neurosci, 21*(10), 2007-2018.

26. Mell, T., Wartenburger, I., Marschner, A., Villringer, A., Reischies, F. M., & Heekeren, H. R. (2009). Altered function of ventral striatum during reward-based decision making in old age. *Front Hum Neurosci, 3*, 34.

27. Milham, M. P., Erickson, K. I., Banich, M. T., Kramer, A. F., Webb, A., Wszalek, T., et al. (2002). Attentional control in the aging brain: insights from an fMRI study of the stroop task. *Brain Cogn, 49*(3), 277-296.

28. Nielson, K. A., Langenecker, S. A., Ross, T. J., Garavan, H., Rao, S. M., & Stein, E. A. (2004). Comparability of functional MRI response in young and old during inhibition. *Neuroreport, 15*(1), 129-133.

29. Paxton, J. L., Barch, D. M., Racine, C. A., & Braver, T. S. (2008b). Cognitive control, goal maintenance, and prefrontal function in healthy aging. *Cereb Cortex, 18*(5), 1010-1028.

30. Prakash, R. S., Erickson, K. I., Colcombe, S. J., Kim, J. S., Voss, M. W., & Kramer, A. F. (2009). Age-related differences in the involvement of the prefrontal cortex in attentional control. *Brain Cogn, 71*(3), 328-335.

31. Zhu, D. C., Zacks, R. T., & Slade, J. M. (2010). Brain activation during interference resolution in young and older adults: an fMRI study. *Neuroimage, 50*(2), 810-817.

32. Zysset, S., Schroeter, M. L., Neumann, J., & Yves von Cramon, D. (2006). Stroop interference, hemodynamic response and aging: An event-related fMRI study. *Neurobiol Aging*.