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Review

Reliable differences in brain activity between young and old adults: A quantitative meta-analysis across multiple cognitive domains

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ABSTRACT

We conducted a systematic review of the neuroimaging literature examining cognition in old and young adults and quantified these findings in a series of meta-analyses using the activation likelihood estimation technique. In 80 independent samples, we assessed significant convergent and divergent patterns of brain activity across all studies; where task performance was equated or different between age groups; and in four specific cognitive domains (perception, memory encoding, memory retrieval and executive function). Age differences across studies predominantly involved regions within the 'task-positive network' of the brain, a set of interconnected regions engaged during a variety of externally driven cognitive tasks. Old adults engaged prefrontal regions more than young adults. When performance was equivalent, old adults engaged left prefrontal cortex; poorly performing old adults engaged right prefrontal cortex. Young adults engaged occipital regions more than old adults, particularly when performance was unequal and during perceptual tasks. No age-related differences were found in the parietal lobes. We discuss the reliable differences in brain activation with regards to current theories of neurocognitive aging.

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1. Introduction

In recent years, functional neuroimaging has become an ever more popular tool to study the neural correlates of differences in cognitive function between young and old adults. When brain activity in young and old adults is compared on a task, there are at least three possible outcomes in any given brain area: (1) young and old groups could have equivalent brain activity, (2) old adults could show less activity, or (3) old adults could show greater activity. Equivalent activity is generally considered evidence for spared function in the elderly, although if performance is lower in the old group this may indicate less effective use of neural resources (Zarahn et al., 2007). Reduced activity in the elderly can reasonably be assumed to reflect a reduced level of functioning, particularly when accompanied by poorer performance on the task (e.g., Anderson et al., 2000; Grady et al., 2006; Rypma and D'Esposito, 2000). Increased recruitment of brain regions in old compared to young participants is the most intriguing result, but poses a major challenge of interpretation. For example, over-recruitment of brain activity in old adults could potentially be due to compensation, inefficiency in utilization of some neural processes, or a reduction in the differentiation and/or specificity of response during a given task (for reviews, see Cabeza, 2002; Grady, 2008; Rajah and D'Esposito, 2005).

This growing literature on the neuroscience of cognitive aging has suggested that there are some reliable age-related differences in brain activity found across studies. From the earliest experiments in this field, which involved perceptual matching tasks, it was clear that age differences in brain activity could take the form of both decreases and increases of activity in old adults compared to their younger counterparts, with increases found in prefrontal cortex and decreases found in occipital regions (Grady et al., 1994).

Age-related changes in neural activity have been observed across numerous cognitive domains, including perception (e.g. Grady et al., 1994), memory encoding (e.g. Madden et al., 1996), memory retrieval (e.g. Schacter et al., 1996), working memory and executive functions (e.g. Grady et al., 1998). Studies of perception often involve the presentation of a stimulus, paired with a decision about that stimulus. Encoding information is not dissimilar to perception; however, entails later verifying the retention of perceived information. Memory retrieval, on the other hand, involves a test of previously learned information. Finally, working memory and executive functions are examined by a diversity of tasks involving the maintenance and manipulation of information online or response inhibition and selection according to task goals.

Many subsequent studies have replicated age-related increases in frontal cortex (e.g., Cabeza et al., 2002; Madden et al., 1999; Morcom et al., 2003; Nielson et al., 2002; Rosen et al., 2002) and decreases in visual areas (Anderson and Grady, 2004; Davis et al., 2008; Madden et al., 2002, 2004). Increased activity in old adults initially led to the suggestion that additional frontal activity can compensate for reduced activity elsewhere in the brain, providing a benefit to cognitive performance (Cabeza et al., 1997; Grady et al., 1994), and much of the subsequent work has continued to explore this idea. When old adults recruit a brain region or regions that are not active in young adults, but have performance equivalent to that seen in young adults, then the over-recruitment has generally been interpreted as compensatory (Cabeza et al., 1997; Grady et al., 1994, 2008; Reuter-Lorenz et al., 2000).

However, other interpretations of over-recruited activity in old adults are also possible. For example, inefficient use of brain activity in old adults has been invoked when there is no age difference in behavior but old adults have more activity in task-related brain regions than do young adults (Morcom et al., 2007; Zarahn et al., 2007). That is, old adults may need to allocate greater neural resources in general, but this may not necessarily translate into better task performance. However, the possibility that this engagement of new areas represents non-selective recruitment or dedifferentiation in the elderly cannot be ruled out entirely (Logan et al., 2002). Indeed, some recent work suggests that over-recruitment of prefrontal cortex is found primarily in old adults who perform poorly on the task at hand (Colcombe et al., 2005; Duverne et al., 2009; Grady et al., in press). Finally, perhaps the strongest evidence for compensation occurs when old adults recruit brain activity that is not seen in young adults, and the engagement of this area or areas is directly correlated with better performance only in the old adults and not in the young (Grady et al., 2002, 2005, 2003; McIntosh et al., 1999; Stern et al., 2005). This would indicate the recruitment of a unique pattern of neural activity that supports task performance in an age-specific manner. At the current time, it seems likely that at least some age-related differences in brain activity are compensatory, but certainly one cannot make this claim for all such differences, and it is not clear how widespread this phenomenon would be across tasks or cognitive domains.

There have been a few reviews and meta-analyses attempting to identify common trends across papers in the aging neuroscience literature (Anderson and Grady, 2001, 2004; Cabeza, 2002; Grady, 1999; Park and Reuter-Lorenz, 2009; Rajah and D'Esposito, 2005; Reuter-Lorenz and Lustig, 2005). Although these have shown what appear to be relatively robust findings across independent studies, primarily related to memory, there has not yet been a meta-analysis using quantitative methods to identify common age-related changes across all the cognitive domains that have been studied. It seemed to us that sufficient data had appeared in the literature for this to be a worthwhile undertaking. In addition, reliable findings across studies could provide information about areas of the brain that are most vulnerable to the effects of aging (i.e., those with age-related reductions in activity) and those that might show the most plasticity (i.e., those with age-related increases in activity) in response to these effects.

In this paper we have carried out a quantitative meta-analysis using the activation likelihood estimation (ALE) approach for neuroimaging data (Laird et al., 2005; Turkeltaub et al., 2002). Because we were looking for age differences that are reliable across cognitive domains, we expected involvement of brain areas that mediate cognitive processes underlying multiple types of tasks. An example of such a set of brain areas is the so-called 'task-positive network' (Fox et al., 2005; Toro et al., 2008), or TPN. The TPN is active during a wide variety of externally-driven cognitive tasks, and consists of regions thought to be involved in attention and cognitive control (e.g., Corbetta et al., 2008; D'Esposito et al., 1995; Dosenbach et al., 2007; Dove et al., 2006; Vincent et al., 2008). The regions generally considered to be part of the network are: (1) dorsolateral prefrontal cortex (DLPFC), rostrolateral prefrontal cortex (RLPFC) and anterior insula/frontal operculum (alFO); (2) superior parietal cortex near the intraparietal sulcus (IPS) and anterior inferior parietal lobes (aIPL, particularly the supramar-

ginal gyri); (3) frontal eye fields (FEF); (4) supplementary motor area (SMA and/or preSMA); (5) ventral occipital cortex (vOC); and (6) postcentral gyrus (PCS) (Fox et al., 2005; Toro et al., 2008). A different network, called the 'default network', increases its activity when people are in a quiescent state and attending to internally driven cognitive processes, and reduces its activity when an external task-based focus is required (Gusnard et al., 2001; McKiernan et al., 2003; Raichle et al., 2001; Shulman et al., 1997). Recently it was shown that the degree of anti-correlation between the task positive and default networks is related to performance on cognitive tests (Kelly et al., 2008), suggesting that the balance between the default and task positive networks is critical for effective cognitive processing. Several studies have found that old adults show less reduction of default mode activity during cognitive tasks, and reduced functional connectivity in this network, relative to young adults (Grady et al., 2006; Lustig et al., 2003; Miller et al., 2008). In contrast, a recent study indicated that old adults have greater recruitment of the TPN across several cognitive domains, and preserved functional connectivity, relative to young adults (Grady et al., in press). Over-recruitment of the TPN as a whole is consistent with reports of increased activity in prefrontal and parietal regions in old relative to young adults during both episodic memory retrieval (Morcom et al., 2007) and attention (Townsend et al., 2006) tasks.

