Episodic Memory Encoding and Retrieval in the Aging Brain

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DOI:10.1093/acprof:oso/9780199372935.003.0013

Abstract and Keywords

The current chapter, Episodic memory encoding and retrieval in the aging brain, reviews event-related functional MRI (fMRI) studies of aging and episodic memory—the cognitive domain most affected in healthy aging. Within, we provide summaries of studies of subsequent memory (i.e., encoding success and failure), retrieval success and failure, and functional connectivity that compare older adults to younger adults. These findings are further considered in the context of prominent hypotheses regarding differences in neural activity in aging, such as compensation, hemispheric asymmetry (HAROLD), and the posterior-to-anterior shift (PASA). Lastly, methodological limitations of existing studies and future directions for the field of cognitive neuroscience of aging and episodic memory are discussed.

Keywords: fMRI, memory, encoding, retrieval, aging

With healthy aging comes a host of cognitive changes. Compared to young adults (YAs), older adults (OAs) are impaired in many cognitive abilities, including episodic memory, executive function, attention, and processing speed, whereas abilities such as language and semantic knowledge are relatively preserved (Light, 1991; Salthouse, 2004). Functional neuroimaging methods allow researchers in the new domain of cognitive neuroscience of aging to associate age-related differences in cognition and brain function. In particular,
techniques such as event-related fMRI can identify age effects on brain activity associated with successful vs. failed cognitive performance.

The current chapter reviews event-related fMRI studies of episodic memory encoding and retrieval, as well as fMRI studies of episodic-memory-related functional connectivity. Before turning to these studies, we first provide a brief summary of relevant background areas: (1) episodic memory and its neural mechanisms; (2) age-related episodic memory decline and its neural mechanisms; (3) task-independent age effects on brain activity and the concept of compensation.

Episodic Memory and its Neural Mechanisms

Episodic memory refers to conscious memory for personally experienced past events (Tulving, 1984). This includes memory for what events happened (item memory), as well as memory for where, when, and how they happened (context memory). The term (p.302) associative memory is broader than context memory, as it includes both item-context and item-item associations, and for this reason, we prefer it in this review. We use “associative memory” and “item memory” to refer to forms of memory while the terms “associative tasks” and “item tasks” refer to memory tests that explicitly test for associative or item memory. Associative tasks include context memory (spatial, temporal, etc.) and associative recognition (e.g., word pairs) tests, and item tasks, old/new item recognition tests. The distinction between forms of memory and tasks is important because tasks are not process pure. For example, even if participants are only asked to decide if an item is old or new, if they can retrieve associations about the item, they can use it infer or confirm the item decision (e.g., remembering where it happened confirms that it happened). It is also important to note that the associative and item distinction largely overlaps with the recollection and familiarity distinction (Yonelinas, 2002). Recollection can be generally defined as associative memory plus item memory, whereas familiarity as item memory without associative memory. The Remember/Know recognition paradigm allows us to isolate the associative component in recognition tests by contrasting “Remember” (i.e., associative plus item) to “Know” (i.e., item only) responses. Similarly, because high-confidence “old” recognition responses are thought to reflect recollection (Yonelinas, 2001; Koen and Yonelinas, 2010), they can sometimes be used as an associative measure when compared to low-confidence “old” recognition responses (item only) or all other responses.

Episodic memory is primarily dependent on the medial temporal lobe (MTL), prefrontal cortex (PFC), and posterior cortical regions, as well as on their interactions (Simons and Spiers, 2003; Eichenbaum et al., 2007; Cabeza et al., 2008; Uncapher and Wagner, 2009; Rugg and Vilberg, 2013). During encoding, MTL—and particularly the hippocampus (HPC)—is assumed to store mnemonic representations as well as pointers to posterior cortical memory traces (e.g., visual cortex for visual memory representations), and during retrieval, MTL
mediates the reactivation of posterior cortices and access to stored memory traces (Alvarez and Squire, 1994; McClelland et al., 1995; Nadel et al., 2000; Sutherland and McNaughton, 2000; Norman and O’Reilly, 2003; Danker and Anderson, 2010; Ritchey et al., 2013). According to a three-process MTL model (Davachi, 2006; Eichenbaum et al., 2007), perirhinal cortex primarily mediates memory for items, parahippocampal cortex, memory for contexts, and HPC, memory for associations between items and contexts (i.e., associative binding). During encoding, ventrolateral PFC is assumed to mediate controlled semantic processing (Prince et al., 2007) while dorsolateral PFC is thought to regulate organizational processes (Blumenfeld and Ranganath, 2007). During retrieval, dorsolateral PFC is presumed to mediate memory search and monitoring processes (Achim and Lepage, 2005; Hayama and Rugg, 2009). In posterior cortices, modality-specific regions (visual, auditory, etc.) are assumed to hold perceptual memory representations, and lateral/ventral temporal cortices, semantic memory representations. Dorsal parietal cortex (DPC; including medial precuneus) is hypothesized to mediate top-down attention during encoding and retrieval (Cabeza, 2008; Uncapher and Wagner, 2009), whereas ventral parietal cortex (VPC) is presumed to mediate bottom-up attention to (Cabeza et al., 2008) or maintenance of (Vilberg and Rugg, 2008) recovered memories during retrieval.

(p.303) Age-Related Episodic Memory Decline and its Neural Mechanisms

Episodic memory is arguably the cognitive function most affected by healthy aging and early Alzheimer’s disease. However, not all forms of episodic memory are equally affected: whereas associative deficits in healthy OAs are substantial, item deficits are small and usually nonsignificant (for reviews, see Kausler, 1994; Spencer and Raz, 1995; Yonelinas, 2002; Koen and Yonelinas, 2016). The dissociation between associative and item memory is one of the main topics in this review. According to a resource deficit hypothesis (Craik, 1986), age-related associative deficits reflect a reduction in executive control and attentional resources, which are more critical for associative than item memory. Consistent with this hypothesis, when control resources are reduced in YAs using a divided attention manipulation, YAs’ memory performance resembles that of OAs (Craik and Byrd, 1982; Rabinowitz et al., 1982). According to the associative deficit hypothesis (Naveh-Benjamin, 2000), associative impairments in OAs reflect a deficit in memory binding, which is essential for associative but not item memory. There is a growing agreement that both executive control and binding deficits are required to explain age-related associative impairments (Castel and Craik, 2003; Naveh-Benjamin et al., 2004). In keeping with this idea, factor analyses of OAs’ associative deficits have identified two quasi-orthogonal factors: an “executive” factor that correlates with tests primarily dependent on PFC function, and a “memory” factor that correlates with tests primarily dependent on MTL function (Glisky et al., 1995; Glisky et al., 2001; Prull et al., 2006).
This two-factor model fits well with evidence that PFC and MTL are among the brain regions most affected by healthy aging. PFC displays the largest age-related atrophy in the brain, (Raz et al., 1997; Raz, 2000; Raz et al., 2005) (Raz et al., 1997; Raz, 2000; Raz et al., 2005) and its function is also impaired by age-related deficits in dopamine function (Bäckman and Farde, 2004). Within MTL, age-related atrophy is substantial in HPC but minimal in perirhinal cortex (Raz et al., 2005). Given that HPC has been linked to associative memory and perirhinal cortex to item memory (Davachi, 2006; Eichenbaum et al., 2007), this atrophy pattern fits well with the aforementioned associative-item dissociation. However, brain regions cannot operate independently, and hence episodic memory also depends on the integrity of white-matter tracts linking regions such as PFC and MTL to each other and to the rest of the brain. Thus, it is not surprising that age-related episodic memory deficits are significantly correlated with age-related white matter decline (Davis et al., 2009; Kennedy and Raz, 2009; Charlton et al., 2010; Daselaar et al., 2015).

