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Review

Age differences in the neural correlates of novelty processing: The effects of item-relatedness

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ARTICLE INFO

Article history:
Accepted 5 August 2014
Available online 19 August 2014

Keywords:
Aging
Episodic memory
False memory
fMRI
Novelty detection
Medial temporal lobe

ABSTRACT

Past research finds that age-related increases in false recognitions are a key contributor to age-related memory decline, suggesting that older adults have difficulty in correctly distinguishing between new and old information, particularly when new items at retrieval are semantically or perceptually related to items from encoding. However, little work has examined the neural mechanisms older adults engage to avoid false recognitions and successfully identify information as novel. In the present study, young and older adults were scanned during a retrieval task in which new items were exemplars from studied categories (related lures) or unstudied categories (unrelated lures) in order to detect age-related differences in the neural correlates of related and unrelated novelty processing. Results showed that, unlike young adults, older adults did not differentially recruit regions such as the anterior cingulate and bilateral middle/inferior temporal gyrus to capitalize on the salient categorical differences in unrelated items. Likewise, older adults did not differentially recruit regions of early visual cortex or anterior hippocampus, suggesting that older adults have difficulty using item-specific details to make successful related novelty decisions. Instead, older adults recruited bilateral ventrolateral prefrontal cortex differentially for successful novelty processing and particularly for related novelty processing. Overall, results suggest that age deficits in novelty processing may arise because older adults process related and unrelated lures similarly and do not capitalize on categorical or item-specific properties of novel items. Similar to aging patterns in memory retrieval, results also showed that older adults have the strongest novelty success activity in lateral PFC regions associated with control and monitoring processes.

This article is part of a Special Issue entitled SI: Memory & Aging.

Contents

1. Introduction . . . 3
2. Results . . . 6
   2.1. Behavioral results . . . 6
   2.2. Imaging results . . . 6

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http://dx.doi.org/10.1016/j.brainres.2014.08.006
0006-8993/

2.2.1. Common novelty success activity in older adults . . . 6
2.2.2. Differential novelty activity across age groups . . . 6
3. Discussion . . . 7
3.1. Common novelty success in older adults . . . 8
3.2. Age differences in novelty processing . . . 9
3.2.1. Age differences in categorical processing . . . 9
3.2.2. Age differences in item-specific processing . . . 10
3.2.3. Age differences in PFC mediated novelty success . . . 10
4. Conclusion . . . 11
5. Experimental procedures . . . 11
5.1. Participants . . . 11
5.2. Stimuli . . . 11
5.3. Procedure . . . 11
5.4. Image acquisition . . . 12
5.5. Image processing . . . 12
5.6. Behavioral analyses . . . 12
5.7. fMRI analyses . . . 12
Acknowledgment . . . 13
References . . . 13

1. Introduction

It is well documented that older adults have more difficulty remembering information than young adults (for reviews see Craik (1994), Light (1991) and Spencer and Raz (1995)) and that this memory deficit is often reflected in age differences in neural functioning during both encoding and retrieval (for reviews see Dennis and Cabeza (2008) and Rajah and D'Esposito (2005)). With regard to retrieval, aging research has typically focused on age-related differences in the neural basis of true memories. However, recent research in the domain of false memory has suggested that older adults also have difficulty in correctly rejecting lures at retrieval (e.g., Koutstaal and Schacter (1997) and McCabe et al. (2009)) and that these behavioral differences are associated with significant age differences in neural recruitment associated with false recognitions (Dennis et al., 2008, 2014; Duarte et al., 2010; Giovanello et al., 2009). Despite the contribution of false recognition to age-related memory decline, relatively little research has examined this issue from the perspective of novelty processing and the successful rejection of retrieval lures. Thus, little is known about the cognitive and neural processes that young and older adults engage to avoid false memories and instead successfully identify information as novel. The present study sought to elucidate the neural basis of novelty processing in young and older adults and assess how factors that increase false recognitions (i.e., item relatedness) moderate neural activity associated with rejecting lures at retrieval.

Research has shown that aging is associated with both declines in true memory and increases in false memories (see McCabe et al. (2009) for a meta-analysis). As such, age deficits in detecting novelty represent a significant contributing factor to age-related memory impairment. Further, behavioral evidence indicates that increasing the similarity or relatedness between retrieval lures and studied items leads to increased false memories (and thus deficits in novelty processing) in both young and older adults (Koutstaal and Schacter, 1997; Norman and Schacter, 1997; Tun et al., 1998). For example, studies using false memory paradigms such as the Deese–Roediger–McDermott (DRM) paradigm and perceptual relatedness paradigms have shown that it is relatively easy to correctly reject lures when they share few perceptual or semantic features with previously encountered items (i.e., unrelated lures; Gallo et al., 2001; Meade et al., 2007). However, both young and older adults have difficulty in correctly rejecting lures that share perceptual or semantic features with previously encountered items (i.e., related lures; Koutstaal and Schacter, 1997; Norman and Schacter, 1997; Tun et al., 1998). While both young and older adults falsely recognize related lures more often than unrelated lures, research has also shown that age-related increases in false memories are significantly greater for related lures (Balota et al., 1999; Butler et al., 2004; Koutstaal and Schacter, 1997; Rankin and Kausler, 1979; Tun et al., 1998). Thus, behavioral research has demonstrated that the degree of relatedness between old and new items is a key factor driving age-related increases in false memories and thus age deficits in novelty processing.

However, as noted previously, neuroimaging studies that have investigated age-related deficits in novelty processing during memory retrieval have typically focused on elucidating the neural correlates of novelty errors (i.e., false memories; Dennis et al., 2008, 2014; Duarte et al., 2010; Giovanello et al., 2009) and have not focused on novelty success (i.e., correct rejections). These studies find that older adults' increase in false memories results from an overreliance on gist or familiarity processing in lateral temporal and parahippocampal (PHG) regions for related items presented at retrieval (Dennis et al., 2008, 2014; Giovanello et al., 2009) as well as a reduced reliance on item-specific processing within sensory regions for unrelated items (Duarte et al., 2010). This shift in processing makes new items more likely to be confused with old items, particularly when they share semantic and/or perceptual properties. While these previous studies shed light on the processes underlying novelty errors, it is also critical to identify the neural resources older adults utilize when they make *successful* novelty decisions (i.e., by

