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The Effects of Healthy Aging, Amnestic Mild Cognitive Impairment, and Alzheimer's Disease on Recollection and Familiarity: A Meta-Analytic Review

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Abstract

It is well established that healthy aging, amnestic Mild Cognitive Impairment (aMCI), and Alzheimer's Disease (AD) are associated with substantial declines in episodic memory. However, there is still debate as to how two forms of episodic memory – recollection and familiarity – are affected by healthy and pathological aging. To address this issue we conducted a meta-analytic review of the effect sizes reported in studies using remember/know (RK), receiver operating characteristic (ROC) and process dissociation (PD) methods to examine recollection and familiarity in healthy aging (25 published reports), aMCI (9 published reports), and AD (5 published reports). The results from the meta-analysis revealed that healthy aging is associated with moderate-to-large recollection impairments. Familiarity was not impaired in studies using ROC or PD methods but was impaired in studies that used the RK procedure. aMCI was associated with large decreases in recollection whereas familiarity only tended to show a decrease in studies with a patient sample comprised of both single-domain and multiple-domain aMCI patients. Lastly, AD was associated with large decreases in both recollection and familiarity. The results are consistent with neuroimaging evidence suggesting that the hippocampus is critical for recollection whereas familiarity is dependent on the integrity of the surrounding perirhinal cortex. Moreover, the results highlight the relevance of method selection when examining aging, and suggest that familiarity deficits might be a useful behavioral marker for identifying individuals that will develop dementia.

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Keywords

Aging; Recollection; Familiarity; Alzheimer's disease; amnestic Mild Cognitive Impairment

Healthy aging is associated with impairments in episodic memory (Drag and Bieliauskas 2010; Hoyer and Verhaeghen 2006; Light 1991; Verhaeghen et al. 1993), although not all forms of episodic memory are equally impaired. For instance, healthy older adults show larger deficits on free recall tests compared to yes/no recognition tests (Craik and McDowd 1987; Schonfield and Robertson 1966; Whiting and Smith 1997; for review, see La Voie and Light 1994), and on tests of associative recognition compared to tests of single item recognition (for review, see Old and Naveh-Benjamin 2008; Spencer and Raz 1995). Such findings have been taken as evidence that healthy aging selectively impairs some episodic memory processes while leaving others unaffected.

A dual-process account of these findings suggests that aging leads to a relatively selective deficit in recollection, which is the ability to retrieve qualitative information about a prior study event, that leaves familiarity-based recognition judgments unaffected (Anderson et al. 2008; Luo et al. 2007; Parkin and Walter 1992; Yonelinas 2002). A growing number of studies have been conducted to assess this possibility using various methods to estimate the contributions of recollection and familiarity to overall performance in young and older adults. However, there is still disagreement about the nature of recollection and familiarity impairments in healthy aging. Some have reported that healthy aging is associated with selective declines in recollection-based episodic memory (Cohn et al. 2008; Jennings and Jacoby 1993; 1997; McCabe et al. 2009; Parkin and Walter 1992; Wolk et al. 2013; Yonelinas 2002), whereas others have found that healthy aging is associated with declines in both recollection- and familiarity-based episodic memory (Belleville et al. 2011; Duarte et al. 2006; Düzel et al. 2011; Friedman et al. 2010; Parks 2007; Peters and Daum 2008; Prull et al. 2006; Wang et al. 2012).

Understanding how recollection and familiarity-based episodic memory change during the course of healthy aging is critical not only in developing behavioral interventions aimed at slowing age-related cognitive decline, but also in determining the potential utility of using recollection and familiarity to identify individuals that will develop dementia. A hallmark of Alzheimer's disease (AD) – the most common form of dementia associated with aging – is severe memory impairment, and a substantial body of work has indicated that symptoms predictive of developing AD occur well before a diagnosis can be made (for reviews, see Didic et al. 2011; Petersen 2004; Salmon 2012). Amnestic Mild Cognitive Impairment (aMCI) is believed to represent the transitional period between healthy aging and AD where early AD symptoms can be detected (Petersen 2004; Petersen et al. 2009; Salmon 2012). Although not all individuals with aMCI will progress to AD (Petersen et al. 2009), abnormally low episodic memory performance is associated with conversion to AD (e.g., Landau et al. 2010).

There is a growing interest in determining how aMCI and AD affect recollection-based and familiarity-based episodic memory. Results from studies comparing performance on tasks believed to rely primarily on recollection (e.g., free recall and associative recognition) to

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tasks thought to depend more on familiarity (e.g., old/new and forced-choice recognition tests) have led some to conclude that aMCI and AD are associated with declines in both recollection and familiarity (Algarabel et al. 2009, 2012; Bennett et al. 2006; Dudas et al. 2005;). For example, aMCI and AD patients show similarly large impairments on tests of free recall and item recognition (Bennett et al. 2006), which, from a dual-process perspective, indicates that recollection and familiarity are similarly impaired in aMCI and AD. However, Westerberg and colleagues (2006, 2013) reported that aMCI patients only show impairments on tasks thought to be rely relatively more on recollection (i.e., old/new recognition) whereas AD patients are impaired on tasks that rely on recollection and tasks that rely primarily on familiarity (i.e., forced choice-recognition; see Bastin and Van der Linden 2003). Such findings suggest that aMCI is associated with specific recollection impairments whereas AD is associated with declines in both recollection and familiarity. Moreover, results from studies that have used methods to estimate the contribution of recollection and familiarity have also led to mixed conclusions. For example, some studies showing that recollection is selectively affected in both aMCI (e.g., Anderson et al. 2008; Troyer et al. 2012) and AD patients (e.g., Genon et al. 2013), whereas other studies find that estimates of both recollection and familiarity are impaired in aMCI (Wolk et al. 2008, 2011, 2013) and AD (e.g., Ally et al. 2009; Wolk et al. 2011). Thus, similar to the studies examining healthy aging, the extant literature is mixed as to the fate of recollection and familiarity in aMCI and AD.

Our aim in this report is to address the above debates by conducting a meta-analytic review of the literature examining how healthy aging, aMCI, and AD affect recollection-based and familiarity-based episodic memory. The review is divided into four main sections. First, we provide an overview of the methods that have been used to measure recollection and familiarity. Second, we briefly discuss some variables to might lead to systematic differences (i.e., moderate) in pattern of recollection and familiarity decreases observed in the extant literature. Third, we present the quantitative meta-analysis of the literature examining recollection and familiarity differences in the three populations of interest. In particular, our goal is to determine if recollection, familiarity, or both are impaired to in these three populations, and to see these decreases are moderated by specific experimental variables. Fourth, we discuss the implications of the findings from the meta-analysis and relate the results to the emerging neuroimaging literature on age-related memory declines.

Measuring Recollection and Familiarity

Many different approaches have been developed to assess the contributions of recollection and familiarity to memory performance (for review, see Light 2011; Yonelinas 2002). The three most widely used process estimation methods are the Remember/Know (RK) procedure (Gardiner 1988; Tulving 1985), Process Dissociation (PD) procedure (Jacoby 1991; for review, see Yonelinas and Jacoby 2012), and the analysis of recognition memory receiver operating characteristics with the dual-process signal-detection model (i.e., the ROC procedure; Yonelinas 1994; 1999; for review, see Yonelinas and Parks 2007; see Supplemental Material)[1]. In the RK procedure, participants are asked to make introspective reports about their memory judgments (Gardiner 1988; Tulving 1985). For items judged to be from the study list, participants are instructed to make a ‘Remember’ response when they

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can recollect specific details of the prior encounter with the item and to make a 'Know' response if no details are recollected but there is a general sense the item was studied. Estimates of recollection and familiarity are derived from RK judgments using the independent RK formulas (Yonelinas and Jacoby 1995) that account for the fact that 'Remember' and 'Know' judgments are mutually exclusive.

The PD procedure relies on the logic that recollection and familiarity will lead to different memory judgments when placed in opposition (Jacoby 1991). In a typical PD experiment, a participant might study two lists of words presented in different modalities (e.g., auditory versus visual), followed by two recognition test phases. The inclusion test is a standard recognition test in which participants judge all studied items as 'old' and items that were not studied as 'new'. On this test, recollection and familiarity act in concert to support accurate recognition decisions. In contrast, the exclusion test is a modified recognition test in which participants identify test items from one source dimension (e.g., aurally presented words during study) as 'old' and words from the other source dimension (e.g., visually presented words during study) as well as words that were not studied as 'new'. On the exclusion tests, recollection and familiarity act in opposition when making recognition decisions about the to-be-excluded studied items (e.g., visually presented words). Specifically, familiarity in the absence of recollecting the critical source detail will lead to incorrect 'old' responses whereas recollecting the source detail will lead to the correct rejection of the to-be-excluded item. Recollection and familiarity estimates are derived from the proportion of 'old' responses given to items on the inclusion test and the proportion of 'old' responses given to to-be-excluded items on the exclusion test (Jacoby 1991; Yonelinas and Jacoby 1996a).

The ROC procedure involves a recognition memory test in which participants make their old/new memory decisions using a confidence scale (e.g., 6-'sure old', 5-'maybe old', 4-'guess old', 3-'guess new', 2-'maybe new', 1-'sure new'). The confidence judgments are used to construct an ROC – a plot of the cumulative hit rate and false alarm rate across confidence bins (i.e., levels of response bias; Yonelinas and Parks 2007). For example, the first (i.e., left-most) point on the ROC is the proportion of old and new words that receive a 6-'sure old' judgments, and the second point of the ROC is the proportion of old and new words that receive a 6-'sure old' or a 5-'sure new' response. Each participant's ROC is fit with the dual-process signal detection model to derive estimates of recollection and familiarity (Yonelinas 1994, 1999).

Although there are many similarities between the three methods regarding the assumptions underlying recollection and familiarity (e.g., the independence assumption), there are important differences between the methods in how the two processes are estimated. The RK method measures recollection and familiarity directly from introspective judgments of when recollection does and does not occur. In contrast, the PD procedure estimates recollection as the ability to remember a specific aspect (i.e., source detail) of the study event and estimates familiarity as the absence of recollecting the to-be-remembered detail. The ROC method is

[1]Here, we adopt the dual-process interpretation of the RK, PD, and ROC procedures. However, we acknowledge that there is still debate surrounding how data from these three procedures should be interpreted (e.g., Donaldson 1996; Dunn 2004; 2008; Wixted 2007; Yonelinas 2001a; 2002). Although this is an important theoretical issue that demands further investigation, we do not intend to add to this debate here because it is beyond the scope of the present article.

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different from both of the above methods in that recollection and familiarity are not measured by asking participants to report a recollective experience per se. Instead, recollection and familiarity are inferred from the parameters obtained by fitting the dual-process signal detection model to the observed ROC constructed from confidence responses. As discussed below, the differences between these methods might account for some of the mixed findings across studies.

Variables Moderating Group Differences in Recollection and Familiarity

As mentioned above, the findings surrounding the effect of healthy aging, aMCI, and AD on recollection and familiarity are mixed. Although some of the variability is likely attributable to random factors across studies, it is possible that there are systematic influences underlying the mixed findings in the literature. One factor that could lead to systematic differences is the degree to which recollection contributes to overall recognition performance. Yonelinas (2002) proposed that high levels of recollection (e.g., recollection estimates greater than 0.60) can inflate estimates of familiarity derived from the RK, PD, and ROC procedures. To the extent that high levels of recollection are isolated to the control group, familiarity differences between older adults relative to young adults and aMCI/AD patients relative to healthy, age-matched controls might be due to artifacts in estimating recollection and familiarity. Yonelinas's (2002) review of the literature supported this hypothesis in healthy aging studies by showing that familiarity estimates were age-invariant when studies had "normal" levels of recollection (i.e., estimates ≤0.60) but the age-related decreases in familiarity were observed for studies with high levels of recollection (i.e., estimates>0.60). Thus, it could be the case that at least some of the variability across studies is accounted for by measurement artifacts caused by high levels of recollection.

A second factor is the method that is used to estimate recollection and familiarity (Light et al. 2000; Prull et al. 2006). As discussed in "Measuring Recollection and Familiarity", this could come about because what constitutes recollection-based and familiarity-based recognition differs across the three estimation methods. Evidence in support of estimation method differences comes from a study by Prull and colleagues (2006) who examined age-related differences in recollection and familiarity derived from each estimation method in the same set of participants. Although the results from this study showed significant age-related differences in recollection in all three tasks, significant age-related differences in familiarity were only observed for the RK and ROC tasks. This difference could potentially arise because of differences in how the instructions are interpreted by different groups of participants, the type of memory judgment required (i.e., subjective or objective), or the assumptions underlying the different methods.