In the current study we sought to identify stable regions of brain activity engaged across tasks and to identify differences in reliable brain activity related to age. To begin, we first identified brain regions reliably involved across all studies and participants. Similar to a previous meta-analysis (Toro et al., 2008), we predicted that reliable task-related activation would be found in regions consistent with the TPN. We then identified brain regions where young and old adults had differences in activity and assessed the overlap between these areas and those active for both age groups. This overlap would indicate that old adults have reliable changes in engagement of the TPN, or a subset of the nodes of the TPN. Age-related reductions would suggest vulnerability in more regional or specific processes, whereas increased activity in old adults might indicate age-specific adaptations or reorganizations of function. In order to identify neural activity associated with changes in cognition with advancing age, we also examined age differences in brain activity related to task performance. For these analyses, we divided tasks where young and old adults had equivalent performance, indicative of more successful cognitive aging, from tasks where old adults performed less well than the young group, indicative of less successful cognitive aging. More activity in old adults who perform as well as their younger counterparts would suggest that these regions, and the processes that they mediate, are more likely to be effective in supporting cognitive function. In contrast, age differences between young adults and poorer performing old adults might indicate those types of processes and brain regions that are more vulnerable in aging, or those processes that are less effective at supporting cognitive function in the elderly. A third set of analyses examined studies within each cognitive domain, including perception, memory encoding, memory retrieval and executive function. The aim of these analyses was to shed light on the functions of the regions showing age differences across cognitive domains.

2. ALE method

2.1. Selection of studies

Neuroimaging studies of cognitive aging were selected using a systematic search process. Peer-reviewed articles, published in English between January 1982 and July 2009, were selected from the search results of three separate databases: Medline, PsycInfo and

Science Citation Index. Searches were conducted using the following terms: (1) keywords: "age" <OR> "aging" <OR> "ageing" <OR> "age-related" <OR> "older adults" <OR> "adult life-span"; AND (2) Keywords: "neuroimaging" <OR> "cerebral blood flow" <OR> "fMRI" <OR> "functional magnetic resonance imaging" <OR> "PET" <OR> "positron emission tomography"; AND (3) Population: "human". As a result, 2798 unique papers were found.

Only studies that reported both healthy young and healthy old adult group results were included. Independent group analysis results were extracted from 55 studies. We also included results from 25 studies that reported within- and between-group analysis results (i.e. combined Young/Old, Young > Old and Old > Young). Combined task effects were duplicated for each group and task by age interaction coordinates were delegated to each respective age group. Theoretical papers and reviews were excluded. Studies that reported combined group results and a region-of-interest analysis (e.g., Rypma and D'Esposito, 2000), reported only brain-behavior correlations (e.g., Springer et al., 2005) or did not report activation foci as 3D coordinates in stereotaxic space (e.g., Hazlett et al., 1998) were excluded because these studies could not be meaningfully analyzed with ALE. For studies that contained multiple non-independent contrasts, the first contrast of interest was included in order to limit the contribution of any one set of participants to the pool of foci. Likewise, subsequent papers reporting results from the same group of participants on a different task were also excluded (e.g., Dennis et al., 2008). Deactivation coordinates were omitted, as were studies that examined patterns of deactivation (e.g., Daselaar et al., 2005). For studies containing multiple independent samples, peak activation foci from each sample were included (e.g., Grady et al., 1994). The reference lists of included papers were searched for additional studies that fit these criteria. In total, 77 appropriate papers were included; three papers reported two independent samples rendering 80 total experiments for both young and old adults.

Tables 1a and 1b contains a list of all original studies, including details of each experiment, participants, and imaging modality. The equivalence of behavioral performance refers to task based measures such as accuracy and not reaction times, which differed between young and old in nearly all cases. Forty-four experiments did not report significant differences between young and old groups in task performance whereas 36 experiments reported significantly poorer performance in old adults.

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. ALE maps are derived based on foci of interest, which comprise statistically significant peak activation locations from multiple studies. GingerALE can also compute statistically significant differences in the pattern of brain activity between two sets of data from several independent experiments.

Twelve separate ALE analyses were conducted, each yielding an ALE map and corresponding cluster report: (A) reliable brain activity combined across all studies in both young and old adults to identify TPN regions; (B) differences in brain activation patterns in young and old adults *across all studies*; (C) differences in brain activity between young and old adults in studies where performance was *equivalent*; (D) differences in brain activity between young and old adults in studies where performance was *unequal*; and (E-L) *Domain-specific* patterns of brain activity common to young and old adults and those that reliably differentiated between groups. For these analyses we used the studies grouped into the domains of perception, memory encoding, memory

Table 1a

Details of included studies. For complete reference, see appendix. See original papers for additional information. Performance refers to task based measures such as accuracy (not reaction time). Exp., experiment; fMRI, functional magnetic resonance imaging; PET, positron emission tomography.

