Episodic Memory in Healthy Older Adults

The Role of Prefrontal and Parietal Cortices

M. Natasha Rajah, David Maillet, and Cheryl L. Grady

Introduction

Healthy aging is associated with deficits in episodic memory. These deficits may be related to changes in neural systems important for mediating episodic memory-specific processes (i.e., encoding and retrieval) and/or to deficits in neural systems implicated in other higher-order cognitive processes, which indirectly impact one’s episodic memory abilities – such as attention, working memory, and cognitive control processes (Zacks et al., 2000). With the advancement and increased availability of brain imaging technologies there has been a marked increase in the number of neuroimaging studies investigating the neural correlates of episodic memory decline in healthy aging. Several studies have found age-related declines in gray matter volume and functional activity of the medial temporal lobes (MTL) that have been associated with deficits in older adults’ episodic memory. Chapters 5, 6, and 18 in this volume discuss the role of the MTL in episodic memory in healthy young and older adults. In the current chapter we review the functional neuroimaging studies published from 2003 to spring 2012 that have examined how age-related changes in prefrontal and parietal cortex impact episodic memory in healthy aging. The majority of studies in this field have used visual stimuli. Two functional neuroimaging studies published since 2003 examined age-related differences in episodic memory that did not employ visual stimuli, one focusing on olfactory–visual associations (Cerf-Ducastel and Murphy, 2009) and the other on auditory verbal memory (Fernandes et al., 2006). These studies have not been included in the current chapter.

Also, in our review of the literature we grouped studies based on whether subsequent retrieval performance was matched between age groups, or was not matched and young adults exhibited significantly better retrieval accuracy than older adults. We did this since assessing brain activity in the context of behavior can be particularly important when there is age-related increase in brain activity in older adults. For example, when performance is matched, increased activation with age might reflect inefficient use of neural resources, but it could also indicate compensatory plasticity in older adults.
In contrast, when performance is lower in older adults, over-recruitment of activity is less likely to reflect compensation but could reflect differentiation of function or the use of strategies or cognitive processes that are detrimental to performance. In the following sections we discuss the anatomy and results from functional magnetic resonance imaging (fMRI) studies of aging and episodic encoding and retrieval for the prefrontal cortex (PFC; also see Chapter 7), and then the parietal cortex. We present a summary of our observations at the end of the chapter.

Prefrontal Cortex

Anatomy

The PFC in humans comprises most of the frontal lobes. It is located rostral to the central sulcus, anterior to the Sylvian fissure, and excludes primary and association motor cortices. Traditionally, neuroscientists have subdivided the PFC into the following “classical” regions based on gross anatomic markers: orbitofrontal cortex (OFC), ventromedial PFC (vmPFC), ventrolateral PFC (vlPFC), medial PFC (mPFC), dorsolateral PFC (dlPFC), dorsal PFC (dPFC), and anterior PFC/frontal pole (aPFC) (Luria, 1962; Mesulam, 1986; Petrides and Pandya, 1999, 2002; Ongur, Ferry, and Price, 2003). In the current section, we focus on age-related changes in dlPFC, vlPFC, mPFC, and aPFC (see Figure 1 in Rajah and D’Esposito, 2005). We define dlPFC as being the brain area within the middle frontal gyrus (MFG) and consisting of Brodmann areas (BA) 8, 9, 46; excluding peaks in BA 10 on the MFG, which we consider to be part of aPFC. vlPFC is defined as the area within the inferior frontal gyrus (IFG), consisting of BA 47, 45, and 44. mPFC is defined as being the brain area within the medial frontal gyrus and consisting of BA 32, 24 and dorsomedial aspects of BA 10. We define aPFC as being the area within the frontal pole of the superior frontal gyrus (SFG) and consisting of BA 10.

Age-related changes in PFC function and episodic memory encoding

Successful encoding has been related to increased activity in vlPFC in young adults, particularly in the left hemisphere (Blumenfeld and Ranganath, 2007; Fletcher, Shallice, and Dolan, 1998; Reber et al., 2002; Spaniol et al., 2009). Young adults also activate bilateral dlPFC during encoding, especially when the encoding tasks are more demanding and employ relational and source/context encoding paradigms (Blumenfeld et al., 2011; Blumenfeld and Ranganath, 2007; Dennis et al., 2008; Maillet and Rajah, 2011).

In writing this chapter we reviewed 23 fMRI studies on aging and episodic encoding. Studies examining age-related changes in episodic encoding have generally employed a subsequent memory paradigm in which encoding activity for subsequently remembered (successfully encoded) items is compared to activity for forgotten items, in young versus older adults. Seventeen of the 23 studies reviewed involved tasks in which older adults’ subsequent retrieval accuracy performance was significantly worse than that of young adults (de Chastelaine et al., 2011; Dennis et al., 2008; Dulas and Duarte, 2011; Duverne, Motamedinia, and Rugg, 2009a; Duzel et al., 2011; Fischer, Nyberg, and Backman, 2010; Grady et al., 2006;
Gutchess et al., 2005; Kensinger and Schacter, 2008; Kim and Giovanello, 2011; Kukolja et al., 2009; Miller et al., 2008; Morcom et al., 2003, 2010; Murty et al., 2009; Sperling et al., 2003; St. Jacques, Dolcos, and Cabeza, 2009). In contrast, in only six studies was subsequent episodic retrieval accuracy matched between older and younger adults (Bangen et al., 2012; Burgmans et al., 2010; Dennis, Daselaar, and Cabeza, 2007; Filippini et al., 2012; Kalpouzos, Persson, and Nyberg, 2012; Leshikar et al., 2010). Figure 17.1 shows a bar graph in which we summarize the fMRI results reported in the 23 studies reviewed on episodic encoding. In creating this graph we tallied the number of activations reported within each PFC region of interest (ROI) (dlPFC, vlPFC, aPFC, and mPFC) from contrasts that identified group differences in regional activations. We summarize these results under conditions when performance was matched between age groups, and when performance was not matched between age groups.