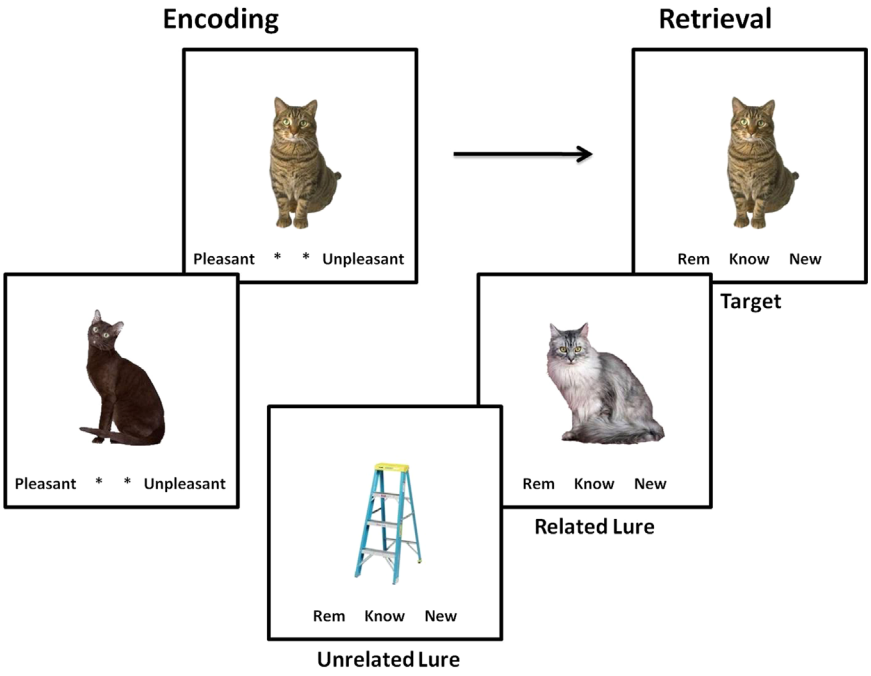

Fig. 1 – Stimuli presentation. During study, participants viewed 8 exemplars from 90 categories (e.g., cats) and made pleasantness ratings for each item. At retrieval, participants saw items from encoding (targets), items from categories presented during encoding (related lures), and items from non-presented categories (unrelated lures). Participants made memory responses using the Remember–Know–New procedure for each item.

contrasting processing supporting correct rejections with that underlying false alarms). Because previous studies of aging have not made such comparisons, the neural resources older adults engage to successfully identify novel information, and thus avoid false memories, remain unclear.

Outside the domain of memory, age differences in novelty processing have been investigated by examining what is known as 'novelty detection'. Novelty detection or stimulus novelty is identified by comparing neural activity associated with the presentation of stimuli that are shown only once (or a small number of times; i.e., novel stimuli) with stimuli that is repeatedly presented (i.e., familiar stimuli; e.g., Bunzeck et al. (2007), Daffner et al. (2006) and Wright et al. (2008)). Research shows that, like young adults (e.g., Daselaar et al. (2006), Kohler et al. (2005) and Kumaran and Maguire (2006)), older adults engage the medial temporal lobe (MTL) memory circuit for novelty processing (Bunzeck et al., 2007) as well as sensory processing in late visual regions (Wright et al., 2008). However, while novelty signals in visual regions have been shown to be reduced in aging (Wright et al., 2008), age differences in MTL novelty processing have not been examined. Thus, it remains unclear whether age deficits in MTL processes associated with age deficits in retrieval success (Dennis et al., 2008; Giovanello and Schacter, 2012; Kukolja et al., 2009) also contribute to age deficits in novelty processing. Further, while novelty detection studies are suggestive of possible neural underpinnings of age-related novelty deficits in memory, they only take into account the true novelty of stimuli, and do not account for memory processes associated with conscious recognition. Therefore, like studies of false memory, studies of novelty detection have not been able to address the neural processes that underlie age differences in *successful* novelty processing.

The present study sought to identify age differences in the neural correlates of successful novelty processing of related and unrelated lures by using fMRI in conjunction with a perceptual false memory paradigm. Related lures at retrieval were drawn from categories of items presented at encoding (e.g., cats, backpacks, clocks) while unrelated lures were drawn from categories not presented at encoding (e.g., ladders; see Fig. 1). The analysis had two main goals. As a first goal, we sought to evaluate cognitive and neural processes older adults engage for novelty success, regardless of the relatedness between old and new items. To do so we assessed the spatial overlap between patterns of neural activity for related and unrelated correct rejections as compared to false recognitions. We predicted that older adults would show novelty success activity in a number of regions typically associated with successful retrieval, including regions of visual and prefrontal cortices.

As a second goal, we sought to evaluate the neural correlates mediating age deficits in novelty processing. To do so, we examined brain regions that young and older adults modulated differently across three types of novelty processing: unrelated correct rejections, related correct rejections, and false recognitions. This analysis allowed us to simultaneously evaluate the effects of age, type of novel stimulus, and novelty success in mediating the neural correlates of novelty processing. Regarding responses to unrelated lures and consistent with previous studies of novelty processing (e.g., Fabiani and Friedman (1995)), we predicted that older adults would not exploit categorical features of retrieval lures when making their novelty decisions.

Table 1 – Demographics and behavioral results.

	YA ($n=17$)	OA ($n=22$)
	M(SD)	M(SD)
Age[a]	21.28(1.79)	74.18(5.20)
Education (y)[a]	14.47(1.37)	18.27(2.71)
Cognitive assessment tasks		
MMSE	29.65(0.61)	29.59(0.80)
WAIS-III		
Symbol Search	13.71(3.08)	14.24(2.99)
Digit Symbol Encoding	12.00(2.68)	13.41(3.34)
Symbol Copy[a]	126.50(13.02)	108.76(19.24)
Digit Span	11.94(3.05)	12.59(2.74)
Arithmetic	11.53(2.40)	12.76(3.40)
Letter Number Sequencing[a]	11.12(2.20)	12.65(1.58)
Vocabulary	14.65(3.02)	12.94(2.46)
BDI	3.18(2.74)	3.76(3.56)
Memory Task – retrieval rates		
Targets		
True recollection	0.47(0.10)	0.49(0.19)
True familiarity	0.31(0.11)	0.36(0.18)
Misses	0.19(0.10)	0.12(0.10)
Related lures		
False recollection[a]	0.19(0.11)	0.34(0.15)
False familiarity	0.30(0.14)	0.40(0.18)
Correct rejections[a]	0.49(0.12)	0.23(0.14)
Unrelated lures		
False recollection[a]	0.04(0.05)	0.09(0.08)
False familiarity[a]	0.04(0.03)	0.20(0.15)
Correct rejections[a]	0.90(0.12)	0.70(0.23)

Key: BDI, Beck Depression Inventory; M, mean; MMSE Mini-Mental State Exam; OA, older adults; SD, standard deviation; YA, young adults.
[a] Age differences: $p<0.05$.

Table 2 – Regions showing common novelty success activity in older adults.