Exp.	First author	Year	Domain	Performance	Modality	Young			Old		
						N	Age	Foci	N	Age	Foci
1	Anderson	2000	Memory: Encoding	≠	PET	12	24.4	23	12	68.5	21
2	Antonova	2009	Memory: Encoding	≠	fMRI	10	23.6	34	10	72.1	31
3	Backman	1997	Memory: Retrieval	≠	PET	7	24.3	3	7	63.4	5
4	Bergerbest	2009	Memory: Repetition priming	=	fMRI	16	28.5	3	15	78.7	7
5	Cabeza	2000	Memory: Retrieval	≠	PET	12	24.7	5	12	68.6	6
6	Cabeza	2004	Executive/Working Memory	=	fMRI	20	22.6	15	20	70.3	23
7	Cabeza	1997	Memory: Encoding	=	PET	12	25.7	13	12	70.5	13
8	Cerf-Ducastel	2003	Perception	≠	fMRI	6	26.5	25	6	78.5	9
9	Chee	2006	Perception	=	fMRI	20	21.3	4	17	66.9	0
10	Colcombe	2005	Executive	=	fMRI	20	23.5	2	40	67.5	3
11	Daselaar	2003	Motor	=	fMRI	26	32.4	18	40	66.4	24
12	Daselaar	2003	Memory: Encoding	=	fMRI	17	32.7	4	19	66.4	4
13	Davis	2008	Memory: Retrieval & Perception	=	fMRI	14	22.2	7	15	69.2	6
14	Dennis	2007	Memory: Encoding	=	fMRI	16	23.5	18	17	69.3	14
15	Dennis	2008	Memory: Encoding	≠	fMRI	14	19.4	7	14	68.4	2
16	DiGirolamo	2001	Executive	≠	fMRI	8	25	31	8	69	47
17	Dreher	2008	Reward Processing	=	fMRI	20	25	4	13	66	2
18	Duarte	2008	Memory: Retrieval	≠	fMRI	17	23.6	18	14	62.7	16
19	Duverne	2009	Memory: Retrieval	=	fMRI	16	21	9	16	71	15
20	Esposito	1999	Executive/Working Memory	≠	PET	20	18–42	8	21	43–80	6
21	Fernandes	2006	Memory: Retrieval	≠	fMRI	12	26.3	5	11	71.2	13
22	Freo	2005	Executive/Working Memory	=	PET	13	27	12	13	65	15
23	Grady	2002	Memory: Encoding	=	PET	12	23.2	10	11	70	13
24a	Grady	1994a	Perception	=	PET	15	26	6	17	67	11
24b	Grady	1994b	Perception	=	PET	9	27	9	9	65	11
25	Grady	1998	Executive/Working Memory	≠	PET	13	25	10	16	66	14
26	Grady	2005	Memory: Retrieval	=	PET	12	25.6	15	12	70.4	13
27	Grady	2000	Perception	≠	PET	10	25	26	10	66	34
28	Grady	2006	Memory: Encoding & Retrieval	=	fMRI	12	23.2	16	16	74.4	16
29	Grady	2008	Executive/Working Memory	≠	fMRI	16	26.1	5	18	65.8	8
30	Grossman	2002	Executive/Working Memory	=	fMRI	13	22.6	8	11	63.5	9
31	Gunning-Dixon	2003	Perception/Emotion	≠	fMRI	8	25.8	13	8	72.3	12
32	Gutchess	2005	Memory: Encoding	=	fMRI	14	21	26	13	70	32
33	Haut	2005	Executive/Working Memory	=	PET	8	23.3	6	8	67.3	5
34	Holtzer	2009	Executive/Working Memory	≠	fMRI	25	19–34	12	25	65–84	17
35	Hubert	2009	Executive/Working Memory	≠	PET	12	22.4	1	12	65	4
36	Iidaka	2002	Perception/Emotion	=	fMRI	12	25.1	7	12	65.2	4
37	Iidaka	2001	Memory: Encoding	≠	fMRI	7	25.7	2	7	66.2	2
38	Johnson	2004	Executive	=	fMRI	6	19.6	7	6	65.3	6
39	Johnson	2001	Language/Semantic Memory	=	fMRI	9	31.9	6	9	72.7	5
40	Jonides	2000	Executive/Working Memory	≠	PET	12	19–30	1	12	61–72	0
41	Kareken	2003	Perception	=	fMRI	5	27.8	16	6	71	19
42	Kensinger	2008	Memory: Encoding	≠	fMRI	17	21.6	7	17	73.3	14
43	Kukolja	2009	Memory: Encoding	≠	fMRI	18	24	3	17	60.3	3
44	Lee	2008	Decision Making	≠	fMRI	12	29.9	4	9	65.2	7
45	Lee	2006	Executive	≠	fMRI	12	29.8	0	9	65.2	12
46	Leinsinger	2007	Perception	=	fMRI	15	28	38	19	71	32
47	Levine	2000	Perception	=	PET	12	27.3	17	14	62.1	7
48	Madden	2002a	Language/Semantic Memory	=	PET	12	23.6	8	12	65	6
49	Madden	1996	Memory: Encoding	=	PET	10	22.5	2	10	68.2	0
50	Madden	1999	Memory: Encoding	=	PET	12	23.2	0	12	71	7
51	Madden	2002b	Perception/Attention	≠	PET	12	23	14	12	66.5	19
52	Maguire	2003	Memory: Retrieval	=	fMRI	12	32.4	11	12	74.8	13
53	Milham	2002	Executive	≠	fMRI	12	23	36	10	68	24
54	Miller	2008	Memory: Encoding	≠	fMRI	17	23.9	19	17	74.9	16
55	Mitchell	2009	Self-relevant processes	≠	fMRI	21	21.7	1	21	69	2
56	Moffat	2006	Memory: Encoding	≠	fMRI	30	27.1	25	21	68.4	21
57	Morcom	2003	Memory: Encoding	=	fMRI	14	21	43	14	68	48
58	Nielson	2006	Memory: Retrieval	≠	fMRI	15	23.6	2	15	70.4	6
59	Nielson	2002	Executive	=	fMRI	10	25.5	8	8	75.1	11
60	Nielson	2004	Executive	=	fMRI	14	29.7	10	14	71.1	24
61	Otsuka	2006	Executive/Working Memory	≠	fMRI	10	24.5	6	10	68.8	6
62a	Paxton	2008b	Executive/Working Memory	=	fMRI	16	21.6	73	16	72.4	55
62b	Paxton	2008a	Executive/Working Memory	≠	fMRI	21	22.8	38	20	73	50
63	Rajah	2008	Memory: Retrieval	≠	fMRI	8	25.6	33	8	72.7	49
64	Raye	2008	Executive	=	fMRI	15	23	5	14	68	6
65a	Reuter-Lorenz	2000a	Executive/Working Memory	≠	PET	8	23.3	9	16	69.9	9
65b	Reuter-Lorenz	2000b	Executive/Working Memory	=	PET	10	21.2	6	10	67.4	10
66	Ricciardi	2009	Executive/Working Memory	=	PET	10	26.2	6	10	68.4	4
67	Rypma	2001	Executive/Working Memory	=	fMRI	6	25.3	41	6	68.6	46
68	Schacter	1996	Memory: Retrieval	≠	PET	8	20.5	3	8	67.9	4
69	Smith	2001	Executive/Working Memory	=	PET	12	22.9	14	12	66.6	11
70	Sperling	2003	Memory: Encoding	≠	fMRI	10	24.9	16	10	74.1	23
71	St Jacques	2009	Memory: Encoding	≠	fMRI	15	24.8	23	15	70.2	8
72	Stebbins	2002	Memory: Encoding	=	fMRI	15	25.3	14	15	76.5	5
73	Stevens	2008	Memory: Encoding	=	fMRI	12	26.2	0	12	70.2	4
74	Tessitore	2005	Perception/Emotion	=	fMRI	12	25	15	15	67	15
75	van der Veen	2006	Memory: Encoding	≠	fMRI	12	25.1	5	12	64.7	8
76	Wierenga	2008	Language/Semantic Memory	=	fMRI	20	25.1	3	20	74.9	7
77	Zysset	2007	Executive	=	fMRI	23	26.6	23	24	57.1	30

Table 1b

Task related details of included studies.

Exp.	Experiment	Task	Comparison task/BASELINE
1	Learning word pairs	Encoding word pairs under full attention	Retrieving paired word
2	Virtual Morris Water Maze (Arena)	Spatial navigation	Rest
3	Likability judgments of words	Stem completion from learned material	Previously unseen stem completion
4	Semantic word judgments	New words	Repeated words
5	Learning verbal material	Item retrieval	Temporal-order retrieval
6	Verbal delayed-response	Intra-trial memory	Baseline
7	Encoding & Retrieval of word pairs	Encoding word-pairs	Recognition & recall of word pairs
8	San Diego Odor Identification Test	Smelling odorant	Smelling deionized water
9	Object processing	Novel object	Old object
10	Flanker Task	Incongruent	Congruent
11	Serial reaction time task	Fixed	Random
12	Pleasant/unpleasant noun judgements	Subsequently remembered nouns	Alternating button press
13	Word recognition & Size comparisons	Conjunction of hits	Baseline
14	Deese-Roediger-McDermott variant	Accurate subsequent memory	Baseline
15	N-back of faces	High confidence hits	Subsequently forgotten items
16	Task-switching	Cued switching	Fixation
17	Slot machine	Anticipation of reward	Anticipation of no reward
18	Retrieval of semantically judged drawings	Correctly remembered items	Correctly rejected new items
19	Retrieval of semantically judged pictures	Successful source recollection	Correctly rejected new items
20	Wisconsin Card Sorting Task	Card sorting to criteria	Immediate matching
21	Auditory presentation of verbal material	Word recognition from full attention	Auditory control
22	Visual working memory for faces	Delayed face matching	Rest
23	Shallow & deep encoding	Old-new judgment of faces	Passive viewing of scrambled faces
24a	Facial processing	Face matching	Alternating button press
24b	Facial processing	Face matching	Alternating button press
25	Match-to-sample with faces	Delayed face matching	Alternating button press
26	Viewing images and words	Old-new judgment	Silent naming
27	Facial processing	Nondegraded face matching	Alternating button press
28	Viewing images and words	Perceptual & Semantic; Old-New judgments	Fixation
29	Auditory 1-back for category and location	Sound category repeat	Sound location repeat
30	Sentence comprehension task	Short antecedent noun-gap linkage (Subject)	Pseudofont target detection
31	Facial processing	Emotion discrimination	Rest
32	Viewing photographs of outdoor scenes	Subsequently remembered photographs	Subsequently forgotten photographs
33	Number-letter sequencing task (WAIS)	Number-Letter Sequencing	Number-Letter Span
34	Delayed item recognition task	Load-dependent processing for retention delay	Baseline
35	Tower of Toronto task	Planning and puzzle solving	Sequential movement of discs
36	Facial processing	Gender judgment to negative faces	Size discrimination of rectangles
37	Paired-picture encoding task	Concrete-related paired encoding	Visual noise control
38	Refreshing information	Refreshing previously seen word	Seeing previously seen word
39	Semantic Memory Decision Making task	Category-exemplar matching	Phonological control
40	Verbal Working Memory & Recognition	High recency	Low recency
41	Olfaction	Odor sensation	Sniffing
42	Semantic decision task for object drawings	Subsequently recognized items	Correctly rejected new items
43	Spatial Source Memory Task	Correct spatial context encoding	False spatial context encoding
44	Risky-gains task	Risky decisions	Safe decisions
45	Arrow task (Simon task variant)	Response incompatible	Response compatible
46	Location processing	Location matching	Button press for abstract image
47	Distinguishing achromatic textures	Viewing even textures	Viewing random textures
48	Lexical decision task (semantic)	Word/nonword Discrimination	Letter identification
49	Word identification task	Letter encoding	Fixation (with manual response)
50	Learning verbal material	Living/Non-living word judgment	Letter case identification
51	Visual Search	Mixed featured target detection with distractors	Target detection with single feature
52	Autobiographical memory	Autobiographical event recollection	Syllable counting
53	Stroop	Congruent & incongruent by color	Neutral
54	Face-name associative encoding paradigm	Subsequently remembered face-name pairs	Subsequently forgotten pairs
55	Focused visualization	Personal hopes and duties	Impersonal semantic concepts
56	Allocentric spatial navigation	Learning spatial layout of virtual environment	Following cues
57	Animacy decisions about words	Correct remembered	Incorrect remembered
58	Recognition of famous faces	Enduring Famous Faces	Non-famous foils
59	Go No-go	Response inhibition	Baseline
60	Go No-go	Response inhibition	Baseline
61	Reading Span Test	Reading and Remembering target words	Cued button press
62a	AX Continuous performance task	Goal maintenance from contextual cues	Fixation
62b	AX Continuous performance task	Goal maintenance from contextual cues	Fixation
63	Recognition and recency judgments	Viewing word pairs	Reverse alphabetizing
64	Refreshing information	Selectively refreshing word	Reading word
65a	Verbal working memory	Delayed letter matching	Immediate matching
65b	Spatial working memory	Delayed location matching	Immediate matching
66	Working memory for faces	Encoding, maintenance and recognition of faces	Sensimotor control
67	Item-recognition task	Six-letter load	One-letter load
68	Stem completion	Shallow encoding (low recall)	Deep encoding (high recall)
69	Operation Span dual-task	Math task (Equation verification)	Arbitrary button press
70	Face-name association encoding task	Novel face-name pairs	Fixation
71	Viewing emotional & neutral photographs	Subsequently remembered photographs	Subsequently forgotten photographs
72	Judgments about words	Semantic encoding	Perceptual encoding
73	Viewing pictures of faces	Subsequently remembered faces	Subsequently forgotten faces
74	Facial processing	Facial expression matching	Geometric shape matching
75	Verbal episodic memory task	Correctly Recognized	Correctly Rejected
76	Object naming	Overt picture naming	Passive abstract picture viewing
77	Stroop	Incongruent	Neutral