**PFC encoding activation when subsequent retrieval performance is not matched**  fMRI results from studies in which retrieval performance was not matched between groups indicated that older adults exhibit increased activity in various PFC regions, compared to younger adults. Left dlPFC most markedly exhibits this pattern of age-related increased activity during encoding, when subsequent memory performance was poorer in older versus younger adults (de Chastelaine et al., 2011; Duzel et al., 2011; Gutchess et al., 2005; Miller et al., 2008; Sperling et al., 2003; St. Jacques, Dolcos, and Cabeza, 2009).

![Pattern of PFC activations in young and older adults during episodic encoding](image)

**Figure 17.1** Pattern of prefrontal cortex (PFC) activations in young and older adults during episodic encoding. This figure summarizes the pattern of PFC activity observed in 23 fMRI studies on age-related differences in encoding (see text for details of studies reviewed). In this bar graph we report the pattern of left and right PFC activations reported in young and older adults when performance was matched (“matched”) and when performance was not matched (“unmatched”). For each PFC ROI we tallied the number of activations in which young adults activated a region more than older adults, and in which older adults activated a region more than young adults. L, left; R, right. PFC abbreviations are: dl, dorsolateral; vl, ventrolateral; a, anterior; m, medial.
Also, when subsequent memory was unmatched between groups, Duverne, Motamedinia, and Rugg (2009a) and Morcom et al. (2003) observed that both young and older adults activated left vlPFC during successful encoding; but lower-performing older adults also activated right vlPFC to a greater degree than young and higher-performing older adults. This finding suggests that right vlPFC recruitment during encoding may reflect attempted compensation in lower-performing elders in response to deficits in left vlPFC processes (de Chastelaine et al., 2011); alternatively, it may reflect dedifferentiation of function with age.

**PFC encoding activation when subsequent retrieval performance is matched**  
In studies when subsequent memory was matched between age groups, the results indicate a similar pattern of age-related increases in brain activity in various PFC regions. However, only one study to our knowledge has reported greater activity in left vlPFC in older than in younger adults when performance was matched (Filippini et al., 2012). Given that young adults engage this region for successful encoding, it is surprising that a greater number of studies did not report age-related increases in left vlPFC activity when performance was matched between groups. This may be due to age-invariance in left vlPFC activity once performance was matched.

Consistent with the findings for studies in which subsequent memory was unmatched (see section above), studies have also reported greater left dlPFC activity in older versus younger adults when subsequent memory was *matched* between age-groups (Burgmans et al., 2010; Dennis, Daselaar, and Cabeza, 2007; Leshikar et al., 2010). In two studies, greater left dlPFC activity in older adults was observed during encoding of verbal stimuli (Dennis, Daselaar, and Cabeza, 2007; Leshikar et al., 2010). The study by Burgmans et al. (2010) reported greater bilateral dlPFC activity in older versus younger adults. This study required subjects to intentionally encode scene stimuli, which may have led participants to utilize both linguistic and spatial relational strategies at encoding.

Therefore, during episodic encoding older adults consistently over-recruit left dlPFC and right vlPFC compared to young adults when performance is unmatched between age groups, and left dlPFC when performance is matched. Again, these age-related increases in activation during encoding may reflect neural compensation or dedifferentiation of function with age.

**Age-related changes in PFC function and episodic memory retrieval**

In young adults, fMRI studies have reported increases in vlPFC and dlPFC activity during retrieval (Cabeza and Nyberg, 2000; Prince, Daselaar, and Cabeza, 2005; Rajah and D’Esposito, 2005). There is evidence that, in general, the dlPFC is more active during retrieval than encoding, compared to vlPFC (Prince, Daselaar, and Cabeza, 2005; Rajah and D’Esposito, 2005; Spaniol et al., 2009). However, right vlPFC activity has been consistently reported during episodic retrieval (Bunge, Burrows, and Wagner, 2004; Donohue et al., 2005; Maillet and Rajah, 2011; Rajah, Ames, and D’Esposito, 2008). In young adults, dlPFC activity during retrieval has been shown to increase as a function of increasing task difficulty (Hayama and Rugg, 2009; Rajah, Ames, and D’Esposito, 2008; Rajah, Languay, and Valiquette, 2010; Spaniol et al., 2009), which may reflect the role of this region in post-retrieval monitoring processes (Hayama and Rugg, 2009; Rajah, Languay, and Valiquette, 2010; Rugg, Henson, and Robb, 2003), in error processing (Garavan et al., 2002),
in response selection (Rajah, Ames, and D’Esposito, 2008), or in mediating relational response strategies (Blumenfeld et al., 2011). Right vlPFC activity during retrieval may reflect this region’s role in selection and/or inhibition of irrelevant stimuli during memory retrieval (Rajah, McIntosh, and Grady, 1999) and in novelty detection (Donohue et al., 2005). However, in general, the neural/cognitive processes mediated by dlPFC and right vlPFC during retrieval remain unclear.