Task-Independent Age Effects on Brain Activity and the Concept of Compensation

Whereas reduced activity in OAs compared to YAs is usually attributed to some cognitive deficit, increased activity in OAs is typically attributed to “compensation” (for reviews, see Dennis and Cabeza, 2008; Cabeza and Dennis, 2013). Some age-related decreases and increases are specific to an individual cognitive domain, such as associative memory, but others have been found to be reliable across several cognitive domains. One of these task-independent effects is the posterior–anterior shift in aging (p.304) or PASA (Davis et al., 2008), which refers to an age-related decrease in occipito-temporal activity coupled with an age-related increase in PFC activity. PASA was first found in a visual matching task by Grady et al. (1994), who suggested that PFC increases compensate for occipito-temporal decreases. Consistent with this hypothesis, there is evidence that PFC activations are negatively correlated with occipito-temporal activations (Cabeza et al., 2004; Davis et al., 2008), and are positively correlated with task performance (Davis et al., 2008).

Another task-independent effect is the Hemispheric Asymmetry Reduction in OLDer Adults or HAROLD, which refers to more bilateral PFC activations in OAs than YAs (Cabeza, 2002). HAROLD was first reported by Cabeza et al. (1997), who suggested that OAs compensate for age-related decline by recruiting both hemispheres instead of one. We, and others, have suggested that the compensation account of HAROLD is supported by evidence that bilateral recruitment is positively correlated with cognitive performance across participants (Reuter-Lorenz et al., 2000; Cabeza, 2002; Rosen et al., 2002). However, we no longer believe that correlations across participants provide good evidence in favor of compensation. Similarly, we believe that negative across-subject correlations—such as between greater PFC activity and performance, which have been couched as evidence for PFC dysfunction (e.g., Rypma and D’Esposito, 2000; Rypma et al., 2007; Stern et al., 2012; McDonough...
et al., 2013)—should also not be attributed to compensation. Given accumulated evidence that both high- and low-performing OAs can display compensatory activity, we now believe that positive correlations with performance support compensation only when they are established within-subjects, as is now possible using event-related fMRI paradigms.

It is also, however, important to note alternative viewpoints of age-related increases in activity. One such viewpoint is dedifferentiation, which posits that older adults have difficulty in recruiting specialized neural mechanisms (Li et al., 2001; Park et al., 2004). This explanation is most commonly supported by evidence from studies of different visual stimuli (Park et al., 2004; Goh et al., 2010; Park et al., 2012) but is also reported in studies of different memory processes (Dennis and Cabeza, 2011; Wang et al., 2015). Alternatively, it has also been proposed that age-related increases may reflect neural inefficiency (Rypma and D’Esposito, 2000; Reuter-Lorenz and Lustig, 2005; Morcom et al., 2007; Nyberg et al., 2014).

Current data do not allow for a clear consensus as to which of these explanations account for age-related increases, although we also note that the concept of compensation is not necessarily incompatible with other explanations of age-related increases in activity. Specifically, dedifferentiation and neural inefficiency can both occur concurrently with compensation. For example, compensatory activity may occur in cohort with dedifferentiation (e.g., Burianová et al., 2013). Additionally, compensatory activity need not be efficient in the same way that using a cane to walk is compensatory but not necessarily efficient.

In the case of episodic memory, event-related fMRI paradigms—as opposed to blocked designs—allow researchers to identify activity associated with successful memory processes both during encoding and during retrieval. During encoding, one can identify Subsequent Memory Effects (SMEs) by comparing activity for subsequently remembered vs. forgotten items (Paller and Wagner, 2002). During retrieval, one can identify Retrieval Success Effects (RSEs) by comparing hits to correct rejections or misses. SMEs and RSEs are assumed to reflect successful encoding and retrieval processes respectively. We interpret larger SMEs/RSEs for OAs than YAs as evidence for compensation—regardless of whether these effects are displayed by high- or low-performing OAs. We do note, however, that these effects may also be interpreted as neural inefficiency (regardless of whether it is compensatory in nature). Thus, the current review focuses on age effects on episodic SMEs and RSEs.

Event-Related fMRI Studies of Episodic Memory and Aging
The fact that OAs are more impaired in associative than item memory (Spencer and Raz, 1995) may reflect difficulties with encoding, retrieval, or both. We review the effects of aging on SMEs and RSEs in separate sections, and then
turn to the effects of aging on “negative” SMEs (nSMEs) and RSEs (nRSEs), which occur when successful memory is associated with reduced rather than increased activity. Throughout the review, we interpret age-related increases and decreases relative to YAs. That is, we consider increases to be compensatory given that they indicate an effect is larger in OAs than YAs; if a region typically shows SMEs in YAs, then increased SMEs in OAs could be interpreted as compensation, and if a region typically shows nSMEs in YAs, then increased nSMEs in OAs could also be interpreted as compensation. Finally, we review evidence regarding age effects on connectivity during episodic memory tasks.

Studies were selected via a pubmed and google scholar search with the following search query: “(fmri OR ‘functional mri’ OR ‘functional magnetic resonance imaging’) AND ‘event related’ AND (aging OR age OR older) AND (memory OR ‘recognition memory’).” Studies were limited to visual stimuli and excluded from the tables reported below if whole brain results or if “memory success” contrasts (e.g., hit versus miss) were not reported.

Subsequent Memory Effects (SMEs)

Table 12.1 displays the results of studies investigating age effects on SMEs. Most studies compared high-confidence hits vs. misses but some exceptions are noted below. To simplify the description of the findings, brain regions are classified very coarsely. Parietal cortex is divided into VPC (Brodmann Areas – BAs 39 and 40) and DPC (BA7 and precuneus). The occipito-temporal pathway (OTP) includes medial and lateral occipital cortex, ventral and lateral temporal cortex, as well as two MTL regions, the parahippocampal gyrus (PHG)—including perirhinal and parahippocampal cortex and HPC. The table also includes a posterior midline region (PMR: retrosplenial and posterior cingulate cortices), the insula, and the anterior cingulate cortex (ACC). Finally, PFC is divided into four large areas: posterior (i.e., premotor, BAs 6 and 8), ventrolateral (BAs 44, 45, and 47), dorsolateral (BAs 9 and 46), and anterior (BAs 10 and 11, including anteromedial) regions. For each of these regions, there are separate columns for the left and right hemisphere. (p.306)

Table 12.1 Subsequent Memory Effects (SMEs)
As for the symbols in Table 12.1, small black diamonds indicate a significant SME in both YAs and OAs with no difference between these groups. Squares indicate that there was a significant SME in only one group (black squares for YAs, white squares for OAs) but no SME x age interaction. Lastly, circles indicate that the interaction was significant either because the SME was smaller in OAs than YAs (black circles) or because it was larger in OAs than YAs (white circles). If the interaction was driven by a large negative SME in one group and a nonsignificant SME in the other, the finding is included in Table 12.3 and discussed in the section on negative SME/RSE effects. For the sake of brevity, black squares/circles are referred to as “age-related decreases” or just “decreases,” and white squares/circles, as “age-related increases” or simply “increases.”

Depending on the encoding and retrieval tasks employed, SMEs may predict item performance or associative performance. Item SMEs and associative SMEs are displayed at the top and bottom panels of Table 12.1, and at the bottom of each panel, a greyed row identifies “recurrent” findings. “Recurrent” is defined as an effect (e.g., increase) reported (1) by at least 25% of the studies in the category, and (2) twice as frequently as the opposite effect (e.g., decrease). Given that there were no notable between-age effects in the left or the right hemisphere (e.g., age-related increases or decreases were not more apparent in one hemisphere than the other), recurrent findings were collapsed across hemispheres. Additionally, we also note that the tables do not display hemispheric asymmetry differences (i.e., HAROLD) and studies that report it are mentioned in the text. For Table 12.1 and all subsequent tables, we categorized imaging contrasts as item memory or associative memory primarily based on the task, unless it specifically tested recollection (which approximates associative
memory) or familiarity (which approximates item memory). Given the caveat that memory tasks are not process pure, we consider whether associative contamination in item tasks—or vice versa—may account for some of the observed patterns across studies in the General Discussion.