retrieval and executive function. Eight studies did not fall into these broad domains (see Tables 1a and 1b).

The original studies contributing these foci are presented in Tables 1a and 1b. Prior to the analysis, coordinates reported in MNI space were converted to Talairach coordinates using the Lancaster transformation (Lancaster et al., 2007). In the approach taken by ALE, localization probability distributions for the foci are modeled at the center of 3D Gaussian functions, where the Gaussian distributions are summed across the experiments to generate a map of inter-study consistencies that estimate the likelihood of activation for each focus (the ALE statistic). The foci were modeled using a full-width half-maximum value 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 to those being tested. In order to determine reliable differences in brain activity between young and old adults, we tested the null hypothesis that the two sets of foci were randomly distributed and the observed difference between them was zero. For all analyses, the false discovery rate method was employed to correct for multiple comparisons at $p < .01$ and subjected to a cluster threshold of 100 mm^3 (Laird, Fox et al., 2005). For greater detail of the ALE method, see Laird, Fox et al. (2005) and Turkeltaub et al. (2002); for a discussion of meta-analytic approaches to neuroimaging data, see Wager et al. (2007).

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. In an auxiliary analysis not presented here, GingerALE 2.0 was used to calculate within group maps for all of the contrasts. We found that all clusters that were significant in the difference analyses (Young vs. Old) were also significant clusters within each group in the random effects analysis. All analyses reported in this paper were conducted with GingerALE 1.1.

Anatomical labels were applied to the clusters using the Talairach Daemon and visual inspection of the ALE maps that were imported into AFNI (Cox, 1996). Coordinates are reported in Talairach space (Talairach and Tournoux, 1988). In order to rule out the possibility that one cognitive domain was biasing the age-related differences when comparing old and young across all studies (B), equal (C) and unequal (D) task performance, we determined which studies were contributing foci to age-related clusters. Unless otherwise stated, clusters from the ALE difference analyses (B–D) comprised peak foci in studies from all four cognitive domains. In some cases, significant clusters in the combined analysis may be driven by one of the age groups. All ALE maps were transformed from a volume image to an average multifiducial surface map using Caret software (Van Essen, 2005) for presentation. Multifiducial surface mapping in Caret maps the volume to 12 individuals in the atlas and then creates an average of these maps thereby reducing bias due to individual variability. Subcortical structures are not displayed.

3. Results

The age of young participants averaged 24.81 years ($SD = 2.8$) while that of old participants was 68.81 years ($SD = 3.9$) across 77 studies. These means do not include three studies that only reported a range of ages (see Tables 1a and 1b). Sample sizes did not differ between age groups ($t < 1$). There were no significant main effects of age group or performance on the number of foci contributed to the analysis, nor was the group by performance interaction significant ($F_s < 1$). Therefore, differences in the number and extent of activation likelihood clusters between age

groups cannot be attributed to the number of foci included in the analysis. There was an effect of imaging modality: fMRI studies had larger sample sizes (fMRI mean $N = 14.54$, $SD = 6.1$; PET mean $N = 11.70$, $SD = 2.8$; Welch's $t = 3.65$, $p < .001$) and reported more activation peaks (fMRI foci mean = 15.59, $SD = 14.2$; PET foci mean = 9.50, $SD = 6.9$; Welch's $t = 4.02$, $p < .001$).

3.1. Combined ALE results

Fig. 1A shows the regions where the old and young groups combined had reliable activity across studies, and Table 2 lists the coordinates of the maxima from these regions. As expected, most of the active regions were part of the TPN, and included bilateral DLPFC, vOC, SMA, IPS, FEF and alfO. Bilateral rostrolateral prefrontal cortex (RLPFC) was also observed, a region associated with cognitive control (Koechlin et al., 1999; Vincent et al., 2008). Additional regions include visual cortex (beyond vOC), superior temporal gyrus, insula, thalamus and putamen. Some default network regions were also found, including the PCC, left angular gyrus and the medial temporal lobes (MTL) bilaterally. Activation of PCC and medial temporal areas could be due to inclusion of memory tasks that engage these areas.

3.2. Young and old ALE difference results

3.2.1. Differences across all studies

Overall, ALE differences were observed between young and old adults primarily in frontal regions corresponding to the TPN (Table 3 and Fig. 1B). Young adults demonstrated reliably greater activation in right VLPFC and left vOC from the TPN, as well as a region in the right hippocampus. Old adults had more activity in several TPN regions including the right DLPFC and PCS. Dorsal to these clusters, greater activity was also seen in old adults near the superior PCS, anterior to the FEF (note: studies in the domain of perception did not contribute foci to this cluster). Additionally, old adults engaged the left DLPFC and left RLPFC. All of these regions with age differences overlapped with clusters identified as common to both age groups (see Table 3), and all but the hippocampus were consistent with the TPN.

3.3. Age differences when performance was equivalent

Given the importance of examining brain activity in the context of performance, additional analyses were carried out after dividing the studies based on whether or not performance was equivalent in young and old adults. In those studies that reported equivalent performance, differences emerged only in three regions, two of which were in left lateral prefrontal cortex (Fig. 1C and Table 3). Young adults had more activity in left VLPFC, whereas old adults had greater activity in the DLPFC. Both of these regions were consistent with the TPN (Table 2) and overlapped with clusters with reliable activation across both age groups shown in Table 2 (see Fig. 1A). Additionally, there was more reliable recruitment of the left posterior insular cortex in old adults (note: studies in the domain of memory retrieval did not contribute foci to this cluster).