A third factor that might moderate the magnitude of group differences in recollection and familiarity is the type of materials (i.e., verbal or nonverbal materials). There is some evidence that age-related memory impairments might be greater for verbal than nonverbal materials. For example, age-related memory impairments are substantially reduced when pictorial stimuli are used compared to verbal stimuli (Ally et al. 2008; Park et al. 1983; Winograd et al. 1982). Such a finding would suggest that pictorial stimuli might lead to reductions in age-related declines in recollection, familiarity, or both processes. Consistent

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with this, a study by Luo and colleagues (2007) found that age-related differences in recollection were not present when words were studied with a corresponding picture. Moreover, using event-related potentials, Ally and colleagues (2008) showed that age-related differences in the left parietal old/new effect, which is the ERP correlate of recollection (Rugg and Curran 2007), were present for words but not pictures. Similarly, a study by Embree and colleagues (2012) reported that familiarity impairments in aMCI patients were robust for word stimuli, but absent for picture stimuli. Thus, reductions in recollection and familiarity in healthy older adults, aMCI, and AD might be dependent on the use of verbal or nonverbal materials.

One additional factor that may turn out to be important in aMCI studies is the inclusion of different subtypes of aMCI patients. As described by Petersen (2004), aMCI can be diagnosed as single-domain or multiple-domain. Single-domain aMCI is associated with selective memory impairments and no detectable impairments in other cognitive domains. By contrast, multiple-domain aMCI patients are impaired in at least one other cognitive domain (e.g., executive functioning) in addition to memory impairments. Although we are unaware of any study that has directly contrasted recollection and familiarity in single-domain and multiple-domain aMCI patients, some of the studies reporting spared familiarity-based recognition in aMCI only tested single-domain patients (Anderson et al. 2008; Serra et al. 2010; Troyer et al. 2012), whereas other studies that reported familiarity impairments in aMCI tested both single-domain and multiple-domain patients (Ally et al. 2009; Embree et al. 2012; Wolk et al. 2008, 2013).

The discussion above highlights that high levels of recollection, estimation method, type of materials, and single-domain or multiple-domain aMCI diagnosis might fully or partially account for the mixed findings in the literature. Thus, we included these variables in the meta-analysis reported below when the extant literature allowed us to do so. Specifically, the moderator variables examined for healthy aging studies included the level of recollection (i.e., high vs. “normal”), the process estimation method (i.e., RK, PD, or ROC), and the type of materials (verbal vs. nonverbal). Because of the limited number of relevant studies, the only moderator variable examined for aMCI studies was the type of patients examined (i.e., single-domain only vs. single-domain and multiple-domain patients). No moderator variables were examined for AD studies because only 5 articles reported enough data to be included in the meta-analysis.

Meta-Analysis of Published Studies

The primary focus of the meta-analysis was to determine if recollection, familiarity or both are impaired in healthy older adults, and aMCI and AD patients. A meta-analysis of the extant literature is useful in addressing the debates described above because it allows the magnitude of recollection and familiarity declines to be quantified across studies. We focused on studies that estimated recollection and familiarity using the RK, PD, or ROC procedures discussed previously. The studies examining healthy aging, aMCI, and AD were examined separately because the control group differed depending on the type of study; healthy aging studies used young adults as the control group, whereas studies with aMCI and AD patients used age-matched healthy older adults as the control group. In addition, we

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examined if the recollection and familiarity differences in these three groups varied systematically across the potential moderators discussed above.

Approximately half of the healthy aging studies that examined recognition memory with the RK, PD, or ROC procedures were excluded from the meta-analysis because estimates of recollection and familiarity were not reported (see Methods). Thus, we were concerned that the high proportion of excluded samples from the effect size analysis biased the results of the meta-analysis. To address this concern, we examined all studies with a complementary approach. Specifically, we adopted the approach used by Yonelinas (2002) whereby estimates of recollection and familiarity are derived for each sample from the average data reported in the paper. Although this approach allows us to obtain a recollection and familiarity estimate for all of the studies, it does not allow us to estimate an effect size measure (specifically Cohen's *d*) that takes into account subject-level variability. The results from this approach are described in detail in the Supplemental Material.

Methods

Literature Search

PsycInfo and PubMed database searches were conducted to find articles that examined recollection- and familiarity-based recognition memory in samples of healthy older adults and in patients diagnosed with aMCI or AD. The following search terms were used: *aging, amnestic mild cognitive impairment, Alzheimer's disease, recognition memory, recollection, familiarity, process dissociation, remember, know, receiver-operating characteristic, dual-process theory*. The search period for the database searches were between 1975 and 2013. We identified studies that reported using the RK, PD, or ROC procedures to examine episodic memory in healthy older adults, aMCI patients, or AD patients. Additional studies meeting our inclusion criteria, which are outlined below, were identified by searching the reference section of each article. The literature search was completed at the end of July 2013.

Inclusion/Exclusion Criteria

Only articles published in a peer-reviewed journal in English were included. Furthermore, to be included the meta-analysis, the study must have used the RK, PD, or ROC procedure to estimate recollection and familiarity using previously published formulas (e.g., Jacoby 1991; Yonelinas 1994, 1999; Yonelinas and Jacoby 1995, 1996a) in a recognition memory task. Studies using the RK procedure were excluded if they did not include false alarm rates for 'Remember' and 'Know' responses (e.g., Fell 1992; Friedman and Trott 2000; Larsson et al. 2006; Lovden et al. 2002; Mark and Rugg 1998).

The inclusion criteria specific to healthy aging studies were similar to Old and Naveh-Benjamin (2008). Specifically, experiments must have included a young adult group with a mean age below 30 years and a healthy (i.e., no memory pathology, such as AD), community-dwelling older adult group with a mean age of greater than 60 years. Across 49 published papers, we identified 68 independent comparisons of young and older adults (see Table 1). We treated each experiment in a multiple-experiment report as an independent

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observation when a new sample of participants were recruited (e.g., Healy et al. 2005; Jennings and Jacoby 1993; Luo et al. 2007; McCabe and Geraci 2009; Parks 2007; Skinner and Fernandes 2009a). Likewise, experiments that employed a between-subject manipulation crossed with age were treated as providing two independent observations (e.g., McCabe and Geraci 2009; Toth and Parks 2006). For example, the easy and hard source memory groups in Toth and Parks (2006) were treated as two independent samples examining recollection and familiarity in older adults. The one exception to this was Experiment 2 in Parks (2007), where the Easy and Broad groups were treated as a single group because this was the only way to estimate the effect size in this experiment. Studies reporting multiple older adults samples with a single young adult control group were treated as a single older adult group (Davidson and Glisky 2002; Duarte et al. 2006). Note that one experiment that met all of our inclusion criteria for this meta-analysis (Duarte et al. 2010) was excluded because the older adult sample was a subset of a larger sample from a previous study in the same lab (Duarte et al. 2008) that was selected to have low memory performance.

A total of 36 (53 %) of the 68 independent comparisons identified in the literature search used the RK, PD, and ROC methods to provide estimates of recollection and familiarity and reported enough data to estimate effect sizes for both processes. These samples were distributed across 25 published articles. The proportion of samples excluded from the effect size analysis differed as a function of the process estimation method. Specifically, 62 %, 28 %, and 30 % of the excluded samples used the RK, PD, and ROC procedures, respectively[2].

The inclusion criteria for the studies examining aMCI and AD were a healthy, age-matched control group determined to have no memory pathologies and a patient group diagnosed following published guidelines for aMCI (e.g., Petersen 2004; Petersen et al. 2009) and AD (e.g., McKhann et al. 1984). A list of the aMCI and AD studies meeting our inclusion criteria is provided in Tables 2 and 3, respectively. Nine published reports that examined patients diagnosed with aMCI met the inclusion criteria. Each study provided a single, independent sample of aMCI patients, and reported enough data to be included in the effect size analysis. Note that we excluded the aMCI sample reported by Wolk and colleagues (2011) because 12 out of the 14 aMCI patients were also included in a prior study by the same lab (Wolk et al. 2008). We also identified 7 published articles meeting the inclusion criteria that examined patients diagnosed with AD. Each article reported a single comparison of patients diagnosed with probable AD and healthy controls. Five of the seven AD samples provided enough data for the effect size analysis.

Note that three studies examined recollection and familiarity in both healthy aging and aMCI (Anderson et al. 2008; Belleville et al. 2011; Wolk et al. 2013), and two studies compared an aMCI and AD sample to a single healthy older adult control group (Ally et al. 2009; Hudon et al. 2009). Table 4 shows the number of participants and demographic data

[2]This was not too surprising because the RK procedure was not initially developed to estimate recollection and familiarity; this development occurred almost a decade after the procedure was introduced (e.g., Yonelinas and Jacoby 1995). In contrast, the motivation underlying both the PD (Jacoby 1991) and dual-process signal detection model that has been applied to recognition ROCs (Yonelinas 1994) was to quantify the contribution of recollection and familiarity.

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for the samples of the healthy aging, aMCI, and AD studies included in the effect size meta-analysis.

Effect Size Meta-Analysis

Moderator Variable Coding—Each study that examined healthy aging was coded along three dimensions to test for potential moderators of recollection and familiarity declines. First, studies were coded as having high recollection estimates if the mean recollection estimate in the young adult group was ≥60. Four of the 36 samples reported high estimates of recollection (see Table 1).

Second, studies were coded based on the estimation method they employed. Of the 36 samples contributing to the effect size analysis, 15, 13, and 7 samples employed the RK, ROC, and PD methods, respectively. One study (Prull et al. 2006) used all three methods within the same sample of younger and older adults. Therefore, this study was excluded from the analysis examining the effect of the process estimation method.

Lastly, the studies were classified as verbal or nonverbal based on the materials used to test memory[3]. We made this distinction based on the types of materials used during the test phase. For example, a study that included words paired with a picture (Luo et al. 2007) or a face (Skinner and Fernandes 2009a), but only tested memory of the words was coded as a study using verbal materials. The type of nonverbal materials used in the studies included in the effect size analysis included travel scenes (Düzel et al. 2011; Howard et al. 2006), objects (Angel et al. 2013; Duarte et al. 2006), and symbols (Friedman et al. 2010). The only studies in the effect size meta-analysis that used nonverbal materials according to our definition were Angel et al. (2013), Duarte et al. (2006), Düzel et al. (2011), Friedman et al. (2010), and Howard et al. (2006). One study examined memory for words and melodies in the same sample, and was excluded from any comparisons involving this variable (Belleville et al. 2011).

The aMCI studies were coded based on the composition of aMCI subtypes in the sample (Petersen 2004). Three reported a homogenous single-domain aMCI sample and the remaining 6 reported examining an aMCI mixed sample of both single-domain and multiple-domain aMCI patients (see Table 2).

Effect Size Calculation—The effect size measure used to quantify differences between young and older adults and healthy controls and patient groups (aMCI or AD) was the standardized mean difference (Cohen's *d*; Cohen 1988). Two effect size measures were calculated for each sample – one for recollection and one for familiarity. Note that some studies did not subtract out baseline familiarity from the reported familiarity estimates (Anderson et al. 2008; Genon et al. 2013; Hudon et al. 2009; Jacoby 1999). Given that our primary focus is on examining how familiarity is useful in discriminating between studied and new events, we *post hoc* corrected the estimate of familiarity reported for each group by subtracting out the average baseline familiarity estimate. For PD studies, the value

[3]The studies that used nonverbal materials only did so in conjunction with the RK and ROC estimation methods. The data reported in the Results were similar when considering the materials effect using only the RK and ROC studies (data not shown).

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subtracted from the familiarity estimate was the average false alarm rate to new items on the inclusion and exclusion conditions. For RK studies, the value subtracted from the reported familiarity estimate was the familiarity estimate for new items.