**Item Memory SMEs (Item SMEs)**

As illustrated by the bottom row of the item SME panel, these studies yielded four recurrent findings; compared to YAs, SMEs in OAs often showed (1) decreases in OTP (occipital cortex, PHG, and/or HPC), (2) increases in dorsolateral and anterior (except for scene studies) PFC, (3) decreases in DPC, and (4) increases in VPC (except in face/object studies). Taken together, the first two effects constitute the PASA pattern. We will consider the PASA pattern and DPC decreases in the General Discussion. Here, we focus on interesting item memory findings. We group these findings according to the stimuli used (as in Table 12.1: scenes, words, and faces/objects).

Age-related SME increases in VPC are noteworthy given that in YAs, VPC tends to exhibit negative SMEs (Cabeza, 2008; Cabeza et al., 2008; Uncapher and Wagner, 2009). Like other default mode network regions, VPC tends to be deactivated during demanding cognitive tasks (Buckner et al., 2008). There is evidence that healthy OAs and AD patients (Lustig et al., 2003; Persson et al., 2007) may not display deactivations in some default mode network regions. We will return to this issue in the section on negative SMEs and RSEs.

(p.308) Word studies showed prominent SME increases in PFC regions. Interestingly, several of these studies found HAROLD (these findings cannot be seen in Table 12.1, which does not display lateralization differences). For example, in Morcom et al. (2003), SMEs in ventrolateral and dorsolateral PFC were left-lateralized in YAs but bilateral in OAs. This HAROLD finding was replicated by Duverne et al. (2009) and Dennis et al. (2007a) in the true memory condition. Another finding that is not displayed in Table 12.1 is from one study (Dennis et al., 2007b) that found PFC increases when SMEs were measured at the trial level (transient activity), but decreases when they were measured at the block level (sustained activity). The authors attributed the decrease in block-level SMEs to a sustained attention deficit. Turning to OTP, one study (Dennis et al., 2007a) found that increased left temporal activity in OAs predicted subsequent false memory for associated words, possibly reflecting OAs’ greater reliance on semantic gist.

Finally, studies using faces/objects showed the PASA pattern but also two different patterns than studies using scenes and words: they did not show any effect in parietal cortex and showed increases in insula and ACC. The lack of parietal effects might reflect the fact that faces/objects are primarily processed by the ventral pathway (OTP). Both studies using faces reported reduced SMEs in the amygdala (Dennis et al., 2008b; Fischer et al., 2010), which is a region
frequently activated by face stimuli (Breiter et al., 1996; Vuilleumier et al., 2001; Fusar-Poli et al., 2009). Insula increases were found in studies using emotional stimuli (Kensinger and Schacter, 2008; Fischer et al., 2010), consistent with its role in emotion. The ACC increases are consistent with similar increases in associative SME studies.

**Associative Memory SMEs (Associative SMEs)**

In addition to DPC decreases, associative SME studies also report recurrent SME increases in ACC and decreases in OTP and dorsolateral PFC. Despite the variability of associative SME findings, it is worth noting a few interesting findings. First, evidence of dorsolateral PFC decreases (Dennis et al., 2008b; Miller et al., 2008; Morcom et al., 2010; Dulas and Duarte, 2011; Kim and Giovanello, 2011; Bangen et al., 2012) likely reflects deficits in executive functions related to associative encoding. Two studies investigated age effects on face-name associative memory (Miller et al., 2008; Bangen et al., 2012), which is an important topic given OAs’ frequent complaints about difficulties remembering people’s names (Zelinski and Gilewski, 1988; Leirer et al., 1990). Similar to item SME studies, both showed a PASA pattern (i.e., occipital decreases coupled with anterior PFC increases). Bangen et al. (2012), also found a HAROLD pattern as PFC SMEs were left lateralized in YAs but bilateral in OAs.

The two studies investigating word-pair associative memory yielded inconsistent findings: Kim and Giovanello (2011) found mostly SME decreases in OTP and PFC, whereas de Chastelaine et al. (2011) found mostly SME increases in these regions, largely driven by negative SMEs in YAs. Interestingly, in the Kim and Giovanello (2011) study, there was an SME increase in perirhinal cortex (included in PHG column) that is consistent with evidence of age-related perirhinal compensation during retrieval (Daselaar et al., 2006b), as discussed later in that section.

Like Bangen et al. (2012), the scene recollection study by Duzel et al. (2011) and the context recognition study by Dulas and Duarte (2011) found SME increases in HPC. This finding is difficult to explain because it is generally assumed that one of the causes of associative deficits in OAs is a binding impairment during encoding due to HPC dysfunction (e.g., Mitchell et al., 2000). However, HPC increases during associative encoding are consistent with similar findings during associative retrieval, as discussed later in that section. One possibility is that it reflects neural inefficiency or compensation.

Lastly, it is important to note a recurrent null finding—that is to say, three studies reported one or fewer age differences across the entire brain. Interestingly, two of these studies utilized objects (Kukolja et al., 2009; Dulas and Duarte, 2014) while the third utilized object-scene pairs (Leshikar and Duarte, 2014). Although object SME studies did not show a similar pattern,
these results indicate that associative SME differences may be minimized when examining the context under which objects are encoded.

**Age Effects on SMEs: Summary and Discussion**

Similarities and differences between item and associative SME studies can be identified by comparing the bottom rows in the two panels in Table 12.1. Regarding similarities, both item and associative SME studies frequently showed occipital decreases and recurrent DPC decreases. Additionally, item SME studies exhibited a PASA pattern (i.e., OTP decreases and dorsolateral and anterior PFC increases) that was also observed in face-name associative SME studies. We will return to PASA and DPC findings in the General Discussion. Regarding differences in recurrent findings, one disparity is between dorsolateral PFC increases in item studies but decreases in associative studies. This is consistent with evidence that associative memory is more impaired than item memory in OAs. Another is between MTL decreases (both HPC and PHG) in item studies but not in associative studies. Given that SME decreases suggest impaired encoding processes, this difference is surprising because OAs tend to be more impaired in associative than item memory. However, the MTL discrepancy could reflect differences in the stimuli and/or methods used by item and associative studies rather than true differences between item and associative memory.

In fact, the study by Dennis et al. (2008b), which directly compared age effects on SMEs for associative vs. item memory within-participants, found the opposite pattern. The associative and item conditions used comparable stimuli (face-scene pairs vs. individual faces or scenes) and retrieval tests (associative recognition vs. old/new recognition). The results showed significant age-related SME reductions in HPC for associative but not item memory (see Figure 12.1). This was the only associative encoding study to report a significant SME x age interaction (all other studies reported SMEs in only one group but not a significant interaction). Thus, it is possible that the MTL difference in item vs. associative studies in Table 12.1 is more apparent than real and will disappear with the addition of more studies. The same might be true for PFC differences.

**Retrieval Success Effects (RSEs)**

The top panel of Table 12.2 lists item studies while the middle and bottom panels list associative studies. The middle panel includes studies that used recognition tests sensitive to associative memory (associative recognition), such as Remember/Know and (p.310) associative recognition tasks, whereas the bottom panel includes studies that used context memory tests (context memory). Even though both associative recognition and context memory tests are assumed to measure associative memory, the latter are more dependent on the generation and monitoring of contextual information. Similarities and differences among the three groups of studies are discussed in the RSE
summary and discussion section; the sections on each study only mention a few noteworthy findings.