3.4. Differences when performance was unequal

When those studies reporting unequal performance between young and old adults were examined, significant and reliable differences emerged in a number of brain areas. Young adults reliably activated occipital cortex bilaterally, consistent with the TPN (Fig. 1D and Table 3). An additional region in the left MTL also was more active in young adults, but this region did not overlap with any TPN region. In contrast, old adults reliably engaged right DLPFC, and PCS (note: studies from the domain of perception did

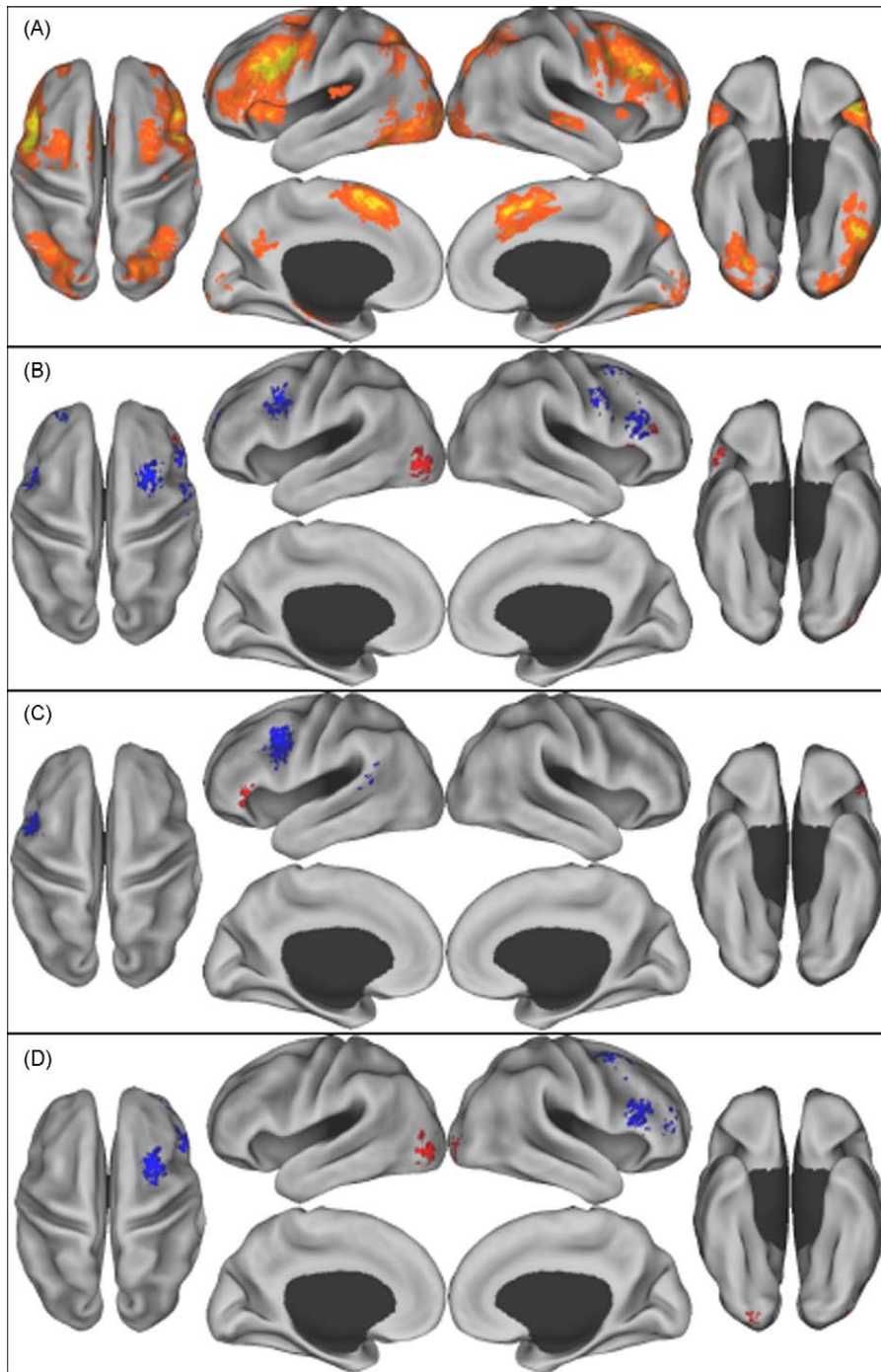


Fig. 1. Reliable patterns of brain activity across studies. A: Activation likelihood clusters across all studies and age groups. B: Age differences from all studies. C: Age differences from those studies where old and young adults had equivalent performance. D: Age differences from those studies where old adults had poorer performance relative to young adults. Red = young adults > old adults, Blue = old adults > young adults. Activation likelihood clusters ($FDR p < .01$) are shown on an inflated surface map in Caret (Van Essen, 2005). Some clusters may not appear contiguous due to mapping clusters on the surface maps; for example, this can occur when neighboring gyri, but not the intermediary sulcus, were included in a statistically reliable cluster in the original image volume.

not contribute to this cluster), consistent with the TPN. Old adults who performed more poorly also activated right RLPFC and the left thalamus (Fig. 1D and Table 3).

3.5. Domain specific results

Perception, memory encoding, memory retrieval and executive function independently demonstrated a pattern of activity consistent with the TPN, including reliable clusters in lateral prefrontal

regions, *alfO*, SMA, and *vOC* (Figs. 2–5). These findings are consistent with a previous large-scale meta-analysis of domain specific cognition (Cabeza and Nyberg, 2000). Notable domain specific clusters were also apparent and the results are discussed in turn.

3.6. Perception

Perceptual studies, most of which were in the visual modality, showed extensive visual cortical activation, as would be expected

Table 2
Areas of activation common to both young and old adults (all studies).

Lat	Region	BA	x	y	z	Vol (mm ³)
Task positive regions						
L	DLPFC	9,46	−42	14	22	13904
L	VLPFC	47	−51	9	2	176
R	DLPFC	9,46	43	17	28	6760
R	DLPFC	9	25	5	26	280
R	RLPFC	10	29	46	11	1472
L	RLPFC	10	−23	49	16	592
L	vOC	19,18	−36	−71	−8	6608
R	vOC	19,18	31	−84	−3	896
R	vOC	19	33	−56	−18	936
R	vOC	19	29	−67	−4	776
B	SMA	6,32	−1	13	46	6112
R	IPS	7	28	−62	40	3504
L	IPS	7	−27	−63	34	3416
R	FEF	6	27	6	48	880
R	FEF	6	29	−9	46	152
L	FEF	6	−26	2	52	784
R	alFO	13	41	13	5	280
Other regions						
L	Fusiform gyrus	20	−39	−31	−15	200
R	Lingual gyrus	17	13	−90	−2	176
B	Lingual gyrus	18	3	−86	0	120
R	STG	22	52	−16	−1	528
L	Thalamus		−13	−18	6	696
R	Thalamus		13	−11	10	272
R	Thalamus		7	−24	−2	144
L	Putamen		−22	4	−1	304
L	Putamen		−22	−8	11	216
L	Insula	13	−28	−26	19	152
Default mode regions						
L	PCC	31	−4	−54	25	176
L	Angular gyrus	40	−42	−54	36	408
L	Hippocampus		−23	−12	−12	640
L	PHC	35	−24	−25	−9	280
R	PHC	28	21	−11	−14	240

Abbreviations: Lat, laterality; L, left; R, right; B, bilateral; X, right/left coordinate; Y, anterior/posterior coordinate; Z, inferior/superior coordinate; Vol, volume; alFO, anterior insula/frontal operculum; DLPFC, dorsolateral prefrontal cortex; FEF, frontal eye field; IPS, intra-parietal sulcus; LOS, Lateral occipital sulcus; MFG, Middle frontal gyrus; MOG, middle occipital gyrus; PCC, posterior cingulate cortex; PCS, precentral sulcus; PHC, parahippocampal gyrus; POF, Parietal occipital fissure; RLPFC, rostralateral prefrontal cortex; SMA, supplementary motor area; STG, superior temporal gyrus; VLPFC, ventrolateral prefrontal cortex; vOC, ventral occipital cortex.