Region	BA	H	Coordinates (T&T)[a]			t	mm^3
			x	y	z		
Anterior PFC	10/11	R	33	60	−4	5.41	1646
Medial frontal gyrus	9/8	M	7	33	46	3.30	1372
Superior frontal gyrus	6	L	−15	−10	69	5.48	1207
Mid/Ventrolateral PFC	46/45	R	52	31	15	3.93	3292
Ventrolateral PFC	47/45	R	30	30	−12	6.81	4225
	47/45	L	−26	23	−8	4.46	3128
Caudate	–	R	15	9	9	3.24	1207
Occipitoparietal cortex	19	L	−41	−77	34	4.49	1591
Late visual cortex	19	R	22	−72	−3	4.74	5981
	19	R	45	−81	17	3.65	988
Cerebellum	–	R	30	−47	−17	4.11	2963

Key: BA, Brodmann's area; H, hemisphere; L, left; M, medial; PFC, prefrontal cortex; R, right; t, t-statistic.
[a] Coordinates from Talairach and Tournoux (1988).

As such, we predicted that older adults would not show a novelty success effect in lateral temporal regions associated with gist processing for rejecting unrelated lures. Regarding responses to related lures and consistent with studies showing age-deficits in visual processing during novelty detection (Wright et al., 2008) and MTL processing during retrieval (Dennis et al., 2008; Giovanello and Schacter, 2012; Kukolja et al., 2009), we predicted that older adults would show reduced processing in both regions for related novelty processing. Lastly, we predicted that older adults' successful novelty processing, particularly with regard to related lures, would be driven by neural activity in prefrontal regions that have been associated with age-related compensation in both working and episodic memory, reflecting a shift to a top-down strategy in order to compensate for declining processing in the MTL and visual cortices (Cabeza, 2002; Cappell et al., 2010; Davis et al., 2008).

Table 3 – Regions showing an interaction in the Age × Novelty ANOVA.

Region	BA	H	Coordinates (T&T)[a]			F	mm³
			x	y	z		
Anterior cingulate	25/32/24	M	4	41	−9	9.25	7792
Dorsomedial PFC	8/9/32	M	−4	29	39	7.76	2030
Ventrolateral PFC	47/45	R	33	23	−8	13.19	2963
	47/45	L	−33	19	−8	11.70	4719
Middle/inferior temporal gyrus	21/20	L	−59	−14	−25	10.72	3018
	21/20	R	56	−11	−28	10.47	3183
Anterior hippocampus/PHG	34/28/36	R	22	−4	−29	8.55	1152
	34/28/36	L	−26	−7	−26	7.88	1207
Occipitotemporal cortex	19/37	L	−63	−53	9	7.48	1152
Late visual cortex	19/37	R	45	−60	2	12.68	12,950
	19/37	L	−45	−64	6	11.14	8944
Early visual cortex	17/18	R	22	−86	4	7.41	1152
Cerebellum	–	R	33	−54	−23	6.88	1646

Key: BA, Brodmann's area; F, F-statistic; H, hemisphere; L, left; M, medial; PFC, prefrontal cortex; PHG, parahippocampal gyrus; R, right.
[a] Coordinates from Talairach and Tournoux (1988).

Overall, the present study sought to assess the neural resources older adults recruit to avoid false recognitions and successfully identify novelty, as well as identify age differences in neural recruitment that help explain age-related increases in false recognitions.

2. Results

2.1. Behavioral results

Table 1 (lower portion) reports means and standard deviations for the rates of 'new' responses to targets, related lures, and unrelated lures. The results of the 2 (Age: young, older) × 3 (Memory: miss, RCR, UCR) ANOVA revealed a significant main effect of age [$F(1)=26.09$, $p<0.001$] showing that young adults responded 'new' ($M=0.53$, $SE=0.03$) at a higher rate than older adults ($M=0.36$, $SE=0.02$). There was also a main effect of novelty trial type [$F(2)=294.16$, $p<0.001$] such that unrelated novel items were labeled 'new' ($M=0.81$, $SE=0.03$) more often than related novel items ($M=0.36$, $SE=0.02$) and targets were labeled 'new' less than either trial type ($M=0.16$, $SE=0.02$). There was also a significant Age × Trial Type interaction [$F(2)=6.62$, $p<0.005$]. Post-hoc t-tests revealed that while the difference in miss rates was not different for young and older adults [$t(37)=1.98$, $p<0.05$], young adults had significantly higher related correct rejection rates [$t(37)=6.11$, $p<0.001$] and unrelated correct rejection rates [$t(37)=3.23$, $p<0.005$] than older adults. Thus, young and older adults had relatively similar performance for target items with age differences being driven largely by reduced performance by older adults in identifying retrieval lures compared to young.

2.2. Imaging results

2.2.1. Common novelty success activity in older adults

Table 2 reports brain regions that showed significant novelty success activity for both related and unrelated novel items in older adults. Results revealed activation in prefrontal regions including bilateral ventrolateral PFC as well as activity in late visual cortex (BA 19). A similar analysis in young adults revealed that young adults engage bilateral anterior MTL, bilateral middle temporal gyrus, and right early and late visual regions across related and unrelated novelty success.

2.2.2. Differential novelty activity across age groups

Table 3 reports brain activity that showed an Age × Novelty interaction. Neural responses for the interaction followed three patterns of activity: (1) regions that young adults modulated for unrelated novelty success but older adults did not [including anterior cingulate (ACC), bilateral middle/inferior temporal gyrus], (2) regions that young adults recruited for related novelty success but older adults did not (including bilateral anterior hippocampus/PHG, right early and bilateral late visual cortex) and (3) regions that older adults modulated for both related and unrelated novelty, but young adults recruited only for related items (including bilateral ventrolateral PFC).

Regarding the first pattern of results, post-hoc t-tests on the beta parameters revealed that young adults showed greater ACC activity for unrelated correct rejections compared to both related correct rejections [$t(16)=3.83$, $p<0.005$] and false alarms [$t(16)=4.63$, $p<0.001$] as well as significantly greater activity for related correct rejections compared to false alarms [$t(16)=2.62$, $p<0.05$]. Older adults showed no differences between novelty trial types in the ACC. In bilateral middle/inferior temporal gyrus, young adults showed greater activation for related [right: $t(16)=2.26$, $p<0.05$; left: $t(16)=4.25$, $p<0.005$] and unrelated [right: $t(16)=4.99$, $p<0.001$; left: $t(16)=5.7$, $p<0.001$] correct rejections compared to false alarms, but significantly greater activation for unrelated compared to related correct rejections [right: $t(16)=5.94$, $p<0.001$; left: $t(16)=3.07$, $p<0.01$]. Older adults showed no modulation between trial types in the right middle/inferior temporal gyrus, and showed increased activity for false alarms [$t(16)=2.71$, $p<0.05$] and unrelated correct rejections [$t(16)=3.83$, $p<0.005$] compared to related correct rejections in the left