**Item Memory RSEs (Item RSEs)**

As indicated by the bottom row of the item RSE panel, OAs exhibited recurrent RSE decreases in DPC, temporal cortex, insula, ACC, and PFC regions, and increases in occipital cortex. Interestingly, in Daselaar et al. (2003) study, RSE decreases in the insula were observed in both high- and low-OAs, suggesting that decreases generalize across individual differences. Dennis et al. (2008a) linked false memories for words in OAs to left temporal increases, which they attribute to greater OAs’ reliance on semantic gist in keeping with the role of left temporal cortex in semantic processing. In contrast, a study using objects (Duarte et al., 2010) found mostly decreased false memory SMEs in OAs, particularly in PFC, fusiform, and DPC. The authors suggest that these decreases affect the ability to discriminate between studied and unstudied stimuli, and may in part explain memory deficits in OAs.

**Associative Memory: Recognition Tasks (Associative Recognition RSEs)**

All recurrent findings in associative recognition studies were RSE reductions, including decreases in parietal, OTP, midline, and PFC regions. The most consistent neural correlate for reduced associative retrieval in OAs was an RSE decrease in VPC (p.311) (p.312) (Daselaar et al., 2006b; Duarte et al., 2008; Duarte et al., 2010; Giovanello et al., 2010; Tsukiura et al., 2011; Dennis et al., 2014). Tsukiura et al. (2011) reported RSE reductions in several regions associated with associative memory, including parietal cortex, dorsolateral PFC, HPC, and PMR when retrieving face-name/job pairs. In fact, HPC decreases were reported by other studies as well (Daselaar et al., 2006b; Giovanello et al., 2010), consistent with associative deficits in aging. Interestingly, studies reported PHG decreases for during both true (Angel et al., 2013; McDonough et
al., 2014) and false (Dennis et al., 2014) recollection. Although Dennis et al. (2014) associated false recollection in OAs with decreases in multiple regions including PHG, Giovanello et al. (2010) associated it with a PHG increase. Another inconsistency emerges from Wang et al. (2016), which did not report any age differences, although this lack of differences is similar to associative studies examining object SMEs.

**Table 12.2 Retrieval Success Effects (RSEs)**

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<thead>
<tr>
<th>First author Year</th>
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<th>Stimulus</th>
<th>Pos</th>
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<td>H &gt; CR</td>
<td>Y = O High-OAs</td>
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<td>word</td>
<td>H &gt; CR</td>
<td>Y = O Low-OAs</td>
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<tr>
<td>Dennis 2008a</td>
<td>16/17</td>
<td>word</td>
<td>H1 + H2</td>
<td>Y = O</td>
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<tr>
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<tr>
<td>Duarte 2010</td>
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<td>object</td>
<td>H1 + CR</td>
<td>Y = O</td>
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<td>Doeshen 2013</td>
<td>27/13</td>
<td>face</td>
<td>H1 + CR</td>
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**Recruitment of R-P(recognition) findings**

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**Recruitment of R-P(recognition) findings**

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<td>Y = O</td>
<td>High-OAs</td>
</tr>
<tr>
<td>Duarte 2014</td>
<td>17/16</td>
<td>object</td>
<td>comb1 &gt; comb2</td>
<td>Y = O</td>
<td>all cond</td>
</tr>
<tr>
<td>Duarte 2016</td>
<td>17/16</td>
<td>object</td>
<td>comb1 &gt; comb2</td>
<td>Y = O</td>
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<tr>
<td>Koldo 2005</td>
<td>25/25</td>
<td>object</td>
<td>Comb comb &gt; combM</td>
<td>Y = O</td>
<td>false</td>
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<tr>
<td>Menon 2007</td>
<td>17/16</td>
<td>object</td>
<td>comb1 &gt; comb2</td>
<td>Y = O</td>
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<td>Menon 2016</td>
<td>17/16</td>
<td>object</td>
<td>comb1 &gt; comb2</td>
<td>Y = O</td>
<td>Low-OAs</td>
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<td>Oldengouhse 2014</td>
<td>22/18</td>
<td>word</td>
<td>comb1 &gt; comb2</td>
<td>Y = O</td>
<td>all cond</td>
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<td>Oldengouhse 2014</td>
<td>22/18</td>
<td>word</td>
<td>comb1 &gt; comb2</td>
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**Recruitment of R-P(recognition) findings**

**Notes:**
- OA = OA (SM)
- OA = OA (SM)
- OA = OA (SM)
- OA = OA (SM)
- OA = OA (SM)
- OA = OA (SM)
- OA = OA (SM)

**Figure 12.2** OAs showed reduced associative-related HPC activity, but increased item-related rhinal activity. These results suggest that OAs compensate for impaired associative processes in HPC by over-recruiting item processes in rhinal cortex.

**Associative Memory: Context Memory Tasks (Context RSEs)**

In stark contrast to associative recognition studies, context studies reported recurrent RSE increases in most brain regions, including parietal, OTP, ACC, and PFC areas. Five studies (Morcom et al., 2007; Dew et al., 2012; Dulas and Duarte, 2012; Dulas and Duarte, 2014; Leshikar and Duarte, 2014) examined context memory for encoding condition (e.g., in which encoding task was this item studied?). Within this group, RSE increases in parietal and most PFC regions disappeared when context memory misses were used as controls instead of correct rejections, and for two of them—one using objects (Dulas and Duarte, 2014) and the other using object-scene pairs (Leshikar and Duarte, 2014)—no age differences were reported. The difference is particularly clear in the two contrasts from Dulas and Duarte (2012), in which the context memory hits were the same and only the control condition was different. (p.313) These findings suggest that parietal and PFC increases for context memory could be partly driven by age-related decreases in control correct rejections. Three studies investigated context memory for background, spatial location, and temporal order. The background memory study by Duverne et al. (2008), which used correct rejections as a control, found not only parietal increases but also decreases in PFC. The object spatial location study by Kukolja et al. (2009) only found HPC decreases (and was the only study to report HPC decreases), the finding most memory models would predict for age effects on associative memory.

**Age Effects on RSEs: Summary and Discussion**

In this section, we summarize and discuss similarities and differences between item memory (top panel of Table 12.2), associative recognition (middle panel), and associative context (bottom panel) studies. Beginning with the comparison between item and associative recognition, both types of studies found RSE decreases in DPC, temporal cortex, ACC, and PFC regions. Both temporal and PFC decreases are consistent with the PASA pattern. Turning to differences, several regions showed reduced RSEs in associative but not item recognition studies, consistent with behavioral evidence that OAs are more impaired in associative than item memory. One of the regions that showed RSE reductions for associative but not item recognition was VPC, which fits well with evidence linking this region to associative memory and recollection (Cabeza et al., 2008; Vilberg and Rugg, 2008). Occipital cortex and PMR also showed more reductions for associative than item recognition, perhaps reflecting the difficulty of associative recognition tasks. The finding of HPC decreases in associative but not item recognition studies is consistent with evidence that HPC is significantly impaired by aging (Raz et al., 2005) and is more critical for associative than item
memory (Davachi, 2006; Eichenbaum et al., 2007). PHG decreases were also observed, which may reflect a deficit in recollecting contextual information.