(Fig. 2E). Due to the emotional nature of some studies (see Tables 1a and 1b), right amygdala activation was also present (e.g. Breiter et al., 1996). We anticipated age differences in posterior regions, which previous work would suggest should be more active in young adults (Anderson and Grady, 2001; Cabeza et al., 2004; Davis et al., 2008; Grady et al., 1994). Consistent with this prediction, young adults had more activity during perceptual tasks than old adults in a number of occipital regions, including bilateral vOC and extended visual cortex (Fig. 2F and Table 4). Young adults also had greater activity in the right amygdala while old adults showed more activation in DLPFC, consistent with a recent observation of age-related changes in the perception of emotional stimuli (Roalf, Pruis, Stevens & Janowsky, in press). Older adults also showed more activation in left alFO.

3.7. Memory encoding

Encoding information, while not dissimilar to perception, involves the verified retention of perceived information. Additionally, comparison tasks are typically matched for perceptual input. As a result, posterior regions differ in their pattern of activity. Visual cortical areas active for encoding tended to be engaged further upstream in ventral temporal cortex, relative to those active for perception (see Fig. 3G). Additionally, mnemonic areas, such as retrosplenial cortex and the medial temporal lobes were engaged. Age-related differences were modest in this modality. Young adults had more activity in right middle frontal

gyrus and medial temporal lobes, as well as right putamen. In contrast, old adults had greater activity in right PCS (Fig. 3H and Table 4).

3.8. Memory retrieval

The pattern of activity seen for retrieval across age groups was largely consistent with recent ALE meta-analyses of episodic memory retrieval in young adults (McDermott et al., 2009; Spaniol et al., 2009), comprising lateral and medial prefrontal regions, alFO, PCC, medial temporal lobes and occipital cortex (Fig. 4I). Notably absent in the present analysis is engagement of inferior parietal regions, which may be accounted for by the relatively small number of studies included ($n = 11$). Young adults engaged cortex within the posterior occipital fissure to a greater degree during memory retrieval, whereas old adults engaged the right RLPFC, left preSMA and middle temporal gyrus more than the young adults (Fig. 4J and Table 4).

3.9. Executive function

Tasks of executive function and working memory engaged a reliable network of lateral parietal and frontal regions in both age groups (Fig. 5K). As would be expected from the predominance of frontal activity during tests of executive function, such as working memory and inhibitory tasks (e.g., Braver et al., 1997; D'Esposito et al., 1995; Jonides et al., 1998), the differences between young

Table 3
Age differences between young and old adults across all studies and by performance.

Lat	Region	TPN	BA	x	y	z	Vol (mm ³)
All studies							
Young > Old							
L	vOC	x	19	-41	-77	-1	360
L	Hippocampus		34	-22	-8	-11	208
R	VLPFC	x	13	40	27	14	144
Old > Young							
R	Superior PCS/FEF	x	6	26	10	47	480
L	DLPFC	x	9	-41	8	29	392
R	DLPFC	x	46	45	24	23	304
R	PCS/DLPFC	x	6	49	2	32	160
L	RLPFC	x	10	-26	44	19	128
Equal performance							
Young > Old							
L	VLPFC	x	47	-47	26	1	136
Old > Young							
L	DLPFC	x	9	-44	7	31	712
L	Posterior insula		13	-50	-37	16	152
Unequal performance							
Young > Old							
L	Hippocampus			-21	-7	-11	296
L	vOC	x	19	-40	-80	0	256
R	MOG	x	18	26	-83	-1	224
Old > Young							
R	Superior PCS/FEF	x	6	26	8	47	632
R	DLPFC	x	46	46	25	21	384
L	Thalamus			-11	-17	12	136
R	RLPFC	x	10	38	44	13	104

Note: TPN = Task positive network. Regions consistent with the TPN are indicated with an "x".

and old adults were seen primarily in frontal regions (Fig. 5L and Table 4). Young adults had more activity in a region of right VLPFC during executive function. Old adults had more activation in bilateral DLPFC, right MFG, left SMA and left RLPFC.

4. Discussion

In this quantitative meta-analysis, we demonstrated reliable age differences in brain activity across multiple cognitive tasks. We found that the TPN, encompassing the DLPFC, RLPFC, alfO, IPS, aPL, FEF, SMA, vOC and PCS, was robustly active across all studies when both young and old groups were combined, consistent with the idea of task-general activation of this network. In addition, many of the areas with age differences were part of the TPN. Some of these TPN regions, such as left DLPFC were more likely to differentiate young and old adults when these two groups performed equally well. In contrast, when young adults outperformed old adults, right lateral prefrontal and occipital regions, both part of the TPN, were more likely to differentiate the groups. For the purposes of discussing these findings, we will first address age differences in anterior regions of the brain and then consider posterior regions of cortex.

4.1. Anterior cortex

Across all studies young adults had more activity in right VLPFC, whereas old adults had more activity mainly in dorsal frontal regions of the TPN, as well as in RLPFC. This extensive over-recruitment of frontal regions in old adults is consistent with the findings of a recent study that also reported more activity in frontal and rostral frontal cortex TPN regions in old adults across multiple cognitive domains (Grady et al., in press). However, the performance level of the old adults relative to the young adults influenced which frontal areas showed an age difference. The most notable influence of performance on the age differences in TPN

Table 4
Age differences between young and old adults by domain.

Lat	Region	TPN	BA	x	y	z	Vol (mm ³)
Perception							
Young > Old							
R	MOG	x	18	29	-80	5	456
L	vOC	x	19	-41	-77	-1	416
R	vOC	x	18,19	33	-68	-6	392
R	Amygdala			25	-3	-12	184
L	POF		31	-23	-63	13	181
L	LOS		19	-18	-62	-9	160
Old > Young							
L	DLPFC	x	46	-41	14	22	912
L	alfO	x	13	-26	20	-3	232
Memory encoding							
Young > Old							
R	MFG		9	41	11	32	168
R	PHC		27	22	-29	-3	128
L	Putamen			-21	2	1	128
Old > Young							
R	PCS/DLPFC	x	9	50	4	29	128
Memory retrieval							
Young > Old							
L	POF		31	-13	-61	21	176
Old > Young							
L	MTG		21	-55	0	-18	232
R	RLPFC	x	10	22	55	5	144
L	preSMA	x	6	-9	26	37	112
Executive functions							
Young > Old							
R	VLPFC	x	47	38	25	16	224
Old > Young							
R	MFG/FEF	x	6	26	9	46	536
R	DLPFC	x	46	46	25	22	488
L	DLPFC	x	9	-46	7	32	344
L	RLPFC	x	10	-26	45	18	240
L	SMA	x	6,32	-5	13	44	160

activity was on the hemisphere that showed an age difference. When performance in the two age groups was equivalent, old adults were more likely to activate left DLPFC and young adults were more likely to activate left VLPFC. These two frontal areas both have been implicated in cognitive control, but may mediate different kinds of control. For example, some have suggested that ventral PFC regions mediate maintenance of information in short term stores (Dove et al., 2006), or represent the salience of such information (Seeley et al., 2007), whereas DLPFC mediates manipulation of information or strategic processes such as monitoring of behavior (D'Esposito et al., 1999; Moscovitch, 1992; Seeley et al., 2007). Our analysis suggests that, for equivalent levels of behavioral output, young adults rely more on control that emphasizes salience or maintenance of information, mediated by left ventral PFC, whereas old adults rely more on strategic control mediated by left dorsal PFC (for a similar conclusion, see Grady et al., 2003). Old adults also had more left DLPFC activity during perceptual and executive function tasks indicating that this strategic control may be utilized primarily for these non-mnemonic cognitive functions.