The effect size for each study was calculated using the online calculator that is a complement to the Lipsey and Wilson (2001) text (http://www.campbellcollaboration.org/resources/effect_size_input.php). In most cases, means and standard deviations (or standard errors) were used to calculate the effect size[4]. If unavailable, the relevant F or t statistic was used to estimate the effect size. Some studies reported the effect of healthy aging on estimates of familiarity to be non-significant, but did not provide means and variance measures or a precise test statistic value (e.g., $F<1$). In such cases, the effect size was conservatively estimated to be 0. Multiple effect size estimates of recollection and familiarity could be derived for some studies (e.g., deep versus shallow encoding; Ally et al. 2009). In these situations, we averaged across the multiple effect size estimates. Next, the small sample bias correction (Hedges 1981) was applied to the effect sizes measures. Negative effect size values indicate impairments in healthy older adults relative to young adults or impairments in aMCI or AD patients relative to controls.

Data Analysis—All of the analyses reported below were carried out using the *metafor* package (Viechtbauer 2010) in R, version 3.0.1 (R Core Team 2013). The mean weighted effect sizes (d_w) and the corresponding 95 % confidence intervals were calculated by fitting the effect sizes with a random effects model using restricted maximum likelihood estimation (Viechtbauer 2005). A random effects model was used because our goal was to make inferences about the magnitude of recollection and familiarity impairments in the population (Hedges and Vevea 1998; Viechtbauer 2010). A mean weighted effect size for both recollection and familiarity estimates were calculated separately for healthy aging studies, aMCI studies, and AD studies. Each study's effect size was weighted by the inverse variance weight (Lipsey and Wilson 2001). The Knapp and Hartung (2003) correction was used to account for uncertainty in the estimated amount of heterogeneity. The test for individual coefficients in the random effects models is based on a t-distribution with $k - p$ degrees of freedom, where k is the number of effect sizes, and p is the total number of coefficients (including the intercept). Homogeneity tests were conducted using the Q-statistic (Lipsey and Wilson 2001). This statistic has a χ^2 distribution with $k - 1$ degrees of freedom. A significant Q indicates that the distribution of effect sizes is heterogeneous (i.e., the variability in effect sizes is larger than expected from sampling error alone).

A series of mixed effects models were fit to the recollection and familiarity effect sizes to investigate if any of the moderator variables influenced the magnitude of recollection and familiarity differences. Specifically, these models examined if high estimates of recollection, the estimation method, and materials moderated differences in recollection and familiarity

[4]The metric reported for estimates of recollection and familiarity varies across the three estimation methods, and also across studies using the same estimation method. For example, recollection in the ROC procedure is calculated as a probability, whereas recollection and familiarity in the RK task can be calculated as a probability or a discrimination index (d'; e.g., McCabe and Geraci 2009). Likewise, in the PD and RK tasks, familiarity can be calculated as a probability (e.g., Jennings and Jacoby 1993) or a discrimination index (e.g., Davidson and Glisky 2002). Effect size estimates were based on means and variances of the metric used to calculate recollection and familiarity in a given study.

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estimates between healthy older adults and young adults. A mixed effect model was fit to the aMCI data to examine how the composition of the aMCI sample (i.e., single-domain only vs. single-domain and multiple-domain patients) affected recollection and familiarity declines. With the Knapp and Hartung (2003) adjustment, the omnibus test to determine if the moderators accounted for a significant portion of the variance (i.e., determine if there was a significant difference between the levels of the moderator variable) is represented by an *F*-distribution with *m* and $k - p$ degrees of freedom, where *m* is the number of moderators in the model excluding the intercept. This *F*-statistic tests the null hypothesis that the coefficients of the model (excluding the intercept) are equal to zero (e.g., H_0: $\beta_1=\beta_2=0$). In the models reported below, one of the levels of a factor (e.g., RK studies when examining the effects of the estimation method) was defined as the reference group (i.e., intercept) of the model. Thus, a significant *F*-statistic indicates that the different levels of a factor have significantly different effect sizes. The significance test for individual coefficients is the same as described above for the random effects models. The specific details of each model will be described in more detail when presenting the results.

Publication Bias—One limitation of meta-analysis is that the results might be influenced by certain publication biases, such as reporting overestimates of the true effect size in experiments with small sample sizes. We addressed the above form of publication bias by examining asymmetry in funnel plots. Specifically, we performed a random-effects version of the Egger's test in which the effect sizes are regressed on the standard error of the effect sizes (Egger et al. 1997; Sterne and Egger 2005). The funnel plots for healthy aging, aMCI, and AD studies are shown in Fig. 1.

Estimating Recollection and Familiarity for Each Study Using the Yonelinas (2002)

In addition to the effect size analysis, we also examined recollection and familiarity deficits in healthy aging, aMCI, and AD following the method outlined by Yonelinas (2002). This approach calculates an estimate of recollection and familiarity for each group in a study (e.g., young and older adults) using the average proportion of responses and the formulas for the corresponding method. The recollection and familiarity estimates derived from this method are provided in Tables 1 for young and healthy older adults, in Table 2 for healthy controls and aMCI patients, and in Table 3 for healthy controls and AD patients. The dependent variable of interest in this analysis was the absolute difference score between young and older adults or between healthy controls and aMCI/AD patients. This difference score was calculated for both recollection and familiarity, with negative values indicating lower estimates of recollection and familiarity in older adults, patients, and AD. Note that our primary purpose for conducting this analysis is to determine if excluding approximately half of the samples biased the results from the effect size meta-analysis reported in the main text. This method and results from this approach are presented in detail in the Supplemental Material. With one exception (discussed below), these results did not alter our conclusions.

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Results

Healthy Aging

Overall—The mean effect sizes for recollection and familiarity differences between young and healthy older adults are shown Fig. 2. Healthy aging led to a significant decrease in recollection, [d_w = −0.75; $LB_{95\%\ CI}$ = −0.85; $UB_{95\%\ CI}$=−0.65; $t(35)$=15.28; p<0.001]. The Egger's test did not find any evidence for publication bias; the coefficient for the standard error (b_{SE}), which indexes funnel plot asymmetry, was not significant, [b_{SE}=−.49, $t(34)$=0.55, p=.59]. The homogeneity test was not significant, [$Q(34)$=41.84; p=0.19], indicating that the variability present in the recollection effect sizes was within that expected from sampling error alone.

Similar to recollection, the overall familiarity effect size was significant [d_w=−0.27; $LB_{95\%\ CI}$=−0.45; $UB_{95\%\ CI}$= −0.09; $t(35)$=2.99; p<0.01], suggesting that healthy aging is associated with reductions in familiarity. However, the mean effect size for familiarity was approximately a third of the magnitude of the recollection effect sizes. Moreover, the 95% confidence intervals did not overlap, which suggests that aging leads to larger declines in recollection compared to familiarity. The Egger's test did not provide any evidence to suggest that publication bias was present for the familiarity effect sizes, [b_{SE}=−.22, $t(34)$=0.14, p=.89]. A significant amount of heterogeneity was present in the effect sizes for familiarity, [$Q(34)$=139.54; p<0.001]. Below, a series of mixed effects models were fit to the data to determine high levels of recollection, the process estimation method, or the type of materials accounts for a portion of the heterogeneity of the familiarity effect sizes. For consistency, the same mixed effects models were conducted on the recollection effect sizes.

High Levels of Recollection—The first model examined if high levels of recollection moderated recollection and familiarity effect sizes. The recollection effect size for studies with high levels of recollection (i.e., Recollection estimates ≥0.60), [d_w=−0.96; $LB_{95\%\ CI}$= −1.23; $UB_{95\%\ CI}$=−0.69; $t(34)$= −7.19; p<0.001], was numerically higher than the effect size for studies with "normal" levels of recollection (i.e., Recollection estimates<0.60), [d_w= −0.72; $LB_{95\%\ CI}$=−0.82; $UB_{95\%\ CI}$=−0.61; $t(34)$=−14.13; p<0.001]. However, a mixed-effect regression model with "normal" recollection studies as the reference group indicated that this difference was not reliable, [$F(1, 34)$=2.86, p=0.10]. The mean familiarity effect sizes nearly identical for studies with "normal" levels of recollection, [d_w=−0.27; $LB_{95\%\ CI}$= −0.47; $UB_{95\%\ CI}$=−0.07; $t(34)$=2.79; p<0.01] and studies high levels of recollection, [d_w= −0.26; $LB_{95\%\ CI}$=−0.80; $UB_{95\%\ CI}$=0.29; $t(34)$=0.95; p=0.35]. A mixed-effect regression model identical to that used for the recollection estimates indicated that these effect sizes did not statistically differ, [$F(1, 34)$=0.003, p=0.96]. This suggests that high levels of recollection do not result in larger age-related recollection or familiarity impairments. However, the lack of an effect on high levels of recollection on age differences in familiarity might have arisen because a large number of studies with high levels of recollection, some of which were included in Yonelinas (2002), were excluded in the effect size analysis reported here. Using the Yonelinas (2002) method, the studies excluded from the effect size meta-analysis showed evidence that age differences in both recollection and familiarity are

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inflated with high levels of recollection, whereas the studies included showed no such effect (see Table S1 in the Supplemental Material).

Process Estimation Method—A second mixed effects model examined the influence of the process estimation method on the magnitude of effect size estimates for age differences in recollection and familiarity. Note that this analysis was performed only on 35 of the samples in the meta-analysis; the Prull et al. (2006) sample was excluded because it used multiple methods with the same group of participants. Figure 2 depicts the recollection and familiarity effect size estimates for the RK, PD, and ROC methods. The recollection effect sizes for RK studies, [d_w=−0.71; $LB_{95\%\ CI}$=−0.86; $UB_{95\%\ CI}$=−0.55; $t(32)$=9.24; p<0.001], PD studies, [d_w= −0.80; $LB_{95\%\ CI}$=−0.97; $UB_{95\%\ CI}$=−0.63; $t(32)$=9.77; p<0.001], and ROC studies, [d_w=−0.67; $LB_{95\%\ CI}$=−0.887; $UB_{95\%\ CI}$=−0.48; $t(32)$=6.96; p<0.001], were all similar in magnitude and significantly different from zero. The familiarity effect size for RK studies was significantly different from zero, [d_w=−0.50; $LB_{95\%\ CI}$=−0.78; $UB_{95\%\ CI}$=−0.23; $t(32)$= 3.70 p<0.001], whereas the effect size for PD studies, [d_w= −0.04; $LB_{95\%\ CI}$=−0.34; $UB_{95\%\ CI}$=0.25; $t(32)$=0.31; p= 0.76], and ROC studies, [d_w=−0.17; $LB_{95\%\ CI}$=−0.56; $UB_{95\%\ CI}$=0.22; $t(32)$=0.90; p=0.37], did not significantly differ from zero. This suggests that the use of the RK procedure might account for some of the variance in reported familiarity differences, but not recollection differences..

To test if the effect sizes were significantly different between the three estimation methods, we created a mixed effects model with two dummy coded variables. One variable coded the studies that used the PD method, and the other coded that studies that used the ROC method, thus making studies using the RK task the reference group. This model revealed no significant effect of estimation method on recollection effect sizes, [$F(2, 32)$=0.57, p=0.57]. However, there was a marginally significant effect of the estimation method on familiarity, [$F(2, 32)$=2.83, p=0.07]. An examination of the model coefficients, which measures the difference between the RK effect sizes with the PD and ROC effect sizes, demonstrated that the mean effect size for PD studies was significantly different from the RK studies, [$t(32)$=2.32, p<0.05], whereas the mean familiarity effect size for the ROC studies did not significantly differ from the RK studies, [$t(32)$=1.41, p=0.17]. The ROC and PD tasks were compared by modifying the above model such that the intercept of the mixed effects model reflected the mean effect size for the PD studies. The coefficient for the ROC studies in this model was not significant, [$t(32)$=0.53, p=0.60], indicated that the PD and ROC effect sizes did not significantly differ from each other. These results show that age differences in familiarity, not recollection, are affected by the estimation method. Specifically, familiarity differences between young adults and healthy older adults were only significant when the RK task was used to assess recollection and familiarity, but not when the PD and ROC tasks were employed. The estimation method accounted for approximately 7.8 % of the estimated heterogeneity in the familiarity effect sizes, and a significant portion of residual heterogeneity remained, [$Q(32)$=122.60; p<0.001].