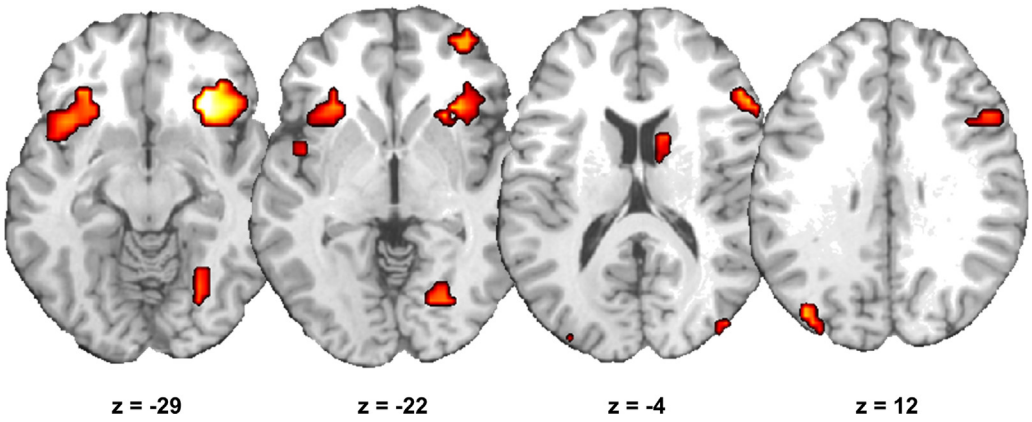

Fig. 2 – Common novelty success activity in older adults. Brain regions showing a novelty success effect (correct rejection > false alarm) in older adults across levels of relatedness include bilateral ventrolateral PFC, right anterior PFC, and late visual regions.

middle/inferior frontal gyrus. In left occipitotemporal cortex, young adults showed greater activity for unrelated correct rejections compared to both related correct rejections [t (16)=3.71, $p<0.005$] and false alarms [t (16)=3.45, $p<0.005$]. Older adults did not show significant differences between novelty trial types in this region.

Regarding the second pattern of age differences, post-hoc t-tests revealed that young adults showed increased activation in bilateral late visual cortex for related correct rejections compared to unrelated correct rejections [right: t (16)=4.64, $p<0.001$; left: t (16)=4.76, $p<0.001$] and false alarms [right: t (16)=3.76, $p<0.005$; left: t (16)=4.35, $p<0.005$]. In right late visual cortex, young adults also showed significantly greater activity for false alarms compared to unrelated correct rejections [t (16)=2.56, $p<0.05$]. Older adults did not show modulation of these visual regions across types of novelty. In right early visual cortex, young adults showed increased activation for related correct rejections compared to unrelated correct rejections [t (16)=3.11, $p<0.01$] and false alarms [t (16)=3.64, $p<0.005$] while older adults showed increased activity for unrelated correct rejections compared to false alarms [t (21)=2.64, $p<0.05$]. In left anterior hippocampus/PHG, analyses revealed that young adults show increased activity for related [t (16)=3.75, $p<0.005$] and unrelated correct rejections [t (16)=3.73, $p<0.005$] as compared to false alarms whereas older adults do not modulate this region across types of novelty. Similarly in right anterior hippocampus/PHG, young adults showed increased activity for related [t (16)=4.23, $p<0.005$] and unrelated correct rejections [t (16)=4.23, $p<0.005$] as compared to false alarms whereas older adults did not modulate this region across types of novelty.

Regarding the final pattern of age differences, post-hoc t-tests revealed that young adults recruited bilateral ventrolateral PFC for related correct rejections [right: t (16)=6.54, $p<0.001$; left: t (16)=5.09, $p<0.001$] and false alarms [right: t (16)=2.3, $p<0.05$; left: t (16)=3.12, $p<0.01$] to a greater degree than unrelated correct rejections. In addition, young adults showed greater right ventrolateral PFC activity for related correct rejections compared to false alarms [t (16)=2.31, $p<0.05$]. Older adults showed greater activity in bilateral ventrolateral PFC for related correct rejections compared to false alarms [right: t (21)=5.53, $p<0.001$; left: t (21)=4.2, $p<0.001$]. In left ventrolateral PFC, older adults also showed greater activity for related compared to unrelated correct rejections [t (21)=2.17, $p<0.05$]. In bilateral ventrolateral PFC, older adults additionally showed greater unrelated correct rejections activity compared to false alarms [right: t (21)=5.59, $p<0.001$; left: t (21)=3.68, $p<0.005$]. In dorsomedial PFC, young adults showed greater activation for related correct rejections [t (16)=3.82, $p<0.005$] and false alarms [t (16)=3.34, $p<0.005$] compared to unrelated correct rejections. Older adults showed greater activity in the dorsomedial PFC for related correct rejections compared to unrelated correct rejections [t (21)=2.35, $p<0.05$] as well as false alarms [t (21)=2.41, $p<0.05$]. In the right cerebellum, young adults showed greater activity for related correct rejections [t (16)=6.88, $p<0.001$] and related false alarms [t (16)=2.32, $p<0.05$] compared to unrelated correct rejections. Older adults showed greater activity for related correct rejections [t (21)=3.07, $p<0.01$] and unrelated correct rejections [t (21)=3.21, $p<0.005$] compared to related false alarms.

3. Discussion

The goal of the present study was to identify the neural mechanisms older adults engage to support novelty success at retrieval and to characterize the neural basis of age-deficits in novelty processing, particularly when new items vary in their relatedness to items presented during encoding. Results revealed that older adults engage prefrontal regions including bilateral ventrolateral PFC and late visual cortex to support successful novelty processing for both related and unrelated items. These findings indicate that older adults utilize general visual properties of objects to make novelty judgments and show increased evaluation and monitoring processing in the PFC for successful responses to novel items compared to false recognitions. Age differences in novelty success took the form of three distinct patterns of neural modulation. The first pattern, found in regions such as the ACC and bilateral middle/inferior temporal gyrus, showed that young adults but not older adults engaged these regions to support