Given that it relates to nRSE effects reviewed in the next section, it is worth noting here that although HPC is associated with associative memory and recollection, perirhinal cortex, another MTL region, is associated with item memory and familiarity (Davachi, 2006; Eichenbaum et al., 2007). Consistent with the idea that OAs are impaired in associative but not item memory, aging has different effects on retrieval activity in these two regions. Whereas Table 12.2 shows that HPC effects related to associative memory were reduced in OAs, Table 12.3 below shows that perirhinal effects related to familiarity were actually increased in OAs (i.e., the nRSEs were increased). For example, Daselaar et al. (2006b) compared the effects of aging on the responses of HPC and perirhinal cortex to associative memory in the form of recollection and item memory in the form of familiarity. Recollection-related activity was quantified by the exponential rate, and familiarity by the slope of the linear decreases (Brown and Aggleton, 2001; Henson et al., 2003; Daselaar et al., 2006a; Montaldi et al., 2006; Wang et al., 2014). As illustrated by Figure 12.2, this contrast yielded a clear cross-over dissociation: OAs showed a reduction in an associative-related effect in HPC, but an increase in an item-related effect in perirhinal cortex. The authors suggested that OAs compensated for deficits in HPC-mediated recollection by relying more on perirhinal-mediated familiarity. (p.314) (p. 315) This interpretation was supported by functional connectivity data and by a logistic regression analysis showing that perirhinal cortex had a stronger effect on recognition accuracy in OAs than in YAs.

Table 12.3 Negative SMEs and RSEs
Finally, the most dramatic difference effect in Table 12.2 is that associative recognition showed mainly RSE decreases whereas context studies displayed primarily RSE increases. On the basis of preexistent hypotheses, one would have expected that the main difference between the three panels of Table 12.2 would be between associative and item memory, not between two types of associative memory. As mentioned above, one speculative explanation for some RSE increases in context studies is the use of correct rejections as the control condition, as several of the increases seem to disappear when context misses are used as controls instead of correct rejections (e.g., Dulas and Duarte, 2012). RSE increases could partly reflect a reduced novelty response for correct rejections in OAs. In a study specifically examining novelty responses, YAs but not OAs exhibited greater activity for correct rejections in OTP and ACC; moreover, the region showing the strongest novelty effects in OAs was ventrolateral PFC (Bowman and Dennis, 2015). Consistent with this, OTP and ACC exhibit RSE increases in many context studies that compare context hits to correct rejections, while ventrolateral PFC generally does not exhibit RSE increases (Table 12.2). However, this account cannot explain why the studies that used context misses also yielded mostly increases, rather than mostly decreases as in associative recognition studies. We will return to the marked difference between associative and context recognition findings in the General Discussion.

Negative SMEs (nSMEs) and Negative RSEs (nRSEs)

Previous sections focused on positive SMEs and RSEs, which occur when memory success is associated with increased activity. However, there are also negative SMEs (nSMEs) and negative RSEs (nRSEs), which happen when...
memory success is associated with reduced activity. Table 12.3 summarizes age effects on nSMEs and nRSEs. The symbols are similar to those used in Tables 12.1 and 12.2, but in the negative direction (e.g., a black square indicate a significant nSME/nRSE in YAs but not in OAs, and a black circle means that YAs had a larger nSME/nRSE than OAs). Although we mention a few recurrent findings, given the small number of studies, these trends should be interpreted carefully as many could disappear with the addition of new studies.

Starting with nSMEs, OAs showed reduced nSMEs in VPC, DPC, and dorsolateral PFC. The nSME reduction in VPC is interesting because VPC typically shows nSMEs in YAs (Otten and Rugg, 2001; Wagner and Davachi, 2001; Cabeza, 2008; Uncapher and Wagner, 2009). The typical explanation for nSMEs in VPC, PMR, and other regions in YAs is that encoding activity in these regions predict subsequent forgetting because these regions are involved in the processing of, or bottom-up attention to, distracting information (Otten and Rugg, 2001; Wagner and Davachi, 2001; Cabeza, 2008; Uncapher and Wagner, 2009). Given that VPC and PMR are part of the default mode network, which has been linked to daydreaming and task-independent thoughts (Buckner et al., 2008), reduced nSMEs (p.316) in these regions can be described as a failure to suppress the default mode network (Daselaar et al., 2004). Reduced nSMEs in OAs were first explained in the context of OAs having difficulty suppressing the default mode network (Lustig et al., 2003; Persson et al., 2007).

The nSME reduction in VPC is consistent with evidence that nSMEs in default mode network regions tend to be attenuated in OAs. As illustrated by Figure 12.3, for example, a large cross-sectional fMRI study including YAs, middle-aged adults, and OAs found that nSMEs in typical default mode network regions, including VPC, PMR, and ACC, decreased as function of age (Park et al., 2013). Also, a recent meta-analysis of SMEs and aging found that within default mode network regions, negative SMEs in YAs partially overlapped with positive SMEs in OAs (Maillet and Rajah, 2014).

Moreover, studies examining connectivity within default mode network regions support the idea that OAs may differentially utilize default mode network regions during memory encoding (Stevens et al., 2008; Rizio and Dennis, 2014). However, it is important to emphasize that in the present review, only VPC showed evidence of nSME reductions. Other core default mode network components, including PMR and ACC, did not show these effects. Even in VPC, only two item studies and two associative studies showed the effect (see Table 12.3).

Turning to nRSEs, there are two main accounts of these effects in YAs. First, when nRSEs reflect more activity for correct rejections (new) than hits (old), one common explanation is “repetition suppression,” which refers to less activity for old than novel items. Repetition suppression is assumed to mediate not only implicit memory (priming) effects but also familiarity-related item memory during episodic recognition tasks (Brown and Aggleton, 2001; Henson et al., 2003). Second, nRSEs could also reflect greater activity in regions mediating control processes when correct rejections or misses are more demanding than hits. As illustrated by Table 12.3, OAs showed increased nRSEs in PHG (item memory), and nRSE decreases in ACC (item memory) and anterior PFC (associative memory). The age-related increases in PHG occurred within perirhinal cortex (Daselaar et al., 2003; Daselaar et al., 2006b) and could reflect
greater reliance on familiarity, as previously discussed (see Figure 12.2). In contrast, decreases in ACC and anterior PFC could reflect a difficulty in recruiting control processes for correct rejections. Clearly, these interpretations are speculative and further research is required.

Task-Based Functional Connectivity Studies of Recognition Memory

Previous sections reviewed age-related differences in the contribution of individual brain regions to successful episodic encoding (SMEs) and retrieval (RSEs). However, successful encoding and retrieval cannot be achieved by the operation of individual brain regions; it also requires close interactions among these regions. FMRI studies can investigate these complex interactions by measuring whether activity in different regions co-varies over time, a measure typically known as functional connectivity (here, just connectivity). Few studies have investigated connectivity associated with encoding and retrieval tasks, and even fewer have examined how this task-based connectivity is affected by aging. The review of these studies suggests at least four different patterns of age-related episodic-related connectivity differences.