In contrast, several regions in right lateral prefrontal cortex differentiated young and old adults when their performance was unequal. Two right frontal regions, one in RLPFC (BA 10) and one in DLPFC (BA 46), showed more activity in poorly performing old adults. In addition, RLPFC distinguished the age groups during memory retrieval, where old adults may engage in more top-down strategic retrieval processes. Executive function tasks also showed greater engagement of right DLPFC in old adults, suggesting that this region is not only important for executive function in general

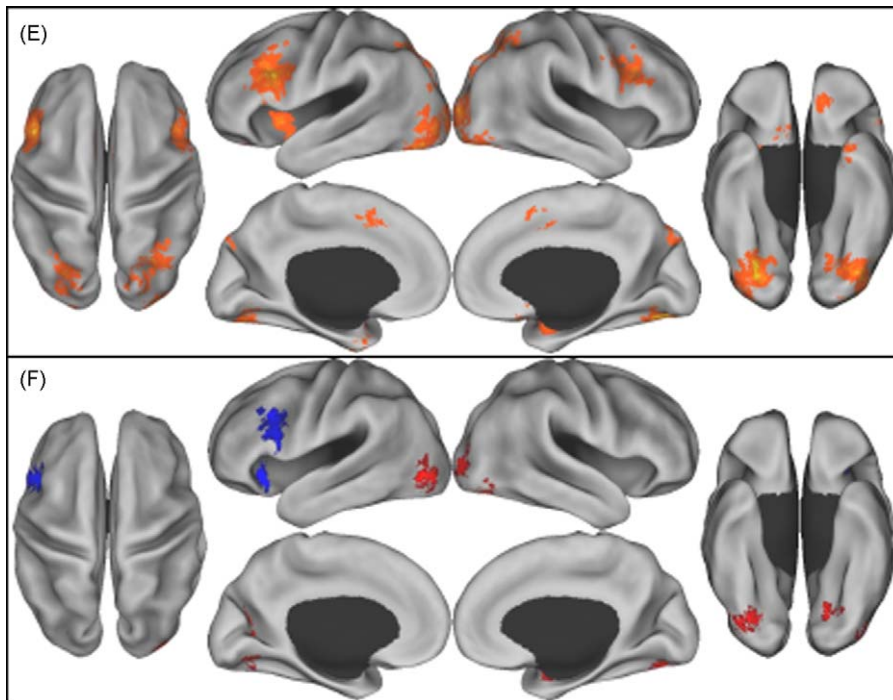


Fig. 2. Perception. E: Combined ALE map. F: Age related differences. Red = young adults > old adults, Blue = old adults > young adults. Activation likelihood clusters (FDR $p < .01$) are shown on an inflated surface map in Caret (Van Essen, 2005).

(e.g., Stuss and Alexander, 2000, 2007) but that use of these regions for executive functions increases with age.

Although our understanding of the roles of these frontal areas in cognitive control is far from complete, the results seen here would suggest that different kinds of control are brought on line in young and old adults when required to perform cognitive tasks. Also, DLPFC activity in old adults is higher at low levels of working

memory demand but then does not increase to the same degree as seen in young adults when demand increases (Mattay et al., 2006). All these results, taken together, suggest that brain activity in young adults has a larger dynamic range than that of old adults; i.e., young adults can perform relatively easy tasks without engaging prefrontal cortex but also show larger increases than old adults when tasks become more difficult. In addition, the

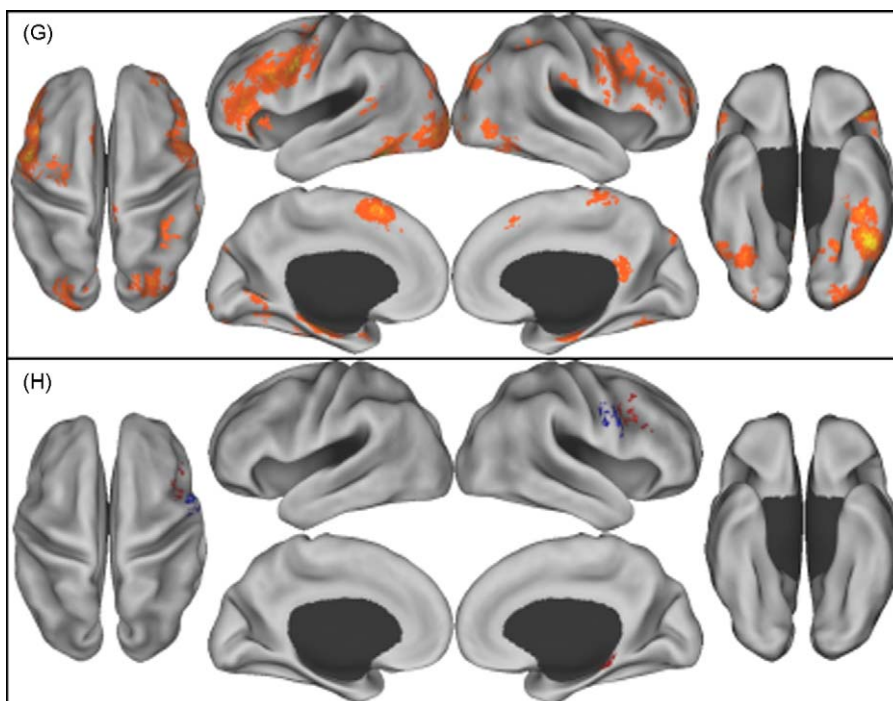


Fig. 3. Memory encoding. G: Combined ALE map. H: Age-related differences. Red = young adults > old adults, Blue = old adults > young adults. Activation likelihood clusters (FDR $p < .01$) are shown on an inflated surface map in Caret (Van Essen, 2005).

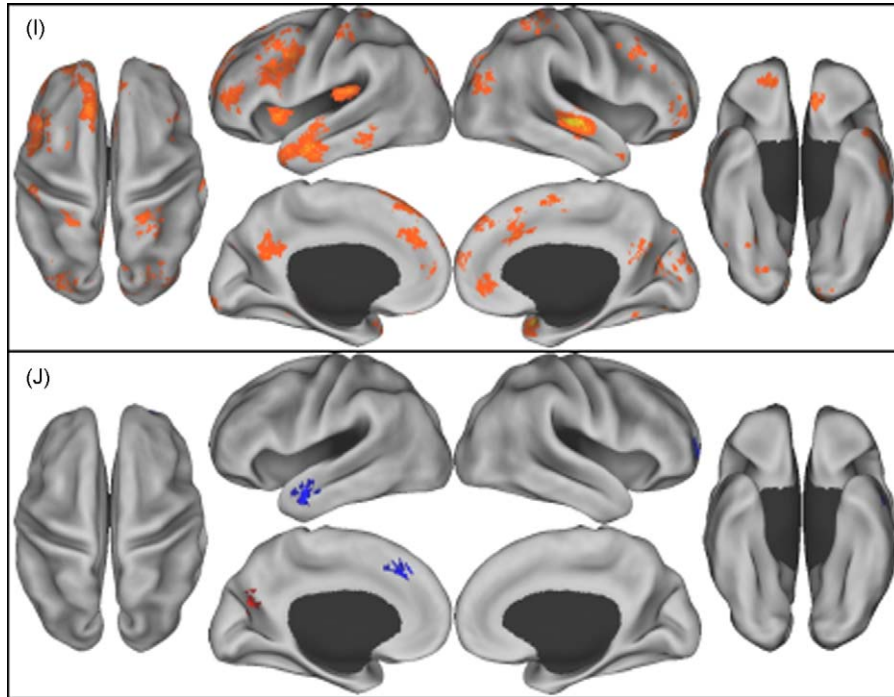


Fig. 4. Memory retrieval. I: Combined ALE map. J: Age-related differences. Red = young adults > old adults, Blue = old adults > young adults. Activation likelihood clusters (FDR $p < .01$) are shown on an inflated surface map in Caret (Van Essen, 2005).

hemispheric difference that we noted, left for better performing old adults and right for poorer performing old adults, is consistent with a recent hypothesis that age-related recruitment of left prefrontal activity will increase in order to compensate but right prefrontal activity is likely to reflect dysfunction of this region (Rajah and D'Esposito, 2005). It is not clear why left prefrontal cortex might be more associated with better performance in old adults, but one possibility is that recruitment of semantic

processes mediated by left prefrontal cortex (Thompson-Schill, 2003; Wagner et al., 2001), and preserved with aging (e.g., Grady et al., 2006; Madden, 1986; Spaniol et al., 2006), may facilitate some aspect of cognitive performance.