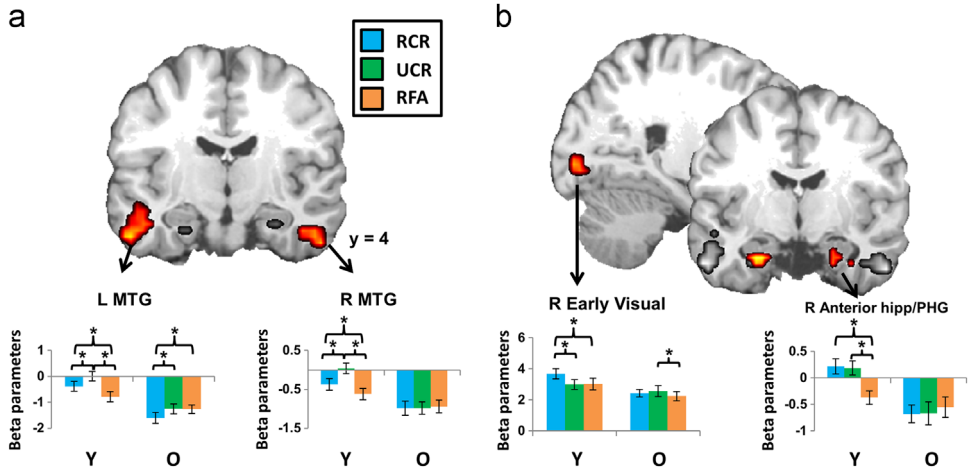

Fig. 3 – Age differences in categorical and item-specific processing. (a) Brain regions that young but not older adults engaged to support successful unrelated novelty processing include bilateral middle temporal gyrus (MTG) extending into inferior temporal gyrus. (b) Brain regions that young but not older adults engaged to support successful related novelty processing include bilateral anterior hippocampus/parahippocampal gyrus and bilateral visual cortex. Activity in gray represents brain regions showing an Age × Novelty interaction that is not consistent with the pattern presented in the current figure. Hipp, hippocampus; L, left; MTG, middle temporal gyrus; O, older adults; PHG, parahippocampal gyrus; R, right; RCR, related correct rejection; RFA, related false alarm; UCR, unrelated correct rejection; Y, young adults.

successful unrelated novelty. The second pattern, found in early and late visual cortex as well as the anterior hippocampus and parahippocampal gyrus, showed that young adults but not older adults engaged these regions to support successful related novelty. The final pattern, found in bilateral ventrolateral PFC and dorsomedial PFC, indicated that both young and older adults utilized the aforementioned PFC regions to support novelty processing, but young did so for related novelty and false alarms while older adults showed novelty success effects for both related and unrelated novelty. The interpretation of each activation pattern is discussed below.

3.1. *Common novelty success in older adults*

Common novelty success across both related and unrelated lures showed enhanced neural activity in right late visual cortex as well as several PFC regions including right anterior PFC, left superior frontal gyrus, and ventrolateral PFC in older adults (see Fig. 2). Studies investigating memory retrieval in young and older adults have often found activity in visual regions (Dobbins et al., 2003; Duarte et al., 2008; Tsukiura et al., 2011) and prefrontal regions (Cabeza et al., 2002; Dobbins et al., 2003; Grady et al., 2005) to support retrieval success (for meta-analysis see Spreng et al. (2010)). Regarding retrieval-related activity in visual regions, it has been posited that such activity represents the reinstatement of cortical activity from encoding (McDonough et al., 2014; Vaidya et al., 2002; Wheeler et al., 2000), with activity in late visual cortex specifically reflecting reinstatement of general object properties (Dennis et al., 2014; Garoff et al., 2005; Slotnick and Schacter, 2004). While lures leading to correct rejection responses have not been previously encountered and thus sensory details from these items cannot be reinstated, this signal may reflect reactivation of true details from studied items to aid in detecting mismatch between new and old items (Brainerd and Reyna, 2002; Gallo et al., 2010; Lampinen et al., 2004). Thus the current findings are consistent with previous research suggesting that older adults rely on general object properties when making retrieval decisions (Dennis et al., 2014; Koutstaal, 2003; Remy et al., 2008).

Additionally, the present results extend previous findings by showing that sensory reinstatement in late visual regions also contributes to successful novelty processing in older adults. This conclusion is counterintuitive to previous research in the domain of priming which typically finds increased visual activity for novel compared to familiar stimuli (Grill-Spector et al., 2006; Henson et al., 2002; Schacter et al., 2007). However, the analysis was quite different as well, as both components of the analysis included stimuli that were novel with respect to their past presentation history. Thus, as this activity was greater for successful novelty responses compared to false recognitions, the present results indicate that activity in this region does not merely represent the absence of an implicit priming signal for new items (for reviews see Habib (2001) and Schacter and Buckner (1998)), but rather a sensory signal that contributes to older adults' detection of mismatch between old and new items to support conscious memory responses.

Regarding novelty success activity in the aforementioned PFC regions, previous research has established a critical role of PFC in mediating control and monitoring processes during retrieval (Cabeza et al., 2003; Gallo et al., 2006; Henson et al., 1999; McDonough et al., 2013). Additionally, ERP studies of novelty detection have identified a novelty signal over frontal electrodes that is hypothesized to support evaluative processes associated with novel stimuli (Friedman et al., 2001). The present results show that this pattern of PFC-supported memory success extends beyond successful retrieval and novelty detection to novelty success during retrieval,

indicating that such monitoring and evaluation processes are also critical to older adults' ability to successfully reject retrieval lures. Thus, these results provide initial evidence that neural activation supporting retrieval success may also support novelty success. Results also suggest that the PFC is critical to novelty success above-and-beyond stimulus novelty. Further discussion of PFC activation in novelty processing with regard to age differences is continued below.

3.2. *Age differences in novelty processing*

In addition to determining neural mechanisms older adults engage for successful novelty processing across levels of relatedness, we also sought to determine differences in the patterns of neural modulation between novelty trial types for young and older adults. An Age × Novelty interaction revealed three distinct patterns of modulation. The first represents activity that young but not older adults utilized to support unrelated novelty processing. The second represents activity that young but not older adults utilized to support related novelty processing. The third represents differences in regions young adults utilized in the face of interference that older adults utilized for novelty success. Each pattern is discussed below.

3.2.1. *Age differences in categorical processing*

The first pattern of age differences included regions such as the ACC and bilateral middle/inferior temporal gyrus where young adults modulated neural activity in support of unrelated novelty processing compared to both related novelty and false alarms but older adults did not show unrelated novelty success effects (see Fig. 3a). Regarding the ACC, young adults showed an unrelated novelty success effect while older adults showed no differential activity across novelty responses. Given the role of the ACC in monitoring processes associated with task demands such as changes in task difficulty (Botvinick et al., 2001) and detecting salient information (Menon and Uddin, 2010), the current results are consistent with the notion that older adults have difficulty modulating neural activity in response to stimuli characteristics (such as relatedness) or changes in task difficulty (Garrett et al., 2013; Payer et al., 2006; Voss et al., 2008).