First, the most reliable task-based connectivity finding is an age-related increase in PFC connectivity. In several studies, this PFC connectivity increase was coupled with a decrease in connectivity with posterior brain regions, resembling the PASA pattern often found in regional activity. Like PASA, the PFC connectivity increase has usually been attributed to functional compensation (Daselaar et al., 2006b; Dennis et al., 2008b; Murty et al., 2009; Oh and Jagust, 2013; Waring et al., 2013; Oedekoven et al., 2015). In several studies, age-related increases in PFC connectivity were found using neutral stimuli. For example, in the aforementioned word recognition study by Daselaar et al. (2006b), OAs showed reduced MTL connectivity with posterior cortical regions (VPC and retrosplenial cortex), but increased MTL connectivity with bilateral dorsolateral PFC regions (Figure 12.4A), resembling a PASA pattern. This pattern was also found in a previously reviewed study in which OAs showed SME reductions in HPC during associative but not item encoding (Dennis et al., 2008b). In this study, HPC connectivity in OAs was reduced with posterior temporal regions, but was increased with PFC (Figure 12.4B). Moreover, two other studies reported greater PFC connectivity with MTL in OAs, one during face-name recognition (Oedekoven et al., 2015), and another during successful scene encoding (Oh and Jagust, 2013). (p.318)
Figure 12.4 PASA-like effect in functional connectivity. (A) OAs exhibited reduced MTL connectivity with parietal and retrosplenial cortices, but increased connectivity with dorsolateral PFC. Adapted with permission from Daselaar SM, Fleck MS, Dobbins IG, Madden DJ, Cabeza R (2006) Effects of healthy aging on hippocampal and rhinal memory functions: An event-related fMRI study. Cereb Cortex 16: 1771–1782. (B) OAs displayed reduced HPC connectivity with OTP regions, but increased HPC connectivity with PFC regions. Adapted with permission from Dennis NA, Hayes SM, Prince SE, Madden DJ, Huettel SA, Cabeza R (2008) Effects of aging on the neural correlates of successful item and source memory encoding. J Exp Psychol Learn 34: 791–808. (C) OAs showed reduced amygdala connectivity with HPC, but increased connectivity with dorsolateral PFC. Adapted with permission from St. Jacques PL, Dolcos F, Cabeza R (2009) Effects of aging on functional connectivity of the amygdala during subsequent memory for negative pictures: A network analysis of fMRI data. Psychol Sci 20: 74–84. (See color plate also)
In another group of studies, greater PFC connectivity in OAs was found during tasks involving emotional stimuli. In one study (St. Jacques et al., 2009), amygdala activity during the encoding of emotional pictures was similar in YAs and OAs while amygdala connectivity differed across groups: it was stronger with HPC in YAs and with bilateral dorsolateral PFC regions in OAs (Figure 12.4C). Murty et al. (2009) reported similar findings: OAs displayed reduced amygdala connectivity with HPC but increased amygdala connectivity with dorsolateral PFC, both during encoding and retrieval of emotional pictures. A third study (Addis et al., 2010) found age effects in HPC connectivity during successful encoding (i.e., SMEs) of positive stimuli: HPC connectivity was stronger with the thalamus in YAs but with PFC in OAs. Finally, in a study in which participants viewed neutral scenes paired with positive or negative items (Waring et al., 2013), parahippocampal connectivity with fusiform cortex was reduced in OAs, whereas parahippocampal connectivity with PFC was increased in OAs, particularly for subsequently remembered pairs (i.e., SMEs).

Second, another type of age-related effect on connectivity is reductions in OAs among components supporting memory in the specific task employed. For example, Tsukiura et al. (2011) found an age-related reduction in connectivity between HPC and anterior temporal cortex for faces paired with names and jobs.
(i.e., associative memory). Given that anterior temporal cortex was associated with memory for names in this study, as well as in other studies, the authors suggested the reduced (p.319) temporal connectivity could contribute to OAs’ difficulty with memory for names. Another example comes from a study of picture associative encoding (Leshikar et al., 2010) where OAs exhibited reduced connectivity between HPC and occipital cortex. Furthermore, when restricting the analyses to unrelated pictures, OAs were found to have reduced connectivity between HPC and several OTP and PFC regions. A study examining face recognition reported parietal connectivity with a DPC seed in both age groups, but decreased connectivity with fusiform cortex (Oedekoven et al., 2013), a region critical for face representations. A graph theory analysis showed significant connectivity reductions in “long-range connections” between fronto-temporal, fronto-occipital, fronto-parietal, and tempero-parietal regions during both memory encoding and retrieval (Wang et al., 2010). The authors propose that this reduced connectivity supports the idea that white matter declines across cortical regions may at least partially explain cognitive deficits found in aging (O’Sullivan et al., 2001; Davis et al., 2009). Lastly, a study from Gutchess et al. (2005) reported positive connectivity in YAs but negative connectivity in OAs between parahippocampal cortex—a critical scene processing region—and PFC during scene encoding. The authors suggest that because parahippocampal cortex exhibited reduced SMEs, this negative correlation reflects PFC compensation for impaired SMEs.

Third, some age-related increases in connectivity suggest a failure of inhibitory control processes. For example, a face encoding study (Stevens et al., 2008) found an age-related increase in nSMEs in auditory cortex (not shown in Table 12.1 because only nSMEs for predicted ROIs were reported), possibly because OAs were distracted by scanner noise. Consistent with this interpretation, auditory cortex in OAs displayed stronger connectivity with temporal and parietal cortex and PFC regions, including several default mode network regions typically suppressed during successful encoding. The authors suggest that auditory distraction from the scanner environment may explain the nSMEs in auditory cortex as well as its connectivity with default mode network regions. A second study also found increased connectivity in OAs related to impaired inhibitory control, but this increase was attributed to compensatory processes (Rizio and Dennis, 2014). This study investigated a directed forgetting manipulation in which participants were instructed to forget some stimuli. This intentional forgetting was compared to naturally occurring, incidental forgetting. Interestingly, VPC exhibited negative connectivity with HPC and parahippocampal cortex in OAs during intentional but not incidental forgetting. The authors suggested that negative VPC connectivity mediates inhibitory processes in OAs, who displayed a failure in PFC-mediated inhibition.
Finally, some age-related connectivity differences during episodic memory tasks have been associated with a dedifferentiation of memory systems and subsystems. For example, one study comparing episodic memory encoding and implicit learning (Dennis and Cabeza, 2011) found that YAs showed a clear dissociation between memory systems, recruiting MTL during episodic encoding and the striatum during implicit learning, whereas OAs showed no preferential recruit for either task. Consistent with the idea of dedifferentiation, YAs displayed negative connectivity between MTL and the striatum while OAs did not. Thus, the opposing relationship between episodic and implicit learning systems (Poldrack et al., 2001) seems to disappear in OAs, with an associated attenuation of negative connectivity. A similar age-related dedifferentiation finding was recently reported by our laboratory between two subsystems of episodic memory (p.320) memory: associative and item memory (Wang et al., 2015). In a word recognition task, each word was preceded by a masked word that was either conceptually related to the target word or unrelated. The presence of the conceptual prime increased familiarity-based false alarms and perirhinal activity reductions (repetition suppression) in both age groups. OAs also exhibited activity increases in HPC, possibly due to dedifferentiation (i.e., fluency response in both HPC and perirhinal cortex in aging). Increased connectivity between HPC and perirhinal cortex was also observed in OAs during false alarms that were primed by a conceptual cue, further supporting the possibility that HPC may be recruited during familiarity-based decisions in healthy aging.

In sum, four different age effects on connectivity have been reported. First, the most reliable pattern, reported in eight different studies, was stronger PFC connectivity in OAs than YAs. This age-related increase in PFC connectivity was observed during both encoding and retrieval using a variety of different tasks and stimuli. In several cases, this effect was coupled with an age-related reduction in connectivity with posterior regions, yielding a connectivity effect that resembles the PASA pattern. Second, another age effect on connectivity is a reduction among components of the network supporting task performance, such as reduced connectivity with anterior temporal cortex during a face-name association task. Third, other studies reported an age-related increase in connectivity consistent with a deficit in inhibitory control. Finally, a fourth age-related difference in connectivity is consistent with a hypothesized dedifferentiation between different memory systems.

General Discussion

FMRI studies have made an important contribution to our understanding of the effects of aging on the neural correlates of episodic memory. Event-related fMRI studies have been particularly useful because they can be used to directly compare successful and unsuccessful memory trials during encoding (i.e., SMEs) and during retrieval (i.e., RSEs), allowing the identification of compensatory activity within-participants (i.e., increased SMEs or increased RSEs). Although there is substantial variability across studies, our review has revealed several
recurrent findings. In this section, we first discuss the most consistent recurrent findings, and then consider factors that could explain inconsistencies across studies.

Main Recurrent Findings

We focus here on the most frequent age-related findings on SMEs and RSEs: (1) the PASA pattern in SMEs, (2) DPC reductions in SMEs and RSEs, (3) widespread RSE increases during context recognition, and (4) increases in PFC connectivity.