We reviewed 28 fMRI studies that compared the neural activity in young versus older adults during episodic memory retrieval. In 10 of these studies, memory performance was matched between young and older adults for the fMRI activation analyses discussed in this chapter (Addis, Roberts, and Schacter, 2011; Burgmans et al., 2010; Cabeza et al., 2004; Daselaar et al., 2006; Davis et al., 2008; Giovanello and Schacter, 2012; Giovanello et al., 2010; Kalpouzos, Persson, and Nyberg, 2012; Spaniol and Grady, 2012; St-Laurent et al., 2011). In 18 of the studies reviewed, younger adults’ retrieval accuracy was significantly better than that of older adults (Daselaar et al., 2003; Dew et al., 2012; Brassen et al., 2009; Dennis et al., 2008; Duarte, Graham, and Henson, 2010; Duarte, Henson, and Graham, 2008; Dulas and Duarte, 2012; Grady, McIntosh, and Craik, 2005; Grady et al., 2006; Kukolja et al., 2009; McDonough, Wong, and Gallo, 2012; Morcom, Li, and Rugg, 2007; Murty et al., 2009; Rajah, Ames, and D’Esposito, 2008; Rajah, Languay, and Valiquette, 2010; Tsukiura et al., 2011; van der Veen et al., 2006; Velanova et al., 2007). Figure 17.2 shows a bar graph in which we summarize the

![Figure 17.2 Pattern of prefrontal cortex (PFC) activations in young and older adults during episodic retrieval. This figure summarizes the pattern of PFC activity observed in 28 fMRI studies on age-related differences in retrieval (see text for details of studies reviewed). In this bar graph, we report the pattern of left and right PFC activations reported in young and older adults when performance was matched (“matched”) and when performance was not matched (“unmatched”). For each PFC ROI we tallied the number of activations in which young adults activated a region more than older adults, and in which older adults activated a region more than young adults. L, left; R, right. PFC abbreviations are: dl, dorsolateral; vl, ventrolateral; a, anterior; m, medial.]
fMRI results reported in the 28 studies reviewed on episodic retrieval. In creating this graph, we tallied the number of activations reported within each PFC ROI (dlPFC, vlPFC, aPFC, and mPFC) from contrasts that identified group differences in regional activations. We summarize these results under conditions when performance was matched between age groups, and when performance was not matched between age groups.

PFC activation during retrieval when performance is not matched

The majority of fMRI studies of aging and episodic memory have compared brain activity during tasks in which retrieval accuracy was not matched between age groups, and young adults performed significantly better. In some of these studies, greater right dlPFC activity was observed in young compared to older adults during memory retrieval (Grady et al., 2006; McDonough, Wong, and Gallo, 2012; Rajah, Languay, and Valiquette, 2010; Tsukiura et al., 2011). However, other studies have reported the inverse effect (older > young adult) in this region (Duarte, Graham, and Henson, 2010; Duarte, Henson, and Graham, 2008; Rajah and McIntosh, 2008). Interestingly, the particular region of right dlPFC where there was greater activity in young compared to older adults was either BA 9 and/or BA 46. In contrast, the right dlPFC region with greater activity in older versus young adults was in more dorsal areas of dlPFC, in BA 8.

Previous studies have also reported age-related increases in left dlPFC, left vlPFC, bilateral aPFC, and bilateral mPFC at retrieval (Dew et al., 2012; Duarte, Henson, and Graham, 2008; Morcom, Li, and Rugg, 2007). Three studies have been published to date in which increased left dlPFC activity was observed in older versus young adults when performance was unmatched (Dew et al., 2012; Duarte, Henson, and Graham, 2008; Morcom, Li, and Rugg, 2007). Moreover, Dew et al. (2012) reported greater early activation of left dlPFC in young versus older adults at retrieval, but greater late activation of this same region in older versus young adults. Overall, episodic encoding and retrieval studies consistently report over-recruitment of left dlPFC in older versus younger adults, regardless of whether memory performance was matched or unmatched between age groups.

Age-related over-activations in mPFC may reflect reduced task-related deactivations in older versus younger adults (Grady et al., 2006; Rajah, Languay, and Valiquette, 2010), and therefore may be detrimental to task performance (Damoiseaux et al., 2008; Sambataro et al., 2010). Alternatively, this effect may reflect age-specific compensatory plasticity reflecting the implementation of novel process/strategies in an attempt to maintain retrieval performance when retrieval task demands are high (Rajah, Languay, and Valiquette, 2010; Stevens et al., 2008). Results from Kukolja et al. (2009) support the former interpretation. They found that young adults exhibited greater task-related decreases in mPFC compared to older adults. They concluded that deficits in task-related decreases in mPFC activity in older adults may reflect decreased attentional processing at retrieval, which may have contributed to older adults’ poorer memory performance.