Verbal Versus Non-Verbal Materials—Lastly, a mixed effects model was specified to examine whether the type of materials moderated the magnitude of the recollection and familiarity effect sizes for healthy aging studies. The recollection effect sizes were nearly

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identical for studies using verbal materials, [d_w=−0.75; $LB_{95\%\ CI}$=−0.86; $UB_{95\%\ CI}$=−0.64; $t(33)$=13.75; p<0.001], and studies using nonverbal materials, [d_w=−0.73; $LB_{95\%\ CI}$=−1.02; $UB_{95\%\ CI}$=−0.41; $t(33)$=5.04; p=.11]. A mixed-effects regression model with studies using verbal materials as the reference group indicated that these two effect sizes did not reliably differ from each other, [$F(1, 33)$=0.02, p=0.88]. There was a numerical difference between the familiarity effect sizes for studies using verbal materials, [d_w=−0.22; $LB_{95\%\ CI}$=−0.42; $UB_{95\%\ CI}$=−0.02; $t(33)$=2.29; p<0.05], and nonverbal materials, [d_w=−0.40; $LB_{95\%\ CI}$= −0.89; $UB_{95\%\ CI}$=0.10; $t(33)$=1.63; p=.11]. However, the difference was not reliable, [$F(1, 33)$=0.45, p=0.51]. Thus, there was little evidence that the age effects on recognition were different for verbal and nonverbal materials.

The results from the healthy aging studies provide evidence that healthy older adults show large decreases in recollection relative the healthy young adults. Familiarity decreases were also significant, but much smaller than the decrease in recollection. Moreover, age differences in familiarity were moderated by the estimation method such that familiarity differences were only significant in studies using the RK method and not in studies using the PD and ROC methods. However, the estimation method only accounted for a small portion of the variance across studies, suggesting that other variables not examined here need to be accounted for in future studies. We will return to this issue in the General Discussion.

Amnestic Mild Cognitive Impairment

Figure 3 plots the mean effect sizes for recollection and familiarity differences between aMCI and healthy controls. The recollection effect size was significantly negative, [d_w= −0.82; $LB_{95\%\ CI}$=−1.16; $UB_{95\%\ CI}$=−0.49; $t(8)$=5.64; p<0.001], indicating decreased levels of recollection in aMCI patients compared to healthy controls. The test for heterogeneity test approached significance, [$Q(8)$=13.81; p=0.09], and there was no indication of publication bias as the Egger's test was not significant, [b_{SE}=−1.31, $t(7)$=.46, p=.66]. The mean familiarity effect size across studies was negative, but not significantly different from zero, [d_w=−0.41; $LB_{95\%\ CI}$=−1.04; $UB_{95\%\ CI}$= 0.21; $t(8)$=1.52; p=0.17]. There was a significant amount of heterogeneity in the familiarity effect sizes, [$Q(8)$=55.87; p<0.001]. Similar to the recollection effect sizes, the Egger's test was not significant, indicating that there was no evidence of publication bias for familiarity estimates in the aMCI studies, [b_{SE}=−5.46, $t(7)$=1.18, p=.28].

As discussed previously, some studies only tested single-domain aMCI patients whereas others tested a patient sample comprised of both single-domain and multiple-domain aMCI patients. To examine if this moderated the magnitude of the recollection and familiarity effect sizes, this variable was dummy coded such that the reference group was studies that only examined single-domain aMCI patients. The recollection effect size for the studies examining only single-domain patients, [d_w=−0.72; $LB_{95\%\ CI}$=−1.34; $UB_{95\%\ CI}$=−0.10; $t(7)$=2.72; p<0.05], and the studies that examined both single-domain and multiple-domain patients, [d_w=−0.88; $LB_{95\%\ CI}$=−1.33; $UB_{95\%\ CI}$=−0.43; $t(7)$=4.60; p<0.01], were both significantly different from zero, but did not significantly differ from each other, [$F(1, 7)$=0.24, p=0.64] (see Fig. 4). The mean familiarity effect size for the studies exclusively testing single-domain aMCI patients was not significant, [d_w=0.11; $LB_{95\%\ CI}$=−0.91;

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$UB_{95\%\ CI}$=1.14; $t(7)$=0.26; p=0.80], whereas the effect size for studies testing a mixture of single-domain and multiple-domain aMCI patients was marginally significant, [d_w=−0.68; $LB_{95\%\ CI}$=−1.42; $UB_{95\%\ CI}$=0.06; $t(7)$=2.18; p=.07]. Although there was a fairly large numerical difference between the two effect sizes, the difference was not reliable, [$F(1, 7)$=2.41, p=0.16], which might reflect the small number of studies included in this analysis. Overall, these results show that the aMCI groups exhibited reduced recollection estimates compared to aged controls. Familiarity estimates were numerically reduced as well but only approached significance for studies that examined a mixture of single-domain and multiple-domain aMCI patients.

Alzheimer's Disease

The effect sizes for both recollection, [d_w=−1.39; $LB_{95\%\ CI}$= −2.07; $UB_{95\%\ CI}$=−0.71; $t(4)$=5.66; p<0.01], and familiarity, [d_w=−1.40; $LB_{95\%\ CI}$=−2.12; $UB_{95\%\ CI}$=−0.68; $t(4)$=5.43; p<0.01], were significant in the AD studies (see Fig. 3), suggesting that AD is associated with large deficits in both recollection and familiarity relative to age-matched controls. The test for heterogeneity was not significant for recollection, [$Q(4)$=6.00; p=0.20], nor familiarity, [$Q(4)$=6.74; p=0.15]. The Egger's test was not significant for the recollection effect sizes, [b_{SE}=13.68, $t(3)$=1.33, p=.28]. However, the Egger's test approached significance for familiarity effect sizes, [b_{SE}= −6.81, $t(3)$=2.63, p=.08], suggesting that publication bias might be present for familiarity. However, it is important to point out that the Egger's test can be unreliable when the sample size is small (Moreno et al. 2009). These above findings indicate that AD is associated with large decreases in both recollection and familiarity-based recognition.

General Discussion

The results from the meta-analysis reported above revealed that healthy aging is associated with significant reductions in recollection, with an effect size in the moderate-to-large range (Cohen 1988).A significant age-related decrease in familiarity was also observed, albeit a small effect size. However, these familiarity differences depended on the test method. Specifically, the familiarity effect size was moderate in magnitude and significant in studies using the RK method, whereas familiarity was not impaired in studies using the PD and ROC methods. There was little evidence that high levels of recollection or the type of materials moderated recollection or familiarity effect sizes.

Large decreases in recollection were observed in aMCI patients. Familiarity deficits in aMCI patients were not significant overall. However, the available data suggests that familiarity decreases in aMCI might depend on the type of patients included in the sample. Specifically, a moderate-to-large decrease in familiarity, which approached significance, was observed in studies that included a mixture of single-domain and multiple-domain aMCI patients whereas no familiarity decrease was evident in studies that included only single-domain aMCI patients.

Finally, the meta-analysis of the AD studies revealed that AD is associated with large and significant decreases in both recollection and familiarity. There were however, too few studies to determine whether those effects were moderated by other experimental or

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individual group differences. We discuss the implications of each of the above findings in turn.

Healthy Aging

The results from all three test procedures converged in showing that recollection is disrupted in healthy aging, a finding that is in good agreement with the widely held belief that recollection is impaired in healthy aging. In addition, the results showing significant decreases in familiarity in the studies using the RK test procedure but not the PD or the ROC test procedures partially explains why there has been disagreement in the literature about the fate of familiarity (e.g., Davidson and Glisky 2002; Duarte et al. 2006; Jennings and Jacoby 1993; Prull et al. 2006; Wang et al. 2012; Yonelinas 2002). While it is often assumed that the different estimation methods are interchangeable (Yonelinas 2001a; 2002), the aging literature reviewed here makes it quite clear that this is not always the case (see also, Prull et al. 2006). Why is it that familiarity is impaired in healthy older adults when it is measured using the RK procedure, but not when it is measured using the ROC or PDP procedures? The current review cannot provide a definitive answer to this question, and future studies that directly contrast the three methods are necessary. However, there are several potential explanations for the difference between the estimation methods that are worth considering.

First, the comparison between the estimation methods presented here relied on comparisons across studies, and so it is possible that older adults sampled in the RK studies had a fundamentally different demographic or neuropsychological profile compared to older adults in the PD and ROC studies. However, the studies included in this meta-analysis randomly sampled older adults from the population, which presumably would result in similar sample characteristics on average. Breaking up the data reported in Table 4 by the estimation method is consistent with this notion; the average age (RK=70.84 years; PD=71.37 years; ROC=70.84 years) and education (RK=15.34 years; PD=14.65 years; ROC=16.22 years) were fairly similar across studies. Although we cannot fully rule out this possibility, we believe this account to be unlikely.

Second, it could be the case that the RK studies are telling us the true story (i.e., healthy aging leads to similar decreases in both recollection and familiarity) and that the PD and ROC methods are biased in such a way to make it appear that familiarity is spared in healthy aging. However, several findings argue against this possibility. First, results from numerous task dissociation studies indicate that recollection is more disrupted that familiarity (e.g., recall and associative recognition are significantly more impaired than item recognition; La Voie and Light 1994; Old and Naveh-Benjamin 2008), which is consistent with the conclusions the PD and ROC methods, and suggests that it is the RK finding that might be anomalous. In addition, the factors that are known to produce potential biasing effects on the PD and ROC procedures do not appear to be playing a role in the current aging studies. For example, in the PD procedure, familiarity estimates can be inflated by noncriterial recollection (i.e., recollection of specific details that do not support the required source memory discrimination; Yonelinas and Jacoby 1996b). However, noncriterial recollection should occur more often in young adults than in older adults because young adults have higher levels of recollection, which would inflate the apparent familiarity deficits in aging

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rather than eliminate them (Parks 2007; Toth and Parks 2006). In the ROC procedure, familiarity decreases in healthy aging could be masked because recollection and familiarity are not as reliably estimated in older adults compared to young adults. However, existing data provides no evidence indicating that the dual-process signal detection model fits data from older adults more poorly than the data from younger adults (e.g., Healy et al. 2005; Parks 2007). Finally, as discussed below, there is growing empirical evidence that the RK procedure may be providing biased estimates in studies of aging.

A third possibility is that the PD and ROC methods are telling the true story (i.e., recollection, not familiarity, is impaired in healthy aging) and that the RK method is biased in some way. One aspect of that could lead to the findings observed for the RK studies is that older adults might interpret the RK instructions differently than younger adults. The RK procedure is unique in that it measures recollection and familiarity on the basis of the participants' introspective reports. The extant literature demonstrates that the specific instructions of the RK procedure significantly impact the results (Geraci and McCabe 2006; Geraci et al. 2009; McCabe and Geraci 2009; Rotello et al. 2005; Yonelinas 2001b). For example, using the standard instructions (e.g., Gardiner 1988; Rajaram 1993) some individuals might not fully understand the distinction between 'Remember' and 'Know' judgments, particularly those individuals with memory impairments (Aggleton et al. 2005; Baddeley et al. 2001; Yonelinas et al. 2002). This has led some researchers to adopt a set of *strict* instructions whereby participants are instructed to make a 'Remember' response only if they can report specific details about the study event to the experimenter to ensure that 'Remember' responses reflect instances in which qualitative information is retrieved (e.g., Yonelinas et al. 2002). Importantly, it is only under these strict instructions that the results of the RK procedure converge with those obtained using the ROC procedure (e.g., Koen and Yonelinas 2010; Yonelinas 2001b; for caveats, see Rotello et al. 2005).

The vast majority of the RK studies included in the current meta-analysis used the standard instructions. Thus, it is possible that, compared to young adults, older adults in these RK studies spontaneously adopted a more lenient definition of what constitutes a'Remember' response or were more likely to confuse the two response options. In either case, if older adults make 'Remember' responses to items that are highly familiar rather than responding 'Know' to these items, this would lead to an apparent reduction in familiarity-based responses. It is not possible to verify that older and younger adults use the RK responses in the same way based on the data presented in the meta-analysis, but there is some evidence in the extant literature favoring this explanation. First, a recent review indicated that older adults typically give more false 'Remember' responses compared to young adults (McCabe et al. 2009). This increased propensity to give a 'Remember' response to new items could potentially decrease familiarity estimates (Yonelinas and Jacoby 1995). Second, McCabe and Geraci (2009) found that source-specific instructions, which placed a prominent emphasis on recollecting specific details of the study episode, increased familiarity estimates in older adults but not in younger adults. These results indicate that older adults are particularly sensitive to the content of the RK instructions. Finally, a recent study (Koen & Yonelinas, under review) that directly compared the RK, PD, and ROC methods in the same sample of participants used strict RK instructions, and found no evidence for age-related

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familiarity impairments in any of the three estimation procedures (but see Prull et al. 2006). Although the above findings suggest that the RK instructions might play a pivotal role, future work that systematically examines how aged and young subjects differ in their interpretation of the RK instructions would be beneficial.

In addition to assessing the moderating effects of the estimation methods, we examined if high levels of recollection and material type moderated age-related differences in recollection and familiarity. In neither case did we find compelling evidence that the results depended critically on either of these factors. The results from the meta-analysis reported above suggested that high levels of recollection – which can inflate familiarity estimates – did not significantly impact the age-related effects on recollection or familiarity. This finding stands in contrast to Yonelinas (2002) who reported that familiarity differences due to healthy aging were more evident when the recollection estimate of young adults was high (i.e., ≥0.60). One potential reason for this difference is that the studies included in the current effect size meta-analysis tended to have lower overall levels of recollection than those considered by Yonelinas (2002), and thus minimized the biasing effects of high performance on the observed familiarity effect sizes (see Supplemental Material).

The results of the current meta-analysis also failed to provide support for the idea that the type of materials moderated recollection or familiarity differences between young and healthy older adults. If anything, the familiarity reduction in healthy older adults was larger for studies using nonverbal materials. However, the meta-analysis might not have been sufficiently sensitive to material effects because the type of nonverbal stimuli varied across the studies and included faces, scenes, visual objects, and symbols. Future studies that use a variety of different types of materials will also be important to determine if and how the type of materials moderates age-related declines in recollection and familiarity. It could be the case that age-related differences in recollection and familiarity might vary with the type of nonverbal materials used. Evidence from individuals with medial temporal lobe damage is consistent with this notion (Aly et al. 2010; Bird and Burgess 2008; Carlesimo et al. 2001). For example, Aly and colleagues (2010) showed that, compared to healthy controls, patients with medial temporal lobe damage have significantly reduced estimates of familiarity for words but normal familiarity estimates for faces. To our knowledge, no study has directly examined age-related differences in recollection and familiarity for verbal stimuli compared to different types of nonverbal stimuli (e.g., scenes, faces, objects).

It is important to point out that although the estimation method accounted for part of the across study variance, a large portion of the variance was unexplained by the moderator variables included in this meta-analysis. While it is possible that the across study variance regarding age differences in familiarity might be due to increased noise in familiarity estimates in both young and older subjects, relative to recollection estimates, this explanation likely cannot account for all of the across study variance. We believe that there are other systematic influences that need to be investigated further. While there are many candidate variables, one factor that we see as critical is how healthy and pathological aging influences the structural and functional integrity of neural regions that support familiarity age-related and disease-related differences in the neural correlates of familiarity. Indeed, as we discuss in more detail below, healthy older adults and aMCI patients show differences in

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regions thought to support recollection and familiarity. However, it is important to point out that other factors, such as the neuropsychological profile of the sample and age differences in encoding and retrieval strategies might also play an important role.

Amnestic Mild Cognitive Impairment and Alzheimer's Disease

The results indicated that both recollection and familiarity were significantly reduced in AD. In addition, although recollection was clearly impaired in aMCI, there was only a numerical reduction in familiarity estimates that was not significant. However, the results provided evidence that the aMCI subtype might play a role in the familiarity decline. Specifically, the mean familiarity effect size for studies that only tested single-domain aMCI patients was near zero and slightly positive, whereas the corresponding effect size for studies that tested a mixture of single-domain and multiple-domain aMCI patients was negative and approached significance. This finding is consistent with recent explanations for why familiarity may be spared in some aMCI patients (Serra et al. 2010; Troyer et al. 2012). The findings from the literature comparing tasks believed to differentially rely on recollection and familiarity (e.g., free recall compared to old/new recognition) are also consistent with the pattern of data reported here. In particular, studies exclusively testing multiple-domain aMCI patients found impairments on tasks believed to rely heavily on familiarity (Algarabel et al. 2009; 2012; but see Westerberg et al. 2006). However, although limited by a small sample of single-domain patients, a recent study by Westerberg and colleagues (2013) did not find differences between single and multiple-domain aMCI patients on a four-alternative forced choice test, which they argued relies heavily on familiarity. Future research with larger samples that directly contrast recollection and familiarity estimates between single-domain and multiple-domain aMCI patients is needed to fully address this question.

Why might familiarity be spared in single-domain patients but impaired in multiple-domain patients? Although the extant literature has no addressed this question directly, one possibility is that multiple-domain aMCI patients have more dense amnesia compared to single-domain patients. However, some evidence indicates that single-domain and multiple-domain aMCI patients only differ in impairments on non-memory cognitive domains (Seo et al. 2007). Alternatively, it could be the case that impairments in non-memory domains are what underlie familiarity decreases in multiple-domain aMCI patients. However, some non-memory domains that are affected in multiple-domain aMCI, such as executive function, are typically associated with recollection, not familiarity (e.g., Bugaiska et al. 2007; Davidson and Glisky 2002; but see Bunce and Macready 2005). Thus, it could be the case that familiarity impairments in multiple-domain aMCI patients are not ubiquitous, but depend on the specific neuropsychological profile of the patient. A third possibility discussed by Wolk and colleagues (2013) is that multiple-domain aMCI patients may have more AD-related neuropathology and contain a higher proportion of prodromal AD individuals. Compared to single-domain aMCI patients, multiple-domain aMCI patients have an increased presence of AD biomarkers (Wolk et al. 2009) and also convert to AD at a higher rate (Han et al. 2012). Determining which of the above factors, if any, contribute to familiarity differences in aMCI and AD is an important endeavor for future research.

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The results of the meta-analysis are consistent with a recent proposal that "context free" memory, which includes familiarity-based recognition, is impaired early in the course of AD (Didic et al. 2011). These data suggest that familiarity impairments might be predictive of which individuals will convert to AD and who will remain stable or even revert back to normal. As discussed previously, the finding that healthy aging can be associated with selective recollection deficits, whereas AD is associated with pronounced deficits in recollection and familiarity suggest that familiarity impairments might be indicative of pathological aging. In addition, the finding that familiarity decreases were evident only in aMCI studies that tested both single-domain and multiple-domain aMCI patients in conjunction with findings that multiple-domain aMCI patients convert to AD at a higher rate (Han et al. 2012) suggest that familiarity may be useful in predicting conversion to AD. Future research, and in particular longitudinal data, is needed to determine if baseline levels of the rate of decline in recollection and familiarity predict conversion to AD.

It is also important to consider whether or not other factors play a role in recollection and familiarity decreases observed in aMCI and AD patients. Currently, there is little evidence examining the role the estimation method, high levels of recollection, or the type of stimuli role in recollection and familiarity differences in aMCI and AD. Although few studies have critically examined these issues, the available evidence suggests that only the type of stimuli might moderate familiarity differences in aMCI patients. For instance, Serra and colleagues (2010) reported similar patterns of recollection and familiarity deficits in aMCI patients tested with the RK and PD methods, and Wolk and colleagues (2013) reported that the pattern of recollection and familiarity deficits were unchanged when individuals with high levels of recollection were excluded from the analysis. Regarding the type of stimuli, a study by Embree and colleagues (2012) recently demonstrated that familiarity deficits in aMCI patients were eliminated when the to-be-learned stimuli were pictures instead of words. Additional work replicating and extending the above findings are needed before any firm conclusions can be drawn.

Linking Memory Changes to Medial Temporal Lobe Changes

What are the neural changes that underlie the declines in recollection and familiarity that are observed in aging? It is well established that the medial temporal lobes (MTL) play a critical role in episodic memory, with damage to these regions causing severe impairments in the ability to form new episodic memories (e.g., Scoville and Milner 1957; Squire and Zola-Morgan 1991). In addition, a growing body of research from studies of lesion patients, neuroimaging and animal studies has indicated that within the MTL, the hippocampus is critical for recollection, whereas the surrounding perirhinal cortex is critical for familiarity (for reviews see Diana et al. 2007; Eichenbaum et al. 2007; Yonelinas et al. 2010; but see Squire et al. 2007). A number of structural and functional neuroimaging studies have begun to explore how age related changes in these regions are related to declines in recollection and familiarity. Aging is associated with a large variety of brain changes and a full neural account of age-related memory declines is undoubtedly quite complex. For instance, aging is associated with robust volumetric reductions in the frontal cortex (e.g., Raz 2005), and a full understanding of age differences in memory must account for these changes. Here, we focus on the MTL because, as discussed above, the extant literature provides strong evidence for a

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dissociation between the involvement of the hippocampus and perirhinal cortex in recollection and familiarity, respectively. The existing results suggest that changes in these two MTL regions are directly related to the types of memory impairment that are observed in different age and patient groups.

Structural neuroimaging studies have shown decreases in hippocampal volume in normal aging, aMCI and AD (for reviews, see Raz 2005; Raz and Rodrigue 2006; Ries et al. 2008). AD and aMCI patients show pronounced volumetric decreases in the parahippocampal gyrus, including the perirhinal and entorhinal cortices (e.g., Ries et al. 2008; Troyer et al. 2012; Westerberg et al. 2013; Wolk et al. 2011), whereas perirhinal and entorhinal volumes are less affected in healthy aging (e.g., Raz et al. 2004; Yonelinas et al. 2007). Thus, it might be the case that recollection impairments in healthy aging, aMCI and AD are due to decreases in hippocampal integrity, whereas the familiarity deficits seen in AD and some aMCI groups could be explained by damage to regions outside the hippocampus, such as the entorhinal and perirhinal cortices.

Support for this idea comes from studies examining the relationship between age-related brain changes and memory performance. A number of studies have revealed that age reductions in MTL volumes correlate with decreases in behavioral measures of episodic memory (e.g., Rajah et al. 2010; Troyer et al. 2012; Westerberg et al. 2013; Wolk et al. 2011; Yonelinas et al. 2007; but see Van Petten 2004). Only a few studies to date have used process estimation methods to examine the relationship between estimates of recollection and familiarity with MTL volumes. Importantly, these studies appear to converge in showing that hippocampal volume correlates with recollection whereas entorhinal/perirhinal volume correlates with familiarity. For example, Yonelinas and colleagues (2007) examined the relationship between hippocampal and entorhinal/perirhinal volumes and recollection and familiarity estimates derived from structural equation modeling (cf., Quamme et al. 2004) in 157 older adults between 65 and 80 years-of-age. The results showed that hippocampal volume correlated with recollection where entorhinal/perirhinal volumes correlated with familiarity. Moreover, hippocampal volume was found to mediate the relationship between age and recollection. Wolk and colleagues (2011) found a similar pattern of results in a sample of healthy older adults, aMCI patients, and AD patients. Specifically, after controlling for age and diagnostic status, the volume of the hippocampus, but not parahippocampal gyrus (i.e., the perirhinal, entorhinal, and parahippocampal cortices) predicted recollection estimates derived from a PD procedure. In contrast, parahippocampal gyrus volume predicted familiarity, but not recollection estimates. Likewise, Troyer and colleagues (2012) reported that hippocampal volume correlated with estimates recollection but not familiarity derived from the PD procedure.

Recently, Wolk and colleagues (2013) examined how cortical thickness in a network of regions which is hypothesized to be a “cortical signature of AD” (see Dickerson et al. 2009) correlated with recollection and familiarity estimates in healthy older adults and aMCI patients. The network includes nine bilateral regions distributed across the frontal cortex (superior frontal gyrus and inferior frontal sulcus), parietal cortex (angular gyrus, superior parietal lobule, supramarginal gyrus, and precuneus) and temporal cortex (anterior medial temporal lobe, temporal pole, inferior temporal gyrus). Critically, the anterior medial

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temporal lobe encompassed the entorhinal and perirhinal regions that have been shown to correlate with familiarity estimates (Wolk et al. 2011; Yonelinas et al. 2007). The mean cortical thickness of the above 9 bilateral regions correlated with familiarity, but not recollection, in both healthy older adults and aMCI patients, such that cortical thinning was associated with lower levels of familiarity. The above finding suggests that familiarity impairments in apparently healthy older adults, when they are observed, may be a result of underlying AD neuropathology that does not result in clinical impairments.

The evidence from functional neuroimaging studies has suggested that young and older subjects recruit similar regions in recollection and familiarity related recognition, but that there might be subtle differences in the roles of these regions and how they interact with other cortical regions to support episodic memory. Some studies have reported that older and younger adults show similar patterns of recollection and familiarity related activity in the hippocampus and perirhinal cortex, respectively (Angel et al., 2013; de Chastelaine et al. 2011; Duarte et al. 2008; 2010). For example, using an RK task, Duarte and colleagues (2008, 2010) found increased hippocampal activity associated with recollection and decreased activity in the perirhinal cortex activity associated with familiarity during retrieval in both young and healthy older adults. However, Daselaar and colleauges (2006) reported that increased hippocampal activity associated with recollection in young adults was reduced in healthy older adults. However, healthy older adults showed larger decreases in perirhinal activity associated with familiarity than did young controls (see also Morcom et al. 2010). Moreover, these changes were associated with differences in the connectivity profiles of the hippocampus and perirhinal cortex, such hippocampal activity correlated more strongly with retrosplenial cortex in young adults and perirhinal activity correlated more strongly with prefrontal cortical regions in older adults (for similar results, see Dennis et al. 2008). In contrast, Duverne et al. (2008) reported that aging was associated with increased recollection-related activity in the hippocampus. Finally, Genon and colleagues (2013) reported decreased recollection related connectivity between the posterior cingulate and hippocampus in AD patients, which suggests that decreased hippocampal function might underlie recollection impairments in AD.

The structural and functional neuroimaging results are broadly consistent with the results showing that the hippocampus and perirhinal cortex are critical for recollection and familiarity in healthy older adults, aMCI patients, and AD patients. Moreover, the above discussion suggests that age-related or disease-related changes in MTL regions might underlie decreases in recollection and familiarity. The extant data also suggest that AD-related neuropathology in aMCI patients and healthy older adults might underlie age-related declines in familiarity.

Future Directions and Conclusions

One general limitation of the studies examined in the current meta-analysis is that they examined cross-sectional samples and compared healthy older adults to college-aged young adults. Future work should focus on examining recollection and familiarity declines with longitudinal experimental designs as well as with cross-sectional designs that treat age as a continuous variable. These studies are needed to address important theoretical questions,

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such as determining if the recollection and familiarity declines onset simultaneously, or if one happens later than the other. Another important issue is to determine if the two processes show linear or nonlinear age-related decreases. A few studies have examined age-related differences in recollection and familiarity using cross-sectional samples, with the results showing that age is negatively correlated with recollection but not familiarity (Koen & Yonelinas, under review; McCabe et al. 2009; Yonelinas et al. 2007). However, these studies did not examine if nonlinear age trends were present in recollection and familiarity.

Additionally, only a small number of studies have examined recollection and familiarity in AD and aMCI, and further studies will be essential in determining the fate of recollection and familiarity in these two patient populations. In AD, the impairments in both recollection and familiarity were large and consistent across studies suggesting that the deficits observed in this group are quite robust. This is important because it suggests that the deficits seen in AD are distinct from those seen in normal aging where only recollection is consistently impaired. In aMCI, recollection impairments were also quite consistent but the fate of familiarity was less clear. The results did suggest that multiple-domain, but not single-domain, aMCI patients might exhibit familiarity deficits, but no study that we are aware of has directly compared recollection and familiarity estimates between these two aMCI subtypes. Additional research directly assessing this issue is needed.

Moreover, the results from this meta-analysis suggested that familiarity does not generally decline in healthy aging when measured with the PD and ROC procedures, but that age-related declines in familiarity are often observed in studies using the RK task. This might be related to differences in how elderly individuals interpret the RK instructions; however, further studies directly contrasting the different measurement methods in aged groups will be critical in assessing this possibility. Moreover, findings from Wolk and colleagues (2013) suggest that another cause of familiarity deficits in healthy older adults might be the presence and load of underlying AD neuropathology.

Taken together, the results presented here highlight the importance of assessing recollection and familiarity when examining the effects of age on episodic memory. In addition, they suggest that the distinction between recollection and familiarity has the potential to play an important role in differentiating between memory changes in healthy aging and neurodegenerative diseases.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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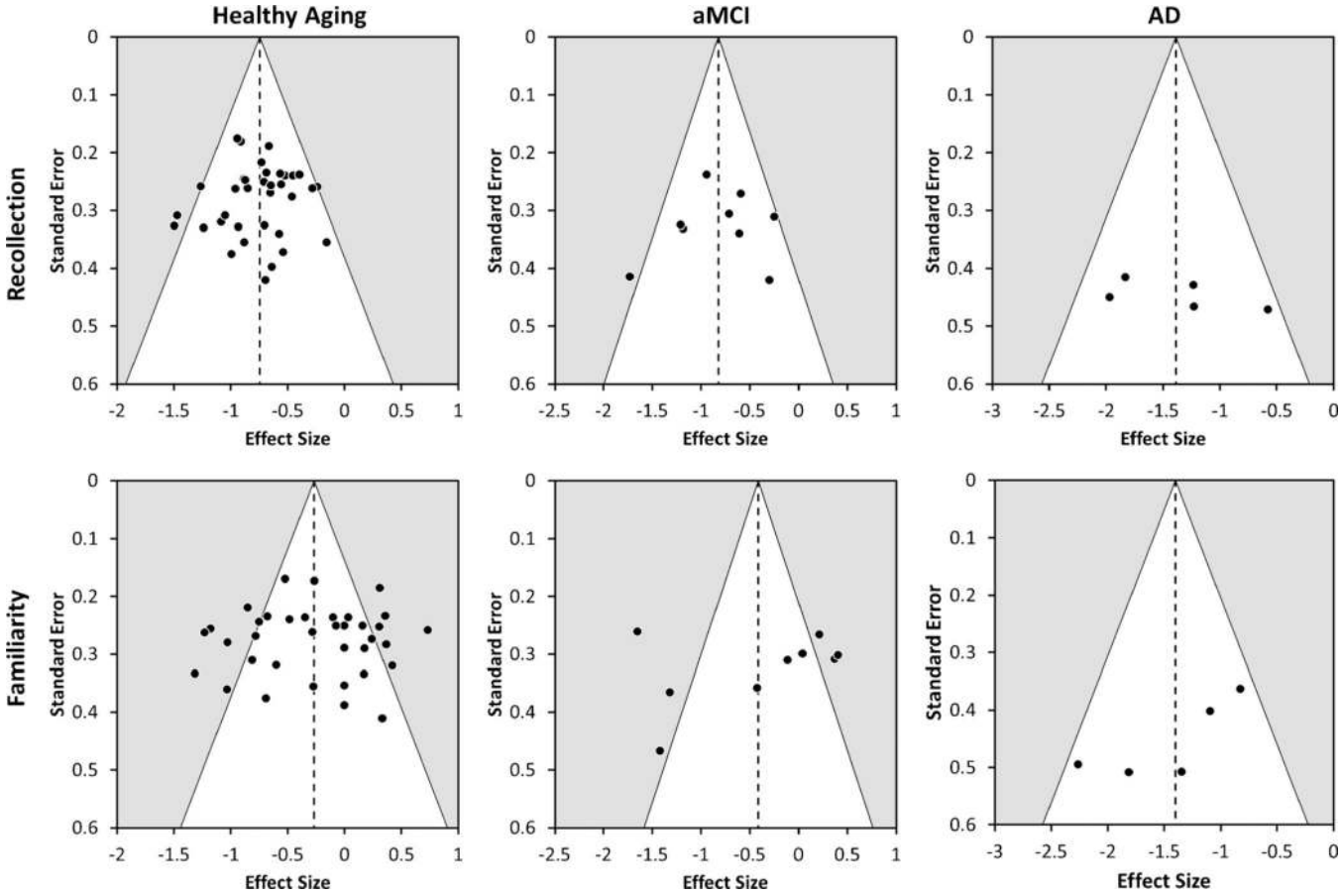

Fig. 1.

Funnel plots with the 95 % pseudo-confidence interval (white area) for recollection (top row) and familiarly (bottom row) differences in healthy aging, amnestic Mild Cognitive Impairment (aMCI), and Alzheimer's disease (AD) studies. Note that the range of the effect sizes on the *x*-axis is differs across the plots.

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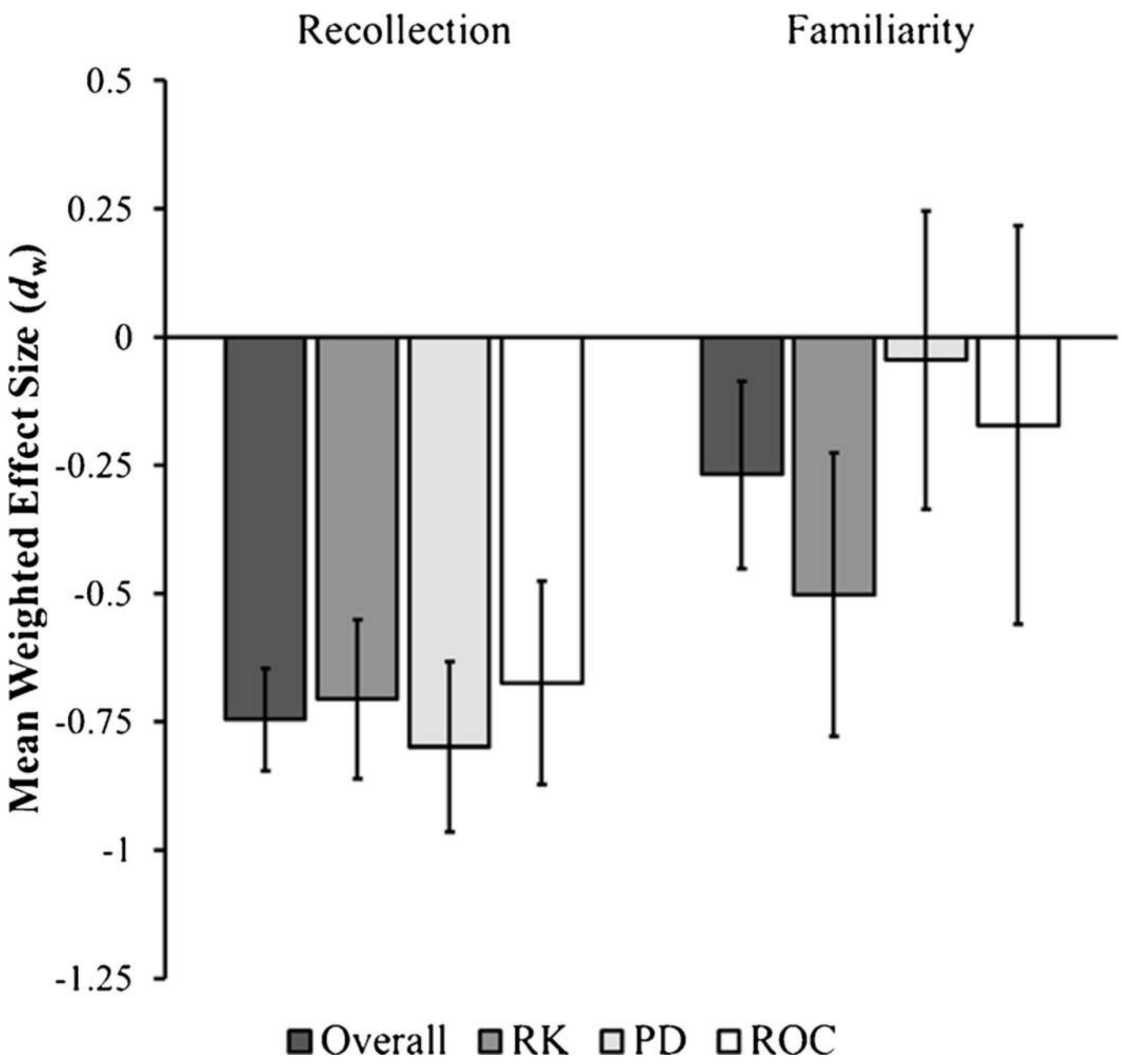

Fig. 2.

The overall mean weighted recollection and familiarity effect size estimates for studies examining healthy aging, and the mean weighted effect sizes for recollection and familiarity divided by the method used to estimate recollection and familiarity. Negative values represent decreases in older adults relative to young adults. Error bars represent the 95 % confidence interval of the effect size estimate. *RK* = Remember/Know Task; *PD* = Process Dissociation Procedure; *ROC* = Receiver-Operating Characteristic Procedure

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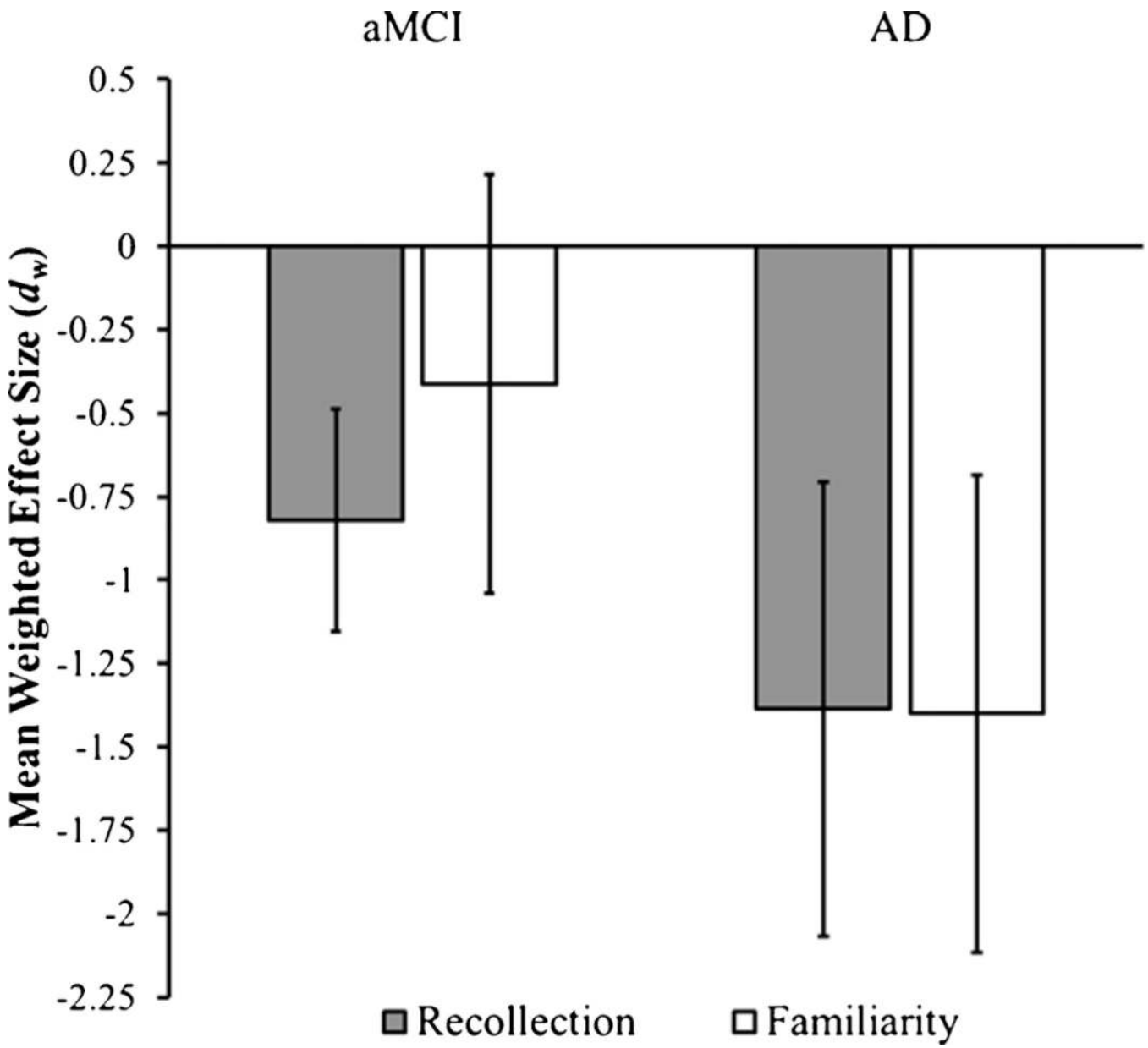

Fig. 3.

Mean weighted effect size estimates for recollection and familiarity differences in studies comparing patients diagnosed with amnestic Mild Cognitive Impairment (aMCI) and Alzheimer's disease (AD) compared to healthy, age-matched controls. Negative values represent decreases in aMCI and AD patients relative to controls. Error bars represent the 95 % confidence interval of the effect size estimate

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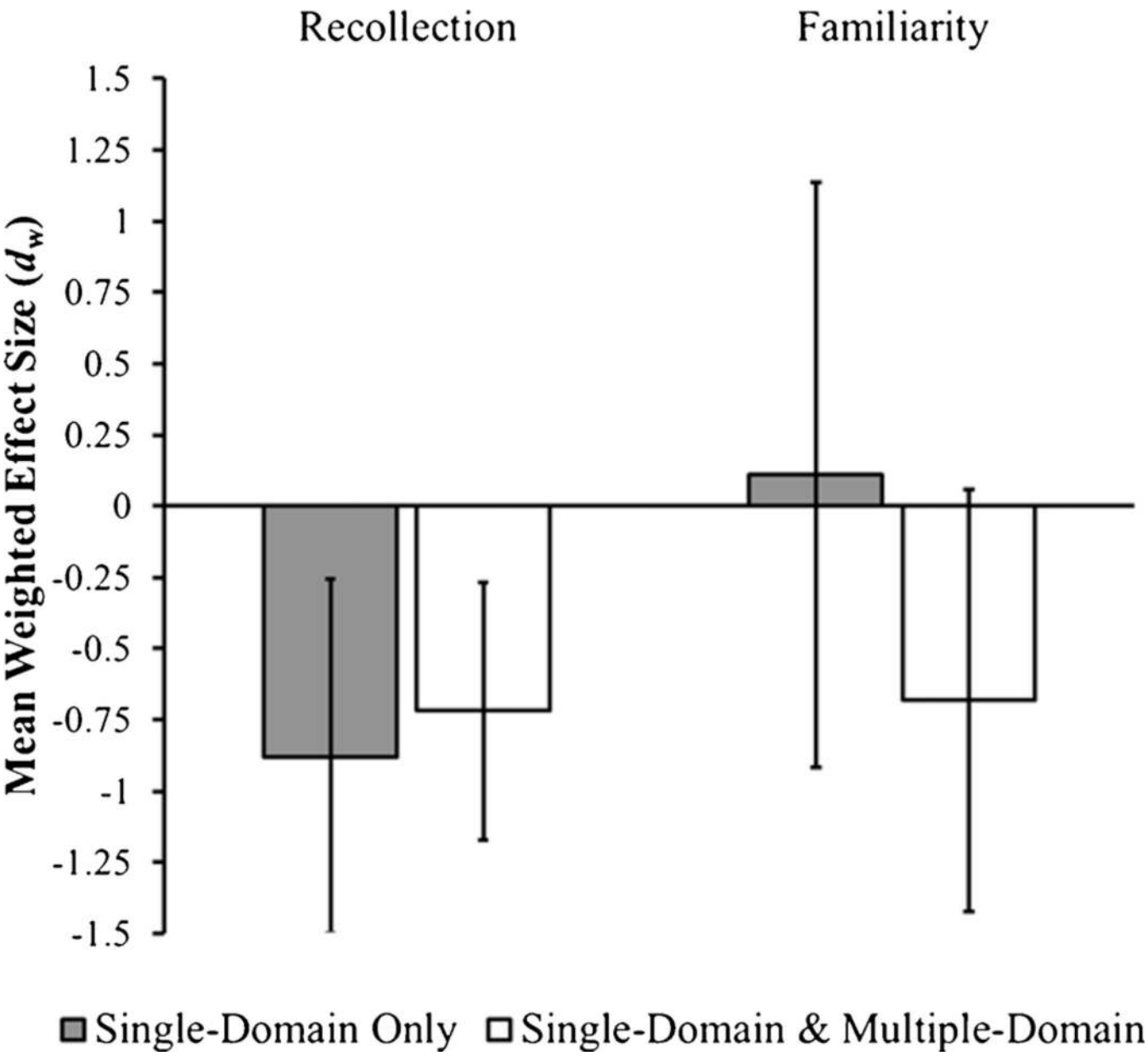

Fig. 4.

Mean weighted effect size estimates for recollection and familiarity differences in studies that compared a sample of single-domain amnestic Mild Cognitive Impairment (aMCI) to healthy, age-matched controls and studies that compared a mixture of single-domain and multiple-domain aMCI patients to healthy, age-matched controls. Negative values represent decreases in aMCI patients relative to controls. Error bars represent the 95 % confidence interval of the effect size estimate

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Table 1

Studies examining recollection and familiarity differences between healthy young and older adults

				Young Adults			Older Adults			Effect Size *d*	
Study	**R>.6**	**Estimation Method**	**Material Type**	***n***	**R (prob.)**	**F (prob.)**	***n***	**R (prob.)**	**F (prob.)**	**R**	**F**
Anderson et al. (2008)	Yes	PD	Verbal	25	0.86	0.44	44	0.76	0.48	−0.56	0.30
Angel et al. (2013)	No	RK	Nonverbal	20	0.40	0.55	20	0.31	0.61	−0.72	0.43
Bastin and Van der Linden (2003)	No	RK	Nonverbal	64	0.35	0.42	64	0.24	0.42	–	–
Bastin et al. (2004)	No	RK	Nonverbal	48	0.44	0.82	48	0.26	0.74	–	–
Belleville et al. (2011)[a]	No	RK	Verbal/Nonverbal	29	–	–	29	–	–	−0.66	−1.04
Benjamin and Craik (2001) – Exp. 2	No	PD	Verbal	18	0.58	0.42	34	0.38	0.53	–	–
Boywitt et al. (2012) – Exp. 1	No	RK	Verbal	40	0.50	0.46	41	0.38	0.41	–	–
Boywitt et al. (2012) – Exp. 2	No	RK	Verbal	44	0.31	0.27	44	0.23	0.20	–	–
Bugaiska et al. (2007)	No	RK	Verbal	24	0.28	0.35	24	0.15	0.28	–	–
Bunce (2003)	No	RK	Verbal	44	0.47	0.69	52	0.35	0.63	–	–
Bunce and Macready (2005)	No	RK	Verbal	52	0.54	0.54	52	0.47	0.48	–	–
Clarys et al. (2002)	No	RK	Verbal	27	0.22	0.28	55	0.14	0.30	–	–
Clarys et al. (2009)	No	RK	Verbal	44	0.37	0.43	44	0.27	0.36	–	–
Cohn et al. (2008) – Exp. 1	No	PD	Verbal	24	0.48	0.21	24	0.25	0.30	−1.07	0.18
Comblain et al. (2004)	No	RK	Nonverbal	20	0.54	0.47	20	0.29	0.29	–	–
Daselaar et al. (2006)	No	ROC	Verbal	12	0.40	0.36	12	0.20	0.46	−0.72	0.34
Davidson and Glisky (2002)	No	PD	Verbal	32	0.40	0.84	48	0.21	0.69	−0.69	−0.69
Duarte et al. (2006)	No	RK	Nonverbal	18	0.55	0.36	24	0.44	0.24	−0.95	−0.61
Duarte et al. (2008)	No	RK	Nonverbal	17	0.51	0.58	27	0.49	0.46	–	–
Düzel et al. (2011)	No	ROC	Nonverbal	24	0.27	0.27	56	0.17	0.17	−0.72	−1.24
Friedman et al. (2010)	No	RK	Nonverbal	18	0.31	0.41	17	0.19	0.24	−0.88	−1.06
Glanzer et al. (2004) – Exp. 5	No	ROC	Verbal	42	0.46	0.34	24	0.29	0.29	–	–
Harkins et al. (1979)	No	ROC	Verbal	8	0.44	0.27	16	0.27	0.18	–	–
Healy et al. (2005) – Exp. 1[d]	No	ROC	Verbal	59	0.41	0.44	60	0.28	0.51	−0.67	0.31
Healy et al. (2005) – Exp. 2[d]	No	ROC	Verbal	31	0.47	0.50	33	0.34	0.48	−0.65	−0.08
Healy et al. (2005) – Exp. 3[d]	No	ROC	Verbal	25	0.37	0.58	36	0.32	0.48	−0.29	−0.29

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Study	R>.6	Estimation Method	Material Type	Young Adults			Older Adults			Effect Size *d*	
				n	R (prob.)	F (prob.)	*n*	R (prob.)	F (prob.)	R	F
Howard et al. (2006)	No	ROC	Nonverbal	43	0.30	0.22	33	0.25	0.24	−0.57	0.36
Jacoby (1999) –Exp.4	No	PD	Verbal	24	0.56	0.39	48	0.29	0.33	−0.97[a]	0[b,c,d]
Jennings and Jacoby (1993) – Exp. 1	Yes	PD	Verbal	24	0.60	0.14	24	0.25	0.10	−1.52[a]	0[b,d]
Jennings and Jacoby (1993) –Exp.2	No	PD	Verbal	16	0.42	0.63	16	0.25	0.60	−1.02[a]	0[b,c,d]
Jennings and Jacoby (1997) – Exp. 2	Yes	PD	Verbal	24	0.87	0.60	24	0.59	0.54	–	–
Kapucu et al. (2008)	No	ROC	Verbal	22	0.29	0.23	23	0.30	0.22	–	–
Kilb & Naveh-Benjamin (2011)	No	RK	Nonverbal	25	0.54	0.70	26	0.29	0.70	–	–
Luo and Craik (2009) –Exp.1	No	PD	Verbal	32	0.27	0.09	32	0.03	−0.05	–	–
Luo and Craik (2009) – Exp. 2	No	PD	Verbal	24	0.40	−0.02	24	0.27	−0.02	–	–
Luo et al. (2007) – Exp. 1	No	PD	Verbal	32	0.53	0.38	32	0.21	0.37	−0.86	0.16[d,f]
Luo et al. (2007) – Exp. 2A	No	PD	Verbal	27	0.44	0.36	27	0.31	0.41	−0.47	0.24[d]
Luo et al. (2007) – Exp. 2B	No	PD	Verbal	18	0.54	0.32	18	0.42	0.36	−0.59	0.18[d]
Luo et al. (2007) – Exp. 2C	No	PD	Verbal	32	0.44	0.39	32	0.31	0.54	−0.57	0.74[d]
McCabe and Geraci (2009) – Exp. 1 (RK Group)	No	RK	Verbal	36	0.29	0.27	36	0.24	0.26	−0.53	−0.10[d]
McCabe and Geraci (2009) – Exp. 1 (AB Group)	No	RK	Verbal	37	0.38	0.33	36	0.25	0.31	−0.90	−0.35[d]
McCabe and Geraci (2009) –Exp.2	No	RK	Verbal	38	0.30	0.34	34	0.22	0.34	−0.46	0.03[d]
McCabe et al. (2009)	No	RK	Verbal	67	0.32	0.35	68	0.23	0.32	−0.92	−0.27[d]
Morcom et al. (2010)	No	RK	Verbal	15	0.36	0.32	12	0.29	0.30	−0.66	0[b]
Norman and Schacter (1997) – Exp. 1 (Exp. Group)	No	RK	Verbal	12	0.52	0.48	12	0.46	0.34	–	–
Norman and Schacter (1997) – Exp. 1 (No Exp. Group)	No	RK	Verbal	12	0.53	0.48	12	0.45	0.40	–	–
Parkin and Walter (1992) –Exp.1	No	RK	Verbal	20	0.51	0.49	20	0.18	0.49	–	–
Parkin and Walter (1992) –Exp.2	No	RK	Verbal	30	0.36	0.65	60	0.14	0.54	–	–
Parks (2007) – Exp. 1	No	RK	Verbal	51	0.41	0.51	41	0.27	0.37	−0.74	−0.86
Parks (2007) – Exp. 2	Yes	ROC	Verbal	72	0.61	0.51	72	0.46	0.42	−0.95[a]	−0.52[b]
Perfect and Dasgupta (1997)	Yes	RK	Verbal	20	0.72	0.59	40	0.39	0.34	–	–
Perfect et al. (1995) –Exp.1	No	RK	Verbal	22	0.48	0.44	22	0.11	0.61	–	–
Perfect et al. (1995) – Exp. 2a (Deep Encoding)	Yes	RK	Verbal	12	0.67	0.90	12	0.67	0.25	–	–

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Study	R>.6	Estimation Method	Material Type	Young Adults			Older Adults			Effect Size *d*	
				n	R (prob.)	F (prob.)	*n*	R (prob.)	F (prob.)	R	F
Perfect et al. (1995) – Exp. 2a (Shallow Encoding)	No	RK	Verbal	12	0.40	0.55	12	0.31	0.25	–	–
Perfect et al. (1995) –Exp.2b	Yes	RK	Verbal	12	0.87	0.81	12	0.22	0.44	–	–
Peters and Daum (2008)	Yes	RK	Verbal	22	0.61	0.55	23	0.36	0.32	−1.10	−0.83
Prull et al. (2006)	No	RK/PD/ROC	Verbal	36	0.45	0.41	36	0.19	0.37	−1.28	−0.49
Schacter et al. (1997) – Exp. 1	Yes	RK	Verbal	32	0.78	0.28	32	0.65	0.16	–	–
Schacter et al. (1997) – Exp. 2	No	RK	Verbal	16	0.58	0.43	16	0.24	0.10	–	–
Skinner and Fernandes (2008)	No	RK	Verbal	30	0.32	0.43	30	0.26	0.33	−0.24	−0.79
Skinner and Fernandes (2009a) –Exp.1	No	RK	Verbal	15	0.45	0.29	15	0.34	0.14	−0.55	−0.71
Skinner and Fernandes (2009a) –Exp.2	No	RK	Verbal	16	0.49	0.20	16	0.46	0.12	−0.16	−0.28
Skinner and Fernandes (2009b)	No	RK	Verbal	24	0.48	0.45	24	0.38	0.65	–	–
Toth and Parks (2006) – Easy Group	No	PD	Verbal	36	0.33	0.40	36	0.15	0.32	−0.88	−0.76
Toth and Parks (2006) – Hard Group	No	PD	Verbal	36	0.05	0.52	36	0.01	0.36	−0.40	−1.19
Tse et al. (2010)	Yes	PD	Verbal	30	0.78	0.66	105	0.63	0.77	–	–
Wang et al. (2012)	No	RK	Verbal	23	0.35	0.67	21	0.22	0.49	−1.26[b]	−1.34[b]
Wolk et al. (2013)	Yes	PD	Verbal	17	0.60	0.75	50	0.36	0.82	−1.49	0.37

The recollection (R) and familiarity (F) estimates under the Young Adults and Older Adults headings refer to the probability (prob.) estimates derived from the Yonelinas (2002) method whereby R and F are calculated based on the average data reported in the study (see Supplemental Material for details). The *n* under these headings refers to the number of young and older adults in the study. The reported effects sizes for R and F are the uncorrected values calculated for each sample. The small-sample bias correction was applied to these effect sizes in the analysis reported in the main text. *RK* Remember-Know; *PD* Process Dissociation; *ROC* Receiver-Operating Characteristic

[a] The probability estimates for recollection and familiarity could not be reliably calculated from the data reported

[b] Effect size estimate based on *t*- or *F*-statistic

[c] Group difference reported as non-significant, and effect size estimate set to 0

[d] Subtracted the average false alarm rate from familiarity *post hoc* before calculating the effect size (see main text for details)

[e] Two ROC estimates of recollection (i.e., R_O and R_n) were derived from an associative recognition task. The R_O measure was selected to compute the recollection effect size estimate because this is analogous to old/new discrimination in item recognition tests

[f] The discrepancy between the age-related differences in the probability estimates of recollection and familiarity and the effect size measures is likely due to the former being calculated based on average data and the latter based on individual means and variance measures reported in the paper

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Table 2

Studies that examined recollection and familiarity differences between healthy older adults and individuals diagnosed with amnestic Mild Cognitive Impairment (aMCI)

			Healthy Controls			aMCI Patients			Effect Size *d*	
Study	**aMCI Subtypes**	**Estimation Method**	***n***	**R (prob.)**	**F (prob.)**	***n***	**R (prob.)**	**F (prob.)**	**R**	**F**
Ally et al. (2009)[a]	SD & MD	ROC	12	0.18	0.31	11	0.09	0.18	−0.32	−1.51
Anderson et al. (2008)	SD	PD	44	0.76	0.48	15	0.63	0.51	−0.72	0.04
Belleville et al. (2011)[b]	SD & MD	RK	29	–	–	28	–	–	−0.63	0.23
Embree et al. (2012)	SD & MD	ROC	16	0.43	0.54	16	0.15	0.45	−1.83	−0.45
Hudon et al. (2009)[a]	SD & MD	RK	23	0.64	0.56	20	0.43	0.59	−1.26	0.39[c]
Serra et al. (2010)	SD	PD/RK	23	0.29	0.18	19	0.18	0.19	−0.27	−0.12[d]
Troyer et al. (2012)	SD	PD	21	0.58	0.31	24	0.26	0.39	−1.29	0.43
Wolk et al. (2008)	SD & MD	PD	21	0.33	0.47	16	0.20	0.32	−0.65	−1.40
Wolk et al. (2013)	SD & MD	PD	50	0.36	0.82	32	0.21	0.50	−0.99	−1.75

The recollection (R) and familiarity (F) estimates under the Healthy Controls and aMCI patients headings refer to the probability (prob.) estimates derived from the Yonelinas (2002) method whereby R and F are calculated based on the average data reported in the study (see Supplemental Material for details). The *n* under these headings refers to the number of healthy controls and aMCI patients tested in the study. The reported effects sizes for R and F are the uncorrected values calculated for each sample. The small-sample bias correction was applied to these effect sizes in the analysis reported in the main text. The estimation method is provided for reference, and was not considered as a moderator variable in the analyses reported in the main text. *RK* Remember-Know; *PD* Process Dissociation; *ROC* Receiver-Operating Characteristic; *SD* Single-Domain aMCI; *MD* Multiple-Domain aMCI

[a] This study examined both aMCI and AD with a single set of healthy controls

[b] The probability estimates for recollection and familiarity could not be reliably calculated from the data reported

[c] Subtracted the average false alarm rate from familiarity *post hoc* before calculating the effect size

[d] The difference between the pattern of probability estimates and effect size measures is likely due to differences in the method used to calculate familiarity. Serra et al. (2010) use a signal-detection PDP calculator, whereas we used the formulas provided in Yonelinas (2002) (see Supplemental Materials for a more detailed description of the method)

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Table 3

Studies examining recollection and familiarity differences between healthy older adults and individuals diagnosed with Alzheimer's disease (AD)

		Healthy Controls			AD Patients			Effect Size *d*	
Study	**Estimation Method**	***n***	**R (prob.)**	**F (prob.)**	***n***	**R (prob.)**	**F (prob.)**	**R**	**F**
Ally et al. (2009)[a]	ROC	12	0.18	0.31	10	−0.02	−0.16	−2.09	−1.16
Barba (1997)	RK	12	0.34	0.21	12	0.15	0.18	–	–
Genon et al. (2013)[a]	PD	16	0.46	0.58	16	0.12	0.38	−0.64	−1.49[b]
Hudon et al. (2009)	RK	23	0.64	0.56	10	0.25	0.22	−1.97	−0.89[b]
Smith and Knight (2002)	PD	14	0.14	0.31	7	0.07	0.17	−1.30	−1.92
Tse et al. (2010)	PD	105	0.63	0.77	48	0.38	0.55	–	–
Wolk et al. (2011)[a]	PD	21	0.36	0.72	9	0.10	0.29	−1.30	−2.39

The recollection (R) and familiarity (F) estimates under the Healthy Controls and AD patients headings refer to the probability (prob.) estimates derived from the Yonelinas (2002) method whereby R and F are calculated based on the average data reported in the study (see Supplemental Material for details). The *n* under these headings refers to the number of healthy controls and AD patients tested in the study. The reported effects sizes for R and F are the uncorrected values calculated for each sample. The small-sample bias correction was applied to these effect sizes in the analysis reported in the main text. The estimation method is provided for reference, and was not considered as a moderator variable in the analyses reported in the main text. *RK* Remember-Know; *PD* Process Dissociation; *ROC* Receiver-Operating Characteristic

[a] This study examined both aMCI and AD with a single set of healthy controls

[b] Subtracted the average