Posterior–Anterior Shift with Aging (PASA) in SMEs

As shown in Table 12.1, item and face-name associative encoding studies showed occipital SME decreases coupled with anterior PFC SME increases. These effects fit (p.321) with the PASA pattern, which was originally attributed to a visual processing deficit in OTP compensated for by the recruitment of higher-order cognitive processes in PFC (Grady et al., 1994). Given that all surveyed SME studies employed visual stimuli, this interpretation could be also applied to the SME findings. Encoding fMRI studies that use visual stimuli frequently report significant SMEs in visual cortex (Kim, 2011), which makes intuitive sense given that better visual processing is likely to lead to better subsequent memory for visual stimuli.

One potential criticism of the idea that OTP reductions reflect visual processing deficits in OAs is that gross occipital volume is well preserved in OAs, particularly when compared with regions such as PFC or HPC (Raz et al., 2005). However, occipital decreases could reflect a reduction of the visual input due to deficits in the peripheral visual system, including impaired crystalline lens transparency (Sekuler and Sekuler, 2000) and reduced axons and myelin in the optic nerve (Peters, 2002). Also, even if gross occipital volume is preserved, there is evidence of significant age-related reductions in synapses (Peters et al., 2001b) and myelin (Peters et al., 2001a) in primary visual cortex. The idea that age-related sensory deficits have a negative impact on higher-order cognitive functions such as episodic memory is consistent with evidence of significant correlations between sensory and cognitive measures in OAs (Baltes and Lindenberger, 1997; Li and Lindenberger, 2002). One explanation for these correlations is that sensory deficits cascade through the processing system, impacting higher-order cognitive abilities. Consistent with this idea, degrading sensory stimuli by adding noise yields cognitive deficits in YAs that resemble the ones associated with aging (Pichora-Fuller et al., 1995; Murphy et al., 2000; Gilmore et al., 2006).

Attributing SME increases in anterior PFC to compensation fits with our conservative application of the term compensation only to cases in which activity is linked to successful performance within-participants. The reason that PFC increases were most frequent in anterior PFC is unclear, but the fact that this
region is associated with higher-order relational and abstract cognitive operations (Badre, 2008) suggests that OAs may be relying on their spared conceptual knowledge to compensate for impaired visual processes.

Although item SME and face-name associative SME studies yielded a PASA pattern, other associative SME studies and RSE studies did not. A speculative explanation of the difference in RSE studies is that memory could be less dependent on executive control than encoding. For example, there is evidence that memory performance suffers when attention is divided during encoding but not when it is divided during recognition (Craik et al., 1996; Anderson et al., 1998). In general, however, it seems that the PASA pattern is not reliably found across episodic memory studies.

**Age-Related DPC Reductions in SMEs and RSEs**

DPC shows recurrent age-related reductions in item SMEs and subthresholded in associative SMEs (Table 12.1) as well as in RSEs during item and associative recognition tasks (Table 12.2). In YAs, DPC frequently shows SMEs (Uncapher and Wagner, 2009) and RSEs (Cabeza et al., 2008), and both effects have been attributed to top-down attention (Cabeza, 2008; Cabeza et al., 2008; Uncapher and Wagner, 2009). During encoding, top-down attention is necessary for focusing processing on relevant new information, and during retrieval, for performing demanding memory search and monitoring processes. Accordingly, age-related SME and RSE reductions in DPC could be attributed to a deficit in top-down attention. As mentioned before, the resource deficit hypothesis postulates that insufficient attentional control resources is one of the main causes of memory deficits in OAs, a hypothesis that is consistent with evidence that divided-attention manipulations can yield memory deficits in YAs that resemble those in OAs (Craik and Byrd, 1982; Rabinowitz et al., 1982). A challenge for the resource deficit hypothesis is explaining why OAs show reductions in top-down attention processes mediated by DPC but not in higher-order control processes mediated by anterior PFC. This is an important question for future research.

**Age-Related RSE Increases in Context Studies**

One of the most interesting patterns that emerged from our review is evidence of widespread age-related RSEs increases in studies assessing associative memory with context memory tasks. These increases are in stark contrast to age-related RSE decreases in studies investigating recognition memory (see Table 12.2). Opposite age effects in context vs. recognition memory RSE studies occurred in most brain regions. These included regions associated with demanding retrieval search, monitoring, and top-down attention processes (“retrieval effort”), such as PFC and DPC, as well as regions associated with memory recovery (“retrieval success”), such as OTP and VPC. Given that the RSE increases were more pronounced when context hits were compared to correct rejections than when context hits were compared to context misses, we
speculated that the increases could be partly driven by decreases in control correct rejections, perhaps related to a reduced novelty response in OAs. Here we consider two alternative explanations.

In the case of regions associated with “retrieval effort,” one possible explanation is that context memory tasks have greater executive control and top-down attentional demands than recognition tests, such as the Remember/Know paradigm. Context memory tasks require a demanding memory search for a specific target (e.g., was this item encoded in context A or B?), as well as an effortful monitoring process (the response can be either correct or incorrect), whereas the Remember/Know paradigm requires only a subjective assessment of the conscious quality of the memories triggered by a stimulus (e.g., are you “remembering?”) that is not constrained to one specific criterion (“non-criterial recollection,” Yonelinas and Jacoby, 1996), and in principle, responses are not correct or incorrect (the response is about a private conscious state). Thus, context memory tasks are more likely to feel demanding and trigger compensatory “retrieval effort” processes than subjective recollection tests such as the Remember/Know paradigm.

A related explanation is that compared to associative recognition tests, context memory tasks are more dependent on late strategic retrieval processes, such as post-retrieval monitoring, which are the ones that could be driving RSE increases in OAs. There is evidence that OAs display a shift from a proactive to a retroactive decision (p.323) strategy (Paxton et al., 2008) and may compensate for deficits in early retrieval processes by extending processing to later retrieval stages (Velanova et al., 2007). Consistent with such a Early-to-Late Shift with Aging (ELSA), in one of the studies listed in the context panel (Dew et al., 2012), we found that OAs showed less activity in PFC (and HPC) than YAs during an early, retrieval preparation phase, but more activity than YAs during a late, retrieval completion phase (see Figure 12.5). As illustrated by Figure 12.5, the ELSA account may apply not only to “retrieval effort” regions such as PFC but also to “retrieval success” regions such as HPC. While it is intuitive that OAs over-recruit control processes to compensate for impaired episodic memory, it is less clear how OAs can over-recruit retrieval success regions given that their episodic memory is impaired. One possible explanation is that top-down modulation from fronto-parietal regions increases activity in posterior regions during demanding context memory tasks. At any rate, all three explanations of the widespread age-related RSE increases during context tasks (correct rejection novelty, control demands of context memory tasks, and ELSA) are highly speculative, and additional evidence is clearly required. Ideally, researchers should directly compare age effects on Remember/Know and context memory tasks within participants, while manipulating variables relevant to the three hypotheses.
Age-Related Increases in PFC Connectivity

At least eight different studies reported age-related increases in PFC connectivity. In some studies, the increases in PFC connectivity were coupled with decreases in posterior connectivity (Daselaar et al., 2006b; Dennis et al., 2008b; Murty et al., 2009; St. Jacques et al., 2009; Waring et al., 2013), whereas in other studies they were not (Addis et al., 2010; Oh and Jagust, 2013; Oedekoven et al., 2015). The former fits with the PASA pattern discussed above, whereas the latter seems to be a PFC-specific phenomenon. In both cases, increases in PFC connectivity have usually been interpreted as evidence of compensation in OAs. This interpretation consistently points to a role for PFC in age-related compensation as PFC regions not only show increased SMEs and RSEs, but are also recruited for task-related functional networks related to episodic memory. One important open question is how the increased connectivity with PFC in OAs relates to disruptions in their white matter tracts (e.g., does increased functional connectivity compensate for reduced structural connectivity?).