Age-related increases in bilateral aPFC may reflect compensation. For example, Rajah, Languay, and Valiquette (2010) reported age-specific increases in right aPFC in older versus young adults. This effect was not due to older adults showing weaker task-related decreases in aPFC activity. Moreover, in older adults,
greater right aPFC activity was moderately correlated with better temporal context memory. Therefore, age-related changes in mPFC versus aPFC may differ, such that age differences in mPFC reflect deficits in task-related decreases in activation and poorer task performance, whereas age-specific increases in aPFC may reflect compensatory plasticity in the aging brain.

**PFC activation during retrieval when performance is matched** Several fMRI studies have compared PFC activity in young versus older adults during memory retrieval, when retrieval accuracy was matched between age groups (Addis, Roberts, and Schacter, 2011; Burgmans et al., 2010; Cabeza et al., 2004; Daselaar et al., 2006; Davis et al., 2008; Giovanello et al., 2010; Kalpouzos, Persson, and Nyberg, 2012; Spaniol and Grady, 2012; St-Laurent et al., 2011; Giovanello and Schacter, 2012). However, only two studies to date have reported greater left vlPFC activity in young versus older adults at retrieval (Giovanello and Schacter, 2012; St-Laurent et al., 2011). Another study reported the opposite age effect (Spaniol and Grady, 2012), a pattern that resembles the age-related under-recruitment of left vlPFC during episodic encoding, and suggests there may be an age-related deficit in left vlPFC during both episodic encoding and retrieval.

In contrast, several studies have reported greater right vlPFC activity in older versus younger adults, when performance was matched between age groups (Cabeza et al., 2004; Giovanello et al., 2010; Grady, McIntosh, and Craik, 2005; Spaniol and Grady, 2012). Verbal stimuli were used in all these studies, and in the Grady, McIntosh, and Craik (2005) study both verbal and pictorial stimuli were employed. In the Cabeza et al. (2004) study, greater right vlPFC activity in older versus younger adults was observed across three verbal tasks: episodic retrieval, a delayed-response working memory task, and a sustained visual attention task. During this study, young adults also activated right vlPFC across tasks, but not to the same degree as older adults. This pattern is similar to what has been found during episodic encoding; however, at encoding this pattern was observed when performance was unmatched between age groups.

Studies have also reported greater activity in left dlPFC in older versus younger adults during episodic retrieval when performance was matched (Burgmans et al., 2010; Davis et al., 2008; Kalpouzos, Persson, and Nyberg, 2012; Morcom, Li, and Rugg, 2007; Spaniol and Grady, 2012). Four studies employed verbal stimuli (Davis et al., 2008; Kalpouzos, Persson, and Nyberg, 2012; Morcom, Li, and Rugg, 2007; Spaniol and Grady, 2012), and one study employed pictorial stimuli of objects and scenes (Burgmans et al., 2010). Overall, greater activity in left dlPFC in older adults has been interpreted as reflecting compensation for reduced neural efficiency within this brain region and for deficits in posterior cortical regions (i.e., the hippocampus) (Morcom, Li, and Rugg, 2007).

Taken together, these findings suggest that when retrieval performance is matched between age groups, task-related increases in left dlPFC and right vlPFC activity in older versus young adults may reflect compensatory over-recruitment in response to neural inefficiency in left vlPFC with age, and in response to deficits in posterior cortical regions such as the hippocampus and occipital cortex. However, Burgmans et al. (2010) reported a negative correlation between left dlPFC activity and object retrieval performance in older adults. Therefore, it remains unclear if left dlPFC over-recruitment in older adults is always indicative of functional compensation. To
help clarify this issue, more studies need to be conducted in which direct correlations between left dlPFC activity and memory performance are examined in young and older adults.

**Parietal Cortex**

**Anatomy**

The human parietal cortex is typically divided laterally into the inferior (IPL) and superior parietal lobes (SPL), and the medial portion is known as the precuneus (Talairach and Tournoux, 1988). The SPL and precuneus comprise BA 7, and anatomical studies in monkeys indicate that both are heavily connected with PFC, with the lateral parietal regions projecting to the principal and arcuate sulci and medial parietal cortex projecting to medial and superior frontal regions (Cavada and Goldman-Rakic, 1989). The IPL is more developed in humans than in other primates (Zilles and Palomero-Gallagher, 2001) and consists of BAs 40 and 39. The IPL has been further subdivided into additional regions based on cytoarchitecture (Caspers et al., 2006) and gyral structure, including the supramarginal and angular gyri. For the purpose of this review we have used the parcellation published by Nelson et al. (2010), which was based on determining areas in the parietal lobe whose activity was related to retrieval success (hits versus correct rejections) and how these regions were functionally connected with the rest of the brain. The set of regions identified by Nelson et al. were SPL (anterior to the intraparietal sulcus), intraparietal sulcus (IPS), angular gyrus (AG), supramarginal gyrus (SMG), and the anterior and posterior IPL (aIPL, pIPL, superior to the SMG and AG). Of these regions, the more posterior ones (IPS, AG, aIPL, pIPL) were directly related to memory, whereas the anterior ones (SPL, SMG) were not. To assign a reported region with age differences to one of these six parietal areas, we determined the proximity of each reported set of coordinates to those reported by Nelson et al. for each region. That is, if a reported region had coordinates that were closest to the IPS as published in Nelson et al., we labeled this region as IPS, regardless of the label ascribed to it in the source paper. We were then able to determine whether parietal age differences were specific to any particular region in the parietal lobe. In addition to these six areas, we also included the precuneus, because age differences have been reported in this area as well (the precuneus was not described by Nelson et al., because their focus was on lateral parietal cortex). We labeled regions as the precuneus if the reported coordinates fell within this region in the MNI152 atlas.