In contrast to the attentional processes associated with the ACC, research in the domains of false memory and language processing have shown the middle and inferior temporal gyri to be critical in categorical or gist processing (Dennis et al., 2008, 2014; Price, 2000, 2010). In the present study, young adults recruited gist processing specifically for successful unrelated novelty processing, suggesting that young adults base memory decisions for unrelated lures on categorical information. However, older adults showed increased neural recruitment of the left middle/inferior temporal gyrus for both unrelated correct rejections *and* related false recognitions compared to related correct rejections. Activity in left middle/inferior temporal gyrus has been associated with false memory in aging (Dennis et al., 2008, 2014), reflecting older adults' susceptibility to interference from overlapping

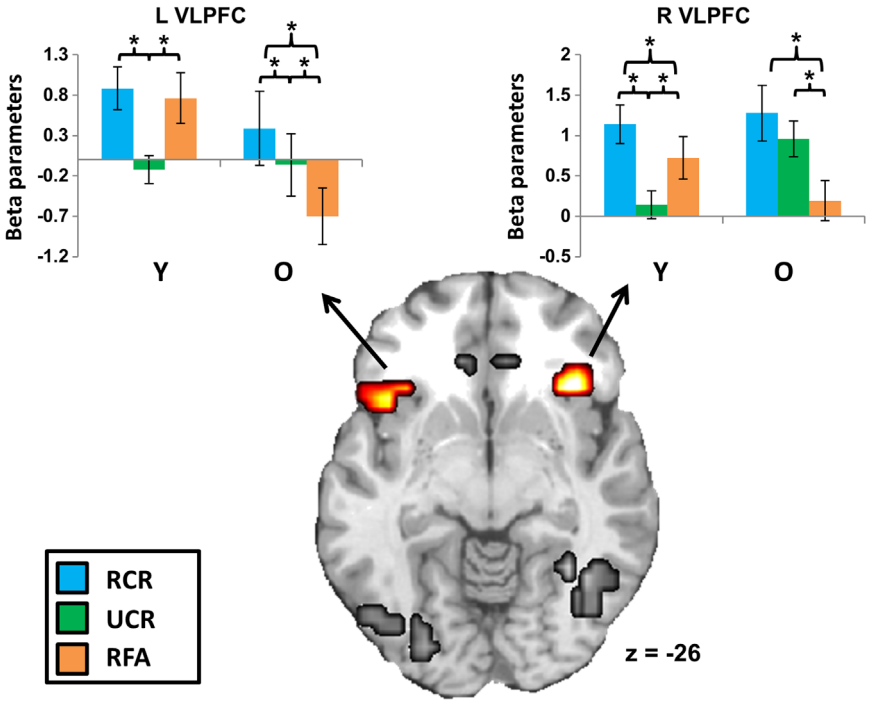

Fig. 4 – Age differences in PFC processing of novelty success. Older adults recruited bilateral ventrolateral PFC for both related and unrelated novelty success, and showed increased activity for related as compared to unrelated novelty success. Young adults, however, recruited bilateral ventrolateral PFC for all related lures compared to unrelated novelty regardless of memory response (correct rejection or false alarm). Activity in gray represents brain regions showing an Age × Novelty interaction that is not consistent with the pattern presented in the current figure. L, left; O, older adults; R, right; RCR, related correct rejection; RFA, related false alarm; UCR, unrelated correct rejection; VLPFC, ventrolateral prefrontal cortex; Y, young adults.

categorical information between old and new items (Dennis et al., 2008, 2014; Koutstaal and Schacter, 1997; Tun et al., 1998). The present results expand on previous false memory studies by demonstrating that older adults also recruit gist processing in left middle/inferior temporal gyrus when rejecting unrelated lures, but not in a manner that also reduces false recognitions. Thus, while both young and older adults recruit gist processes during memory retrieval, only young adults do so in a manner that supports successful unrelated novelty processing. Overall, age deficits in the ACC and bilateral middle/inferior temporal gyrus for unrelated novelty are consistent with the hypothesis that older adults have difficulty exploiting salient categorical information to make successful novelty responses.

3.2.2. *Age differences in item-specific processing*

The second pattern of age differences revealed by the ANOVA included regions where young, but not older adults, showed novelty success effects for either related novelty (visual cortex) or for both related and unrelated novelty (bilateral anterior hippocampus and PHG) compared to false alarms (see Fig. 3b). Instead, older adults showed a lack of modulation across trial types in bilateral late visual regions and bilateral MTL and an unrelated novelty success effect in right early visual cortex.

Regarding the pattern of activity in visual regions, while older adults utilized late visual cortex for common novelty success, no visual region was selectively recruited for related novelty success compared to false alarms in this age group. It is particularly noteworthy that young, but not older adults recruited regions of *early* visual cortex for related novelty success given this region's importance to low-level visual processing that has been shown to support true memories, and specifically true recollections (Dennis et al., 2012; Slotnick and Schacter, 2004). As previously discussed, this visual signal has been posited to reflect the reinstatement of perceptual details from a previous encoding episode (Dennis et al., 2012; Slotnick and Schacter, 2004; Vaidya et al., 2002; Wheeler et al., 2000) such that retrieving true details of a previous episode may be critical to detecting mismatch between new and old items, particularly when such items share perceptual features. Further, aging studies have suggested that older adults' retrieval deficits may result from reduced processing in posterior cortices, including visual cortex (Davis et al., 2008; Grady et al., 2002; McDonough et al., 2014), reflecting older adults' retrieval of fewer perceptual details to support successful memory responses (McDonough et al., 2014). The present results extend these previous findings showing that, while young adults utilize this perceptual signal in early visual cortex to support successful novelty decisions when items share perceptual and semantic features, older adults utilize visual processing in a more general manner, either by recruiting late visual regions across levels of relatedness or by recruiting early visual cortex to support novelty success for items that differ substantially from encoding items.

With respect to hippocampal activity, previous research conducted in young adults has shown that anterior hippocampus is critical to novelty processing (Kaplan et al., 2014; Kohler et al., 2005; Kumaran and Maguire, 2006) and is posited to reflect match/mismatch processes that serve to distinguish between old and new items (Brown and Aggleton, 2001; Kumaran and Maguire, 2007). The fact that young, but not older adults in the present study showed a novelty success effect in anterior hippocampus is consistent with research showing that older adults have difficulty utilizing mismatch processes to support novelty decisions (Yassa et al., 2011). Specifically, aging studies have linked functional deficits in the MTL to deficits in recollection (e.g., Daselaar et al. (2006)), retrieval of associations (e.g., Giovanello and Schacter (2012)), and retrieval of encoding source (e.g., Dulas and Duarte (2012)). Integrating accounts of aging and novelty suggests that novelty deficits and retrieval deficits may result from a common cause: age-related deficits in hippocampal processing make it difficult for older adults to use details of previously encoded episodes to detect mismatch between new and old items. The present study represents critical first evidence that age deficits in hippocampal processing contribute to age deficits in *successful* novelty processing. Further research in the domains of novelty processing and aging will be needed to strengthen this conclusion.