Potential Factors Explaining Inconsistent Findings Across Studies

While we observed several recurrent patterns across studies, there are also many inconsistencies. For example, although several studies reported the HAROLD pattern, or reduced PFC lateralization in OAs, in SMEs (Morcom et al., 2003; Dennis et al., 2007a; Duverne et al., 2009; Bangen et al., 2012), many others failed to find this effect when examining SMEs (Daselaar et al., 2003;
Gutchess et al., 2005; de Chastelaine et al., 2011) or context RSEs (Morcom et al., 2007; Dulas and Duarte, 2012). As another example, there was no consistent evidence of associative SME reductions in HPC—which would be one of the strongest a priori predictions given the role of HPC in associative memory (Davachi, 2006; Eichenbaum et al., 2007) and evidence of binding deficits in OAs (Naveh-Benjamin, 2000)—with some studies reporting reductions (Dennis et al., 2008b; Kim and Giovanello, 2011), and others reporting increases (Duzel et al., 2011; Bangen et al., 2012). Even the findings we identified as recurrent were not necessarily reliable (our definition of “recurrent” was only 25% of the studies). One possibility is that these effects (e.g., HAROLD or HPC-related deficits) are not always present in OAs, but there are also several factors differing between studies that would make it difficult to confirm this possibility with confidence. Within this section we elaborate on several variables that may either separately or in cohort explain these differences.

First, there are many ways to measure age-differences in fMRI studies of episodic memory. As shown in Tables 12.1–12.3, one can be particularly stringent in defining an age difference as an interaction (e.g., SME greater in one group than the other), or simply as the presence of an effect in one group but not the other. Moreover, while we did our best to separate studies reporting nSMEs and nRSEs from those that did not, most studies did not report the direction of the interaction. That is, a positive SME interaction (i.e., white circle) could be due to (1) a larger significant SME in OAs than YAs, (2) a significant SME in OAs but a nonsignificant SME in YAs, (3) a significant SME in OAs and a significant nSME in YAs, (4) a nonsignificant SME in OAs and a significant nSME in YAs, or (5) a larger significant nSME in YAs than OAs. Studies (p.325) reporting these latter two patterns would have only been included in Table 12.3 if the authors noted that such a pattern existed.

Relatedly, studies defined SMEs and RSEs differently. For item SMEs, successful encoding can be defined as either subsequent high-confidence hits contrasted with subsequent low-confidence hits or subsequent misses, subsequent hits contrasted with subsequent misses, or some other possibility. For associative RSEs, this is further complicated by the addition of correct rejection trials and also the utilization of different retrieval paradigms (e.g., Remember/Know or context retrieval). Relatedly, as mentioned in the introduction, item and associative tasks are not process pure. Particularly, many item tasks that ostensibly tap item memory may also recruit associative processes. Thus, some similarities seen between item and associative memory studies may be due to contamination of these two forms of memory across tasks.

The third issue relates to individual differences in memory. While YAs had better memory performance than OAs in many studies, they had balanced performance in other studies. Although event-related studies allow us to examine memory success rather than performance differences per se, differences in memory may
still lead to an interaction between memory differences and univariate activity. For example, a more difficult task (in OAs) may lead to greater activity for hits than misses (while increased activity for both hits and misses would not affect the memory success comparisons).

Lastly, studies utilized vastly different stimuli, which likely also contributed to the inconsistencies across studies. Different cortical areas are critical for different stimuli types (Epstein et al., 1999; Downing et al., 2001; Haxby et al., 2001), which may weaken evidence of any recurrent findings. Regarding stimuli, one interesting null result emerges across associative SME and RSE studies utilizing objects: all studies that reported no age differences (or only one age difference) utilized object stimuli or object stimuli in combination with another stimulus type. However, not all object studies reported no age differences, therefore this remains pattern that requires further study. For example, it may be the case that neural correlates of associative memory are less unaffected by aging than previously thought (e.g., Wang et al., 2016). Together, differences in how contrasts are reported, how memory success is defined, whether memory performance is matched, and what stimuli are used may all contribute to the inconsistent findings found across item and associative encoding and retrieval. Thus, it remains important for future research to develop a more standardized approach to studying age effects on the neural correlates of episodic memory.

Additional Methodological Considerations

We note in this section several methodological concerns that must be addressed in future work in order to better advance our understanding of age-related effects on episodic memory. One methodological issue revolves around the necessity of controlling for vascular changes. Given that fMRI signal is dependent on blood flow, cerebrovascular reactivity changes in aging has significant implications for interpretations of age-related differences in fMRI activity (Ito et al., 2002; D’Esposito et al., 2003; Lu et al., 2011; Tsvetanov et al., 2015). For example, one study recently compared uncorrected fMRI activity compared to cerebrovascular-reactivity-corrected fMRI (p.326) activity during memory encoding (Liu et al., 2013). The uncorrected activity for task vs. fixation yielded results consistent with many studies in the aging literature, namely a PASA pattern. However, the occipital and MTL decreases were no longer present when accounting for cerebrovascular reactivity differences, while the PFC increases became larger. When contrasting subsequent hits and misses, a similar pattern was observed in PFC. Thus it is particularly important for future work to account for cerebrovascular reactivity differences in aging, especially given that posterior cortices most often exhibit age-related decreases (see Tables 12.1 and 12.2).

It is also critical to acknowledge that many of the studies reviewed in the current chapter are cross-sectional rather than longitudinal. In brief, age-related differences in brain and behavior observed in cross-sectional studies are not
necessarily due to aging (for a detailed discussion, see Chapters 6 and 7). Rather, they could be due to differences between the YA and OA samples (i.e., selection bias or cohort effects), or could be simply an age-invariant effect (e.g., worse memory or activity decreases that were present throughout adulthood). For example, a comparison of cross-sectional and longitudinal methods indicates that age-related over-recruitment of PFC in a cross-sectional analysis actually manifest as underrecruitment in a longitudinal analysis (Nyberg et al., 2010). A follow-up study from a subset of the same sample reported that longitudinal increases in PHG activity—approximately in the perirhinal cortex—correlated with longitudinal decreases in memory performance whereas decreases in HPC activity (and volume) correlated with decreases in memory performance (Persson et al., 2012). The former finding is inconsistent with a compensation account, but could reflect inefficient processing. The latter finding is, however, consistent with both cross-sectional studies (see Table 12.1) and theoretical proposals (e.g., Naveh-Benjamin, 2000) that HPC dysfunction in aging contributes to episodic memory deficits. Although these aforementioned studies examine gross activity (i.e., block design) rather than memory success differences, they offer promising insight into age-related changes in episodic memory.

Lastly, the studies reviewed in the current chapter varied vastly in the statistical power afforded by the sample sizes. The sample sizes of studies listed in Tables 12.1–12.3 ranged from 19 (9 YAs, 10 OAs) to 192 (64 YAs, 64 middle-aged adults, 64 OAs). A quantitative meta-analysis that fully accounts for differences in power is beyond the scope of the current study (for meta-analyses, see Spreng et al., 2010; Maillet and Rajah, 2014). Thus, it is possible that the age-related differences found in studies with smaller sample sizes are less reliable than those with larger sample sizes and may explain some inconsistencies seen across studies.

Conclusion
In the current chapter, we reviewed event-related studies of item and associative episodic encoding and retrieval, as well as episodic memory studies of task-based functional connectivity. While the field has advanced greatly over the past decade with the use of these methods, many unanswered questions remain. Future work must seek to adopt more standardized methods for assessing age differences in event-related studies to better understand whether and how compensation—and other explanatory models such as dedifferentiation and neural inefficiency—in the aging brain relate to changes in episodic memory.

References

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