Age-related changes in parietal function and episodic memory encoding

It is not clear that the parietal lobes have a specific role in episodic encoding, except perhaps in learning new spatial routes (Shelton and Gabrieli, 2002). Indeed, a study using transcranial magnetic stimulation (TMS) to interfere with dorsal parietal activity during encoding found little disruption (Rossi et al., 2006). Nevertheless, age differences in parietal activity during encoding are commonly found.
Eleven studies have reported age differences in parietal activity during encoding when older adults performed more poorly than young adults on subsequent memory tests. Reduced parietal subsequent memory effects in AG and SMG have been reported in older relative to younger adults for both pictures (St. Jacques, Dolcos, and Cabeza, 2009) and words (Kim and Giovanello, 2011). However, more often greater subsequent memory effects have been observed in older than in younger adults in the parietal cortex when performance was unmatched between groups. For example, larger subsequent memory effects in IPS were reported for older adults during scene encoding (Dennis et al., 2008; Duzel et al., 2011; Gutchess et al., 2005; St. Jacques, Dolcos, and Cabeza, 2009), in the precuneus for face/name paired associate learning (Miller et al., 2008), and in inferior parietal regions for words (de Chastelaine et al., 2011; Morcom et al., 2003). Additionally, more activity has been found in parietal cortex of older adults during encoding generally (i.e., not related to subsequent memory effects per se) during associative (Sperling et al., 2003) and non-associative (Murty et al., 2009) scene encoding, and during encoding of words and objects (Grady et al., 2006). These age increases during encoding have been found in most regions of parietal cortex, and found bilaterally. Thus, there does not appear to be a consistent pattern of age differences during encoding, at least not based on the type of processing carried out or in the hemisphere that is engaged.

Nevertheless, there may be some specificity in terms of which region of the parietal lobe is more activated by younger versus older adults during encoding. To assess this we have plotted the number of reported age differences in each of the major subsections of the parietal lobes, based on the nomenclature used by Nelson et al. (2010). For encoding (Figure 17.3), it is clear that age differences have been found throughout all parietal areas of interest, although the pIPL and SPL are under-represented. This figure indicates that older adults tend to have more activity for encoding in the IPS and the precuneus, particularly when their performance is worse than that seen in younger adults (red bars). The IPS is functionally connected with dlPFC (Grady et al., 2010; Nelson et al., 2010) and has been implicated in top-down attentional mechanisms (Cabeza et al., 2008; Corbetta, Patel, and Shulman, 2008). Over-recruitment of this region during encoding in older adults might indicate a greater additional demand relative to younger adults. Nevertheless, because all but one of these studies reported better performance in younger adults, there is no evidence that the over-recruitment of the IPS during encoding provided any benefit for later memory, but more engagement of attentional mechanisms may have aided older adults in carrying out the encoding task that was required.

The precuneus is often considered to be part of the default network, which is a set of regions that are more active during internally directed, self-referent thought and have reduced activity during externally driven tasks (Grady et al., 2010; Grigg and Grady, 2010; Gusnard et al., 2001). Research has shown that more activity in this region during encoding is associated with worse subsequent memory (Vannini et al., 2011), and more activity here in older adults suggests less effective encoding, perhaps due to a reduced ability to suppress activity in default regions during encoding (Grady et al., 2006; Miller et al., 2008; Vannini et al., 2012). In general, given the predominance of red bars in Figure 17.3, indicating more activity in older adults associated with worse performance, a tentative conclusion is that over-recruitment of parietal cortex during
encoding probably reflects more engagement of a number of cognitive processes, which do not necessarily support successful memory. However, these conclusions are based on only 11 studies, and further research is needed to corroborate our conclusions.

Parietal activation during encoding when subsequent memory performance is matched  To our knowledge 14 fMRI studies have reported age differences in parietal cortex during encoding. However, only in three of these studies was subsequent retrieval performance matched between older and younger adults (Burgmans et al., 2010; Dennis, Daselaar, and Cabeza, 2007; Leshikar et al., 2010). All three studies reported more activity in younger than older adults in left parietal cortex, although not in the same region. Two of these studies examined activity during encoding per se, rather than examining this activity categorized by whether the encoded item was remembered or forgotten (i.e., the subsequent memory effect). One examined brain activity during paired associate learning of object pairs, and found more activity in the left SMG in younger relative to older adults (Leshikar et al., 2010), and the other found more activity in left IPS in younger adults during encoding of both neutral and emotional scenes (Burgmans et al., 2010). The third found more activity during the successful encoding of words in younger adults in the left precuneus (Dennis, Daselaar, and Cabeza, 2007). In addition to these reductions, Leshikar et al. (2010) also found that older adults activated a number of right parietal regions more than young adults during paired associate encoding, including the AG, precuneus, and IPS. In these studies, more activity was reported in younger than in older adults in left parietal cortex.
Age-related changes in parietal function and episodic memory retrieval

In contrast to encoding, the parietal lobes are quite active during memory retrieval (Spaniol et al., 2009) and have been linked to specific memory processes. One well-known parietal effect in episodic memory retrieval is the so-called “old/new” effect in left parietal cortex that is observed using event-related potentials (ERPs; Rugg et al., 1998). This old/new effect consists of greater positivity in the ERP when participants indicate that a presented stimulus has been seen at study (i.e., they judge the item to be “old”: hits), relative to unseen stimuli (“new” items: correct rejections). Interestingly, studies looking at the parietal old/new effect in aging generally have found that older adults show reduced amplitude of this response (Ally et al., 2008; Angel et al., 2009; Duverne, Motamedinia, and Rugg, 2009b; Friedman et al., 2010; Li, Morcom, and Rugg, 2004; Nessler et al., 2007, 2008). Parietal cortex is also thought to play a role in familiarity, being more active for familiarity judgments than recollection (Cabeza et al., 2008; Vilberg and Rugg, 2008; Wheeler and Buckner, 2004; Yonelinas et al., 2005). Recently there have been suggestions that parietal activity during memory retrieval reflects specific attentional processes that are needed. Dorsal parietal cortex is thought to reflect top-down attention to retrieval search to maintain the relevant goals of the task, whereas ventral parietal cortex is thought to reflect bottom-up responses to retrieved memories (Cabeza et al., 2008; Ciaramelli et al., 2010; Ciaramelli, Grady, and Moscovitch, 2008). This dorsal/ventral distinction is similar to that proposed for attention in general (Corbetta, Patel, and Shulman, 2008; Fox et al., 2006; Shulman et al., 2009), but may not involve exactly the same regions of parietal cortex.

Parietal activation during retrieval when subsequent memory performance is not matched A similar picture of both age increases and decreases was found in studies where older adults performed more poorly than younger adults (12 studies). Parietal activity during word recognition (Dennis, Kim, and Cabeza, 2008; Grady, McIntosh, and Craik, 2005; Velanova et al., 2007), object recognition (Grady, McIntosh, and Craik, 2005), and paired associate retrieval (Tsukiura et al., 2011) was reported to be lower in older adults in a number of areas. Some studies have found reduced parietal activity in some regions in older adults, but increased activity in other areas. For example, Kukolja et al. (2009) tested recall of spatial context and found that younger adults had more activity in IPS whereas older adults had more activity in SMG. Murty et al. (2009) examined scene recognition and found age reductions in a region of the precuneus, but age increases in more superior precuneus regions, as well as in IPS and IPL. Duarte, Graham, and Henson (2010) found reduced AG activity in older adults for object recollection, but more activity in SMG for familiarity in the older group, despite the fact that the older adults had lower measures of both recollection and familiarity. Finally, more activity in older compared to younger adults, in conjunction with age reductions in performance, has been reported for source memory (Duarte, Henson, and Graham, 2008; Morcom, Li, and Rugg, 2007) and context retrieval (Dew et al., 2012).

Thus, as with encoding, there does not appear to be a consistent direction of age difference in episodic retrieval based on the type of retrieval or the kind of information that is retrieved. However, the relatively large number of published studies on memory retrieval allows an assessment of regional specificity in these age
differences. Figure 17.4 plots the number of regions with more or less activity in older adults, using the same nomenclature as in Figure 17.3. For retrieval, there does not appear to be any region where younger adults have a greater tendency to show more activity. However, older adults tend to have more activity than younger adults in IPS, particularly when their performance is as good as that seen in younger adults (Figure 17.4, yellow bars), suggesting that the processes subserved by this region may be compensatory. As noted above, the IPS is thought to be involved in top-down cognitive control, which could indicate a role for attention in supporting successful memory retrieval in older adults. Additionally, its role in familiarity might indicate that more activity in IPS in older adults during retrieval could reflect the tendency for older adults to rely more heavily on familiarity rather than recollection relative to younger adults (e.g., Prull et al., 2006). However, these two roles may actually reflect the same process, as Nelson et al. (2010) suggested that activation of the IPS during familiarity judgments may reflect control processes that are needed when individuals are uncertain about a retrieved memory, or whether a presented item has been previously encoded. The other notable aspect of Figure 17.4 is that the precuneus tends to be over-activated in older adults when their performance is worse than that of younger adults (red bar). As noted above, the precuneus is part of the default network, and older adults show smaller task-related reductions in default network activity when these tasks require responding to external stimuli (Grady et al., 2010; Lustig et al., 2003; Persson et al., 2007; Park et al., 2010). Precuneus over-recruitment in older adults during externally cued memory retrieval would be consistent with this idea of less “deactivation” in default areas with age. Additionally, Miller et al. (2008) found that the degree of precuneus reduction during episodic retrieval correlated with better memory in

![Figure 17.4](image.png)

**Figure 17.4** Pattern of parietal activations in young and older adults during episodic retrieval. This figure summarizes the pattern of parietal cortex activity observed in 21 fMRI studies on age-related differences in retrieval (see text for details of studies reviewed). In this bar graph we report the pattern of left and right parietal activations reported in young and older adults when performance was matched (“matched”) and when performance was not matched (“unmatched”). For each parietal ROI we tallied the number of activations in which young adults activated a region more than older adults, and in which older adults activated a region more than young adults. IPS, intraparietal sulcus; IPL, inferior parietal lobule; SPL, superior parietal lobule; SMG, supramarginal gyrus.
older adults. Thus, it seems that when older adults show over-recruitment of precuneus activity, during either episodic encoding or retrieval, this provides little benefit for memory performance, making a failure to suppress default activity the most likely explanation of this increase. Aside from the precuneus, it appears that parietal over-recruitment during retrieval may have a better outcome for older adults than such activity during encoding (compare yellow and red bars in Figures 17.3 and 17.4). This finding suggests an intriguing aspect of parietal function in older age that deserves further study.