3.2.3. *Age differences in PFC mediated novelty success*

The third pattern of age differences revealed in the interaction included bilateral ventrolateral PFC in which young adults showed increased activity in the presence of all related lures (i.e., related correct rejections and false alarms) whereas older adults showed a novelty success effect, including a stepwise increase in activation from false alarms to unrelated correct rejections to related correct rejections in the right ventrolateral PFC (see Fig. 4). Research in young adults has posited that the ventrolateral PFC is critical to negotiating interference in working (Badre and Wagner, 2005; Postle et al., 2004) and episodic memory (Nee et al., 2007; Wimber et al., 2009), which is consistent with the present finding that young adults engage ventrolateral PFC for all related, but not unrelated lures. While previous research has suggested that ventrolateral PFC interference resolution is disrupted in aging (Jonides et al., 2000), a number of aging studies have identified processing in PFC regions to be critical to older adults' successful memory performance during retrieval (Anderson et al., 2000; Cabeza et al., 2000, 2004; Grady et al., 2002). Such processing in PFC regions has been posited to compensate for deficits in posterior brain regions such as the MTL and visual cortex (Posterior to anterior shift in aging, PASA; Davis et al., 2008). Given both the observed age-related deficits in the MTL and visual cortex, as well as intact ventrolateral PFC functioning in older adults, results from the present study reflect the PASA pattern on neural recruitment in aging, similar to that seen to support successful retrieval (Anderson et al., 2000; Cabeza et al., 2000, 2004; Grady et al., 2002).

Additionally, the CRUNCH theory of aging suggests that age-related increases in PFC activity may represent older adults' engagement of control and monitoring processes at lower levels of difficulty than young adults (Reuter-Lorenz and Cappell, 2008). This theory may explain why older but not young adults recruited ventrolateral PFC activity even for unrelated novelty decisions. The CRUNCH theory also suggests that older adults may not be able to continue to modulate PFC activity at the highest levels of difficulty due to capacity limitations in the recruitment of neural activity. In the present study, however, older adults showed increased activity for the relatively difficult memory decision of related correct rejections compared to

unrelated correct rejections. Thus, further evidence is necessary to establish when and in what situations older adults reach this ceiling in neural recruitment during novelty processing. Thus, despite behavioral deficits in rejecting lures, the current results suggest a means by which older adults are able to modulate neural activity to promote successful novelty decisions, even when retrieval lures are related to items from encoding.

4. Conclusion

The present study sought to characterize the effects of item-relatedness on the neural correlates of novelty processing in older adults and elucidate age differences between young and older adults. Results showed that older adults exhibited novelty success activity largely in PFC regions including bilateral ventrolateral PFC as well as late visual cortex, suggesting that older adults rely on monitoring and control processes as well as visual processing of general object properties to make successful novelty decisions across levels of relatedness. Regarding age differences, results showed that older, unlike young adults, did not differentially recruit regions such as the anterior cingulate and bilateral middle/inferior temporal gyrus to capitalize on the salient categorical differences in rejecting unrelated lures. Likewise, unlike young adults, older adults did not differentially recruit regions of early visual cortex or anterior hippocampus to support related novelty success, suggesting that they have difficulty using item-specific details to support related novelty processing. In contrast, older adults recruited bilateral ventrolateral PFC to support novelty success across levels of task difficulty, suggesting that prefrontal processes may contribute to successful novelty processing when coupled with deficits in posterior cortices (i.e., PASA). Overall, results suggest that age deficits in novelty processing may arise because older adults process related and unrelated lures similarly and do not capitalize on categorical or item-specific properties of lures at retrieval. Similar to aging patterns in memory retrieval, results also showed that older adults have the strongest novelty success activity in lateral PFC regions associated with control and monitoring processes, suggesting that such processes are critical to avoid false recognitions for older adults.

5. Experimental procedures

5.1. *Participants*

Twenty young adults and 23 healthy older adults participated in the current study. Two young participants were excluded from the analysis due to head motion in excess of 4 mm, 1 additional young participant was also excluded for performing below chance, and 1 older adult was excluded for failure to follow task instructions, leaving data from 17 young adults [11 females; mean age=21.28 yr, SD=(1.79), range 18–25 yr] and 22 older adults [11 females; mean age=74.18 yr, SD=(5.20), range 67–83 yr] reported in all analyses. The young adults were recruited from the Penn State University community and older adults from Centre County, PA. All participants were right-handed, native English speakers and were screened for history of neurological disorders and psychiatric illness, alcoholism, drug abuse, and learning disabilities.

In addition, participants completed a battery of cognitive measures including the Mini Mental State Exam (MMSE; Folstein et al., 1975), subtests from the Wechsler Adult Intelligence Scale (WAIS) including Symbol Search, Digit Symbol Encoding, Symbol Copy, Digit Span, Arithmetic, Letter Number Sequence, and Vocabulary tasks (Wechsler, 1997), and the Beck Depression Inventory (BDI; Beck and Steer, 1993). Tests were conducted in order to screen for dementia and depression in the older cohort. All individuals performed well within the normal range for their age, verifying that they were cognitively healthy [see Table 1 (upper portion) for participant demographics]. All participants provided written informed consent and received financial compensation for their participation. All experimental procedures were approved by Penn State University's Institutional Review Board for the ethical treatment of human participants.

5.2. *Stimuli*

Stimuli consisted of 1092 color pictures of common objects. Images were obtained from an internet image search. All backgrounds were removed and pictures were cropped and resized to an approximate size of 480 × 480 pixels (see Fig. 1). Images were presented focally and equated for resolution. Seven hundred twenty images were presented during encoding, including 90 categories of stimuli with 8 exemplars per category. Six hundred and forty two images were presented at retrieval including (a) 270 targets (3 of the 8 exemplars from each encoding category), (b) 270 related lures (3 novel images associated with each encoding category) and (c) 102 unrelated lures (including 3 novel images from each of 34 unrelated categories). Items selected as targets were counterbalanced between participants.

5.3. *Procedure*

Encoding and retrieval both took place in the scanner with approximately 24 h separating the two memory phases (Only retrieval data are presented in the current analyses). Images were displayed by COGENT in MATLAB (Math Works) and projected onto a screen that participants viewed through a mirror attached to the head coil. Images were displayed at a screen resolution of 1024 (*H*) × 768 (*V*) at 75 Hz. At the viewing distance of 143 cm, the display area was 20° (*H*) × 16° (*V*). Behavioral responses were recorded using a 4 button response box. Scanner noise was reduced with headphones and earplugs, and cushioning was used in the head coil to minimize head motion.

Encoding was incidental and participants were instructed to make subjective pleasantness ratings of objects as they were presented. Encoding images were presented for 1 s and participants were given 2 s to make their pleasantness rating, followed by a variable interstimulus interval (M=2 s, range 1.5–3 s). During half of the encoding runs, images from a given categories were presented in a blocked design while in the other half of the runs, categorical images from a given

category were intermixed. The blocked-intermix manipulation was presented every other run and counterbalanced between participants. There were no behavioral or neural differences between trial types of interest based on this manipulation, thus analyses were collapsed with regard to this encoding variable.