Age-related differences were also observed in premotor portions of the TPN, in FEF and SMA/pre-SMA. The SMA has been reported to be more active in old adults during inhibitory tasks (Nielson et al., 2002), but not during motor learning (Daselaar et

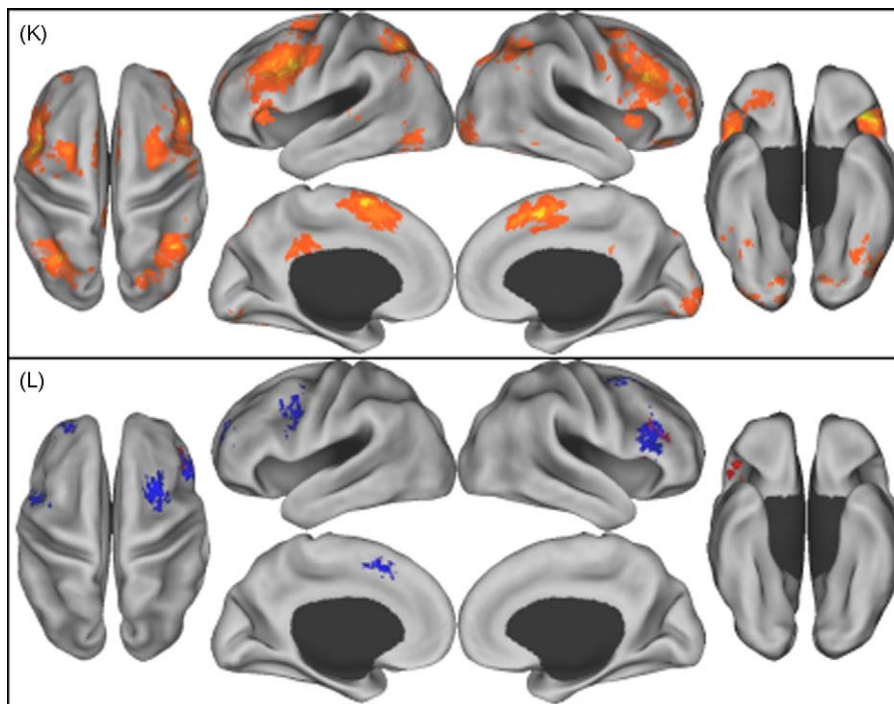


Fig. 5. Executive function. K: Combined ALE map. L: Age-related differences. Red = young adults > old adults, Blue = old adults > young adults. Activation likelihood clusters (FDR $p < .01$) are shown on an inflated surface map in Caret (Van Essen, 2005).

al., 2003); age differences in FEF also have been reported during saccades (Raemaekers et al., 2006). Old adults showed more activity than young adults in these premotor areas when old adults performed more poorly and during executive function and memory retrieval tasks. Given the role of the FEF and SMA in the control of motor responses and eye movements (e.g., Boxer et al., 2006; Everling and Munoz, 2000; McDowell et al., 2008; Petit et al., 1998; Picard and Strick, 1996; Pierrot-Deseilligny, 1994), more activity in these areas suggests that old adults require a greater reliance on cognitive control of motor function than do young adults (Heuninckx et al., 2005), particularly on those tasks that make demands on executive functions or memory that old adults are likely to perform more poorly than young adults. In addition, this extra activity in motor planning areas may reflect the longer response times and slowing of saccades that are commonly found in old adults (e.g., Cerella, 1985; Munoz et al., 1998).

4.2. Posterior cortex

Occipital regions also showed reliable age differences, mostly in favor of young adults. Young adults were more likely to activate occipital regions bilaterally, particularly relative to poorly performing old adults. In addition, young adults activated a number of occipital regions more during perceptual tasks in both hemispheres, including TPN regions and other areas not typically considered part of the TPN. This additional engagement of visual cortex in young relative to old adults is consistent with previous reports (Anderson and Grady, 2004; Davis et al., 2008; Madden et al., 2002, 2004). Indeed, some have suggested that enhanced engagement of frontal resources by old adults may be in response to reduced processing by visual cortices (Davis et al., 2008; Grady et al., 1994). Our meta-analysis result is consistent with this idea and further indicates that this may reflect age differences primarily in the amount or elaboration of perceptual processing rather than mnemonic or executive processing.

Parietal cortices, including IPS and aIPL, were engaged in all analyses that combined young and old adults, yet no age-related changes were seen for these nodes of the TPN. Recent reviews of the cognitive neuroscience literature suggest that parts of lateral parietal lobe are involved in the control of attention and memory functions (Cabeza, 2008; Ciaramelli et al., 2008; Corbetta et al., 2008; Vincent et al., 2008). Superior parietal cortex, in conjunction with frontal regions, may control the activity of visual cortex (Bressler et al., 2008), and inferior regions participate in general attentional functions as well as attention to spatial locations (Alain et al., 2008; Wojciulik and Kanwisher, 1999). Age differences in parietal activity have been reported in old adults in some studies, mostly involving attentional tasks, in which both increases (Grady et al., in press; Madden et al., 2007; Townsend et al., 2006) and decreases (Milham et al., 2002; Rosano et al., 2005) in old adults have been noted, relative to young adults. We did not examine attention specifically here, which may account for our failure to find reliable parietal age differences. On the other hand, the inconsistency in the literature may indicate that age differences in parietal cortex are quite dependent on the specific task demands under investigation. In addition, we also have shown recently that functional connectivity of the aIPL is maintained in old adults (Grady et al., in press). This latter result, along with the current meta-analysis, suggest that the parietal nodes of the TPN are not especially vulnerable to aging, in general, although this certainly does not rule out age differences in any given experiment.

4.3. Neurocognitive aging

Broadly speaking, it is useful to consider whether our results shed light on the different interpretations of age differences in brain

activity that have been considered in the literature. With the meta-analysis reported here, it is not possible to determine individual differences in brain activity and performance, so a strong case for any of the current theories cannot be made. However, our finding that old adults had more TPN activity, particularly in frontal regions, might reflect less efficient or effective use of these regions, i.e. 'less bang for the buck'. That is, old adults may be allocating more neural resources to attentional and cognitive control operations just to maintain behavioral performance at the level seen in the young. On the other hand, we did find evidence that use of different subsets of frontal TPN regions were associated with different behavioral outcomes in the old adults. This might indicate that some regions, particularly left DLPFC, are more likely to be compensatory than others, as suggested above.

Furthermore, reliable patterns of activation across tasks suggest that the TPN is a useful construct, both in general terms and for understanding cognitive aging specifically. However, results from resting-state functional connectivity analysis of MRI data, which may reflect underlying structural neuroanatomical networks (Margulies et al., 2009; Van Dijk et al., 2010), suggest that the TPN can be broken down into sub-components. For example, dissociations may exist between areas of the TPN participating in visuospatial attention and cognitive control (Vincent et al., 2008). Future work will be required to delineate fully the function and connectivity of brain networks related to cognition and age-related changes in the functional neuroanatomy of these networks.

Outside of the TPN, domain specific age differences also were observed, indicating that one age group or the other may uniquely activate domain-specific processes. This result would be consistent with the idea of 'neural compensation' suggested by Stern (2002, 2009), in which old adults use different brain regions than those used by young adults, because the original network may not be functioning optimally. This type of compensation may or may not be associated with performance equivalent to that seen in young adults, but might nevertheless help to support behavior. Unfortunately, it is proving difficult to disentangle these different alternatives (Craik, 2006; Grady, 2008), and our results do not unequivocally support one interpretation over the others. However, given the clear differences in activation that characterized better and worse performing old adults, these results can be used as a starting point for attempting to clarify the roles of these network subsets in supporting cognitive function in old adults.

In conclusion, we found that old and young adults showed activation of a distributed network of regions, the TPN, across a variety of cognitive domains. We confirmed previous reports that old adults have more activity in frontal regions, but young adults recruit visual cortices more than do old adults. We extended this work to show: (1) the performance by old adults on the tasks reliably influenced the laterality of frontal age differences—left prefrontal cortex activity was greater in old adults who performed well on the tasks and right prefrontal cortex activity was greater in old adults who performed less well; (2) frontal over-recruitment in old adults was seen across cognitive domains, but was most extensive in executive function tasks; (3) age differences in occipital cortex occurred primarily when there were age differences in performance and were driven largely by perceptual functions; (4) other nodes of the TPN, such as premotor regions, also showed age differences that were largely domain-specific; and (5) the parietal lobes showed no reliable age differences, suggesting that these TPN nodes are not generally vulnerable to the effects of age. These results taken together suggest that old adults may recruit the TPN differently depending on factors yet to be identified, and that this differential recruitment has an impact on their cognitive functioning.

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Appendix A. Meta-analysis studies

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