**Parietal activation during retrieval when subsequent memory performance is matched** Nine fMRI studies have reported age-related differences in parietal activation when memory performance was matched between young and older adults. In these studies both over- and under-recruitment of parietal regions in older versus younger adults has been reported. In a study that examined both autobiographical recall and “laboratory” episodic memory (St-Laurent et al., 2011), more activity in younger, relative to older, adults was seen bilaterally in lateral parietal areas and medially in the precuneus. An additional study also reported less precuneus activity in older adults for autobiographical retrieval (Addis, Roberts, and Schacter, 2011). Because the precuneus, along with the rest of the default network, is activated for autobiographical memory and other self-referent tasks (Grigg and Grady, 2010; St-Laurent et al., 2011; Spreng and Grady, 2010), less precuneus activity in older adults during autobiographical retrieval suggests a deficit in engaging this area during recall of personally relevant memories. On the other hand, several additional experiments looking at memory for non-personal memories, such as paired associates (Giovanello and Schacter, 2012) and word recognition (Daselaar et al., 2006), also found reduced precuneus activity in older adults, as well as in lateral parietal areas, despite matched performance in the young and old groups.

However, two studies also found regions in parietal cortex where older adults had more activity, in the AG bilaterally for episodic recall (St-Laurent et al., 2011) and in left SMG for autobiographical recall (Addis, Roberts, and Schacter, 2011). Other studies reporting more AG activity for older adults during memory tasks where performance was matched between groups include those examining face/name recall (Kalpouzos, Persson, and Nyberg, 2012) and word recognition (Davis et al., 2008). Similarly, studies of word recognition also have reported over-recruitment in IPS and IPL by older adults when their memory performance is equivalent to that seen in younger adults (Cabeza et al., 2004; Spaniol and Grady, 2012). Only one study found more SPL activity in older adults than in younger adults with matched performance (Burgmans et al., 2010). Across all of these studies with matched performance, age differences were found in both right and left parietal regions, with no clear predominance of one over the other.

**General Summary of Age-related Changes in PFC and Parietal Function**

Three possible patterns of results are observable when comparing task-related brain activity in young versus older adults. (1) There may be no age-related differences in activation in regional brain activations. (2) There may be less...
brain activity within specific brain regions in older than in younger adults (Brassen et al., 2009; Dulas and Duarte, 2011; Rajah, Languay, and Valiquette, 2010). (3) There may be increased brain activity in specific brain regions in older than in younger adults (Park and Reuter-Lorenz, 2009; Dennis and Cabeza, 2008). Cognitive neuroscientists have often interpreted age-related decreases in brain activity as reflecting a deficit in brain function. In contrast, age-related increases in brain activity have often been interpreted as reflecting functional compensation in the aging brain. However, these cognitive/behavioral interpretations of between-group differences in brain activity can differ based on which neural model of age-related functional change one subscribes to: dedifferentiation (Baltes, Staudinger, and Lindenberger, 1999; Li, Lindenberger, and Sikstrom, 2001), neural inefficiency/CRUNCH model (Cappell, Gmeindl, and Reuter-Lorenz, 2010; Morcom, Li, and Rugg, 2007), or compensatory plasticity (Cabeza, 2002; Greenwood, 2007; Park and Reuter-Lorenz, 2009; Reuter-Lorenz and Cappell, 2008). For example, it is possible that age-related decreases in brain activity may be related to dedifferentiation of function, and/or to deficits in function, and/or they may reflect performance differences between age groups. In contrast, increased brain activity in older versus younger adults may be related to dedifferentiation, neural inefficiency, and/or compensatory plasticity in the aging brain. Therefore, based on functional imaging data alone, one cannot clearly interpret age-related decreases versus increases in regional brain activations.

In this chapter we have investigated the patterns of age-related changes in PFC and parietal cortex activations at episodic encoding and retrieval both when performance was matched between age groups and when it was unmatched, with younger adults performing significantly better on retrieval accuracy. Within the PFC, the majority of studies reported greater activity in older than in younger adults in most PFC regions during encoding and retrieval, regardless of whether performance was unmatched or matched between groups. The few exceptions were: (1) left vlPFC, which young adults activated more than older adults at encoding when performance was unmatched, and at retrieval when performance was matched; (2) right dlPFC and right vlPFC, which young adults activated more at retrieval when performance was unmatched; and (3) right mPFC, which young adults activated more at retrieval when performance was matched. Therefore, there appear to be performance-associated deficits in right PFC at retrieval and in left vlPFC at encoding with age. This pattern may reflect dedifferentiation and/or deficits in neural efficiency and function that limit task-related modulation of these PFC regions when task demands are high. In terms of parietal cortex there did not seem to be any specific region where younger adults consistently had more activity.

In terms of age-related over-recruitment, older adults over-activated several PFC regions, such as left dlPFC, during encoding and retrieval both when performance was matched and when it was unmatched between age groups. This age-related increase in left dlPFC activity may reflect reliance on more abstract relational strategies during encoding and retrieval to compensate for neural inefficiency within the left dlPFC itself and/or for deficits in other PFC and posterior cortical regions (i.e., parietal cortex, hippocampus, and occipital cortex). This compensatory recruitment of left dlPFC may be sufficient for maintaining older adults’ performance on easier
memory tasks, in which performance was matched, but not on harder tasks, in which performance was not matched. A similar argument for compensation can be made for the IPS in the parietal lobe, which was over-activated in older adults for both encoding and retrieval. However, in this region the over-recruitment during encoding was associated with poor performance, whereas during retrieval it was associated with performance equal to that seen in younger adults. Thus, like the abstract relational processes underpinned by left dlPFC, the engagement of the attentional processes in which the IPS participates might be useful for boosting performance in some circumstances, but not others. That is, one could argue that left dlPFC or IPS activity in older adults may not always be compensatory, because at times it may reflect the recruitment of cognitive processes that are deleterious to task performance. For example, if left dlPFC activation reflects the use of abstract relational strategies to support memory performance in elders, it is possible that use of such a compensatory strategy may hinder performance on tasks that require item-specific processing.

Older adults also exhibited greater recruitment in several brain regions identified as being part of the default mode network, such as mPFC and the precuneus. These “over-activations” in older adults likely reflect weaker task-related decreases in these brain regions, and may contribute to age-related deficits in memory encoding and retrieval. For example, several studies reported age-related increases in mPFC or precuneus activity at retrieval when performance was unmatched between age groups, and concluded that this may reflect reduced attentional focus in older adults during task performance.

As this review makes clear, it is still difficult to explain exactly why older adults have different patterns of brain activity compared to younger adults. However, we have uncovered some interesting aspects of age differences in our two brain areas of interest. First, older adults frequently have more activity in PFC than young adults, consistent with earlier work prior to 2003. There is now enough evidence to state with confidence that this activity is not always compensatory, if one defines this based on whether older adults can perform the memory task as well as younger adults. This observation suggests that over-recruitment of PFC is sometimes either an inefficient use of neural resources or a less selective use of such resources. Second, parietal cortex is also over-recruited by older adults, but this seems only to be beneficial for performance if it happens at retrieval. This differs from the results seen for PFC, which indicate that over-activation of PFC by older adults during both encoding and retrieval can be associated with good task performance. For both PFC and parietal cortex, it is likely that at least some of the age differences in activity during episodic memory tasks reflect the influence of older age on cognitive control processes rather than on memory processes per se.

Conclusions

There are a number of factors that can potentially influence cognitive aging and which we have not considered here. These include, but are not limited to, health factors such as cardiovascular risk and risk for dementia, genetics, and life experience. For example, parietal over-recruitment in older adults has been linked to apolipoprotein (ApoE) risk genes...
and increased blood pressure (Braskie, Small, and Bookheimer, 2010), and both altered function of the default network (Hedden et al., 2009; Oh et al., 2011; Sheline et al., 2010; Vannini et al., 2011) and cognitive decline (Storandt et al., 2010) have been linked to amyloid deposition in the brains of older adults.

Additionally, we have focused here on age differences as they occur in two brain areas without considering the larger picture of functional interactions among these areas. However, the field may find that using a network approach will ultimately be more useful than considering brain regions in isolation. For example, age differences in several brain networks involving parietal cortex and PFC have been reported, including the default network (Andrews-Hanna et al., 2007; Grady, Grigg, and Ng, 2012; Grady et al., 2010; Park et al., 2010), and other networks engaged during cognitive tasks (Grady et al., 2010; Rajah, Languay, and Grady, 2011; Wang et al., 2010). Measures of functional connectivity are related to performance in both younger and older adults (Andrews-Hanna et al., 2007; Kelly et al., 2008), suggesting that the integrated activity among brain regions is important for behavior and indeed may be more important than activity in any one brain region alone. Experiments looking at functional connectivity in aging are becoming more frequent in the literature and hold great promise for our understanding of cognitive aging.

Furthermore, we have not emphasized here the studies that have assessed individual differences in brain activity in older adults and how these relate to performance, although such studies exist (e.g., Davis et al., 2008; McIntosh et al., 1999; Rajah, Languay, and Grady, 2011). Future fMRI studies of cognitive aging and memory should aim at directly examining correlations between regional patterns of activity and task performance in low- versus high-performing elders. Results from these studies will help us better understand whether over-recruitment of PFC or parietal cortex in general is beneficial to performance, or if over-activation in some regions reflects deleterious effects of aging on memory function.

Finally, it is notable that the majority of studies discussed in this chapter employed cross-sectional designs. Thus, the observed between-group differences in behavior or brain structure/function may not be due to the factor of age, but to developmental, historical, and other cohort factors unique to each group. One cannot determine from cross-sectional designs if age alone contributes to the group differences observed in cross-sectional fMRI studies of aging and episodic memory; however, comparisons of in-vivo volumetric and fMRI studies using cross-sectional versus longitudinal methods have yielded similar results (Fotenos et al., 2005; Kramer et al., 2007; O’Brien et al., 2010; Raz et al., 1997, 2005). Therefore, we argue that longitudinal designs are optimal for studying aging; but results from cross-sectional studies play an important role in providing an initial exploration in the most efficient, economical, and feasible manner.

References