During retrieval, participants completed 6 runs each approximately 8 min in length. All stimulus categories were presented in an intermixed fashion. Each image was displayed for 2.5 s while participants made memory responses using the 'Remember–Know–New' paradigm (see Fig. 1) followed by a variable interstimulus interval (M=2 s, range 1.5–3 s). In accord with typical task instructions, participants were told to respond 'Remember' if they could recollect specific details about the object such as its shape, color, or their thoughts or feelings during its initial presentation. Participants were told to respond 'Know' if the picture looked familiar, but they could not recollect any specific details of its prior presentation. They were told to respond 'New' if they believed the picture was not presented during the encoding session. The images were pseudorandomly sorted, ensuring that no more than 3 images from any one category appeared in a row.

5.4. *Image acquisition*

Images were acquired using a Siemens 3T scanner equipped with a 12-channel head coil. A T1-weighted sagittal localizer was acquired to locate the anterior (AC) and posterior (PC) commissures. Images were then prescribed parallel to the AC–PC plane. An MPRAGE was acquired with a 2300 ms TR, 3.41 ms TE, 230 mm field of view (FOV), 256^2 matrix, 160 axial slices, and 0.9 mm slice thickness for each participant. Echo-planar functional images were acquired using an interleaved acquisition, 2000 ms TR, 30 ms TE, 240 mm FOV, a 64^2 matrix, 34 axial slices with 3.8 mm slice thickness resulting in 3.8 mm isotropic voxels.

5.5. *Image processing*

Functional data were preprocessed and analyzed with SPM8 (Statistical Parametric Mapping; Wellcome Department of Cognitive Neurology, http://www.fil.ion.ucl.ac.uk/spm). Time-series data were corrected for differences in slice acquisition times and realigned. Images were checked for movement artifacts using a time series diagnostic function TSDiffAna (Freiburg Brain Imaging) in MATLAB (MathWorks). Functional images were spatially normalized to a standard stereotaxic space using the Montreal Neurological Institute (MNI) templates implemented in SPM8. The coordinates were later converted to Talairach space (Talairach and Tournoux, 1988). Finally, the volumes were spatially smoothed using an 8-mm isotropic Gaussian kernel.

5.6. *Behavioral analyses*

To determine the effects of age and relatedness on memory accuracy, 'new' response rates to targets and related and unrelated lures were entered into a 2 (Age: young, old) × 3 (Memory: miss, related correct rejection, unrelated correct rejection), mixed factor ANOVA. Where appropriate, a Greenhouse–Geisser correction for sphericity was included to account for differences in variance between conditions. Post-hoc *t*-tests were used to probe significant interactions.

5.7. *fMRI analyses*

Trial-related activity was modeled in the General Linear Model (GLM) with a stick function corresponding to trial onsets convolved with a canonical hemodynamic response function (hrf). Statistical Parametric Maps were identified for each participant by applying linear contrasts to the beta weights for the events of interest. Individual regressors were created for each response option ('Remember', 'Know', and 'New') for each trial type (target, related lure, unrelated lure) resulting in 9 regressors. In addition, regressors for 'no response' trials, motion parameters, and a constant for each run were included in the model and treated as regressors of no interest. For all analyses, related correct rejections (RCR) were defined as 'new' responses to related lures, unrelated correct rejections as 'new' responses to unrelated lures (UCR), and related false alarms (RFA) as both 'remember' and 'know' responses to related lures.

To determine overlap between processes contributing to novelty success across levels of relatedness in older adults, we performed a conjunction of related and unrelated correct rejections as compared to false alarms. As a first step, we created individual contrasts of *RCR* > *RFA* and *UCR* > *RFA*.[1] As a second step, we used the inclusive masking procedure in SPM to determine spatial overlap between these two contrasts, thus determining regions that were commonly active in both contrasts. Use of the conjunction procedure ensured that activity was not driven by only one trial type, but that brain regions were significantly active within each individual contrast before determining spatial overlap between the activation maps. A common baseline of related false alarms was used for both related and unrelated correct rejections because it allowed us to control for the presentation of a lure while isolating brain regions that are associated with a correct 'new' response. As such, these contrasts represent a novelty success contrast (novelty success > novelty error) similar to the traditional retrieval success contrast (hits > misses; e.g., Daselaar et al., 2013; Dobbins et al., 2003; Prince et al., 2005; Slotnick and Schacter, 2004).

In order to identify differential neural activity between young and older adults for novelty processing, we performed a 2 × 3 mixed factor ANOVA using the full factorial ANOVA procedure in SPM. Age group (young, older) was entered as a between-subjects factor. Novelty trial type (RCR, UCR, RFA) was entered as a within-subject factor. Since our primary interest was in differences in how young and older adults modulate neural activity based on the type of novelty and the success of the novelty response, we looked at neural regions that showed an effect in the overall Age × Novelty interaction. Consistent with previous studies using a similar analysis approach (Gamer et al., 2012; Okado and Stark, 2003), we

[1] While unrelated false alarms were included in the model, they were ultimately treated as a regressor of no interest as many participants had an insufficient number of trials to extract an adequate neural signal.

extracted beta parameters from the peak voxel of each cluster in each participant for each of the three trial types and performed post-hoc *t*-tests in SPSS to examine the nature of the interaction in each cluster.

For all contrasts, in order to obtain results that are corrected for multiple comparisons, we used Monte Carlo simulations (https://www2.bc.edu/sd-slotnick/scripts.htm) to define individual voxel and cluster extent thresholds (e.g., Forman et al. (1995), Garoff-Eaton et al. (2007), Quadflieg et al. (2008) and Slotnick and Schacter (2004)). This procedure takes into account the acquisition matrix (64 × 64), number of slices (34), voxel dimensions (3.8 mm^3), intrinsic smoothness (16.1 mm), and resampling of voxels (none) in order to simulate data and estimate the rate of Type I error given the protocol parameters over 10,000 iterations. In this study, an individual voxel threshold of $p<0.01$ was used in combination with a cluster extent threshold of 18 voxels (988 mm^3) in order to identify results corrected for multiple comparisons at $p<0.05$. In addition, we used the aal pickatlas (Maldjian et al., 2003; Tzourio-Mazoyer et al., 2002) to restrict all analyses to cortical and subcortical regions. This whole-brain mask ensured that no cluster contained spurious activity in white matter or cerebrospinal fluid.

Acknowledgment

Funding of this research was supported by a National Science Foundation (NSF) Grant BCS1025709 awarded to N.A.D. and was conducted while N.A.D. was an AFAR Research Grant recipient from the American Federation for Aging Research. Thanks to the Penn State Social, Life, & Engineering Sciences Imaging Center (SLEIC), 3T MRI Facility. Thanks to Courtney Allen, Christina Johnson, Kristina Peterson, Avery Rizio, and Indira Turney for helpful comments throughout the writing process. Thanks to Simon Vandekar for assistance with data collection and analysis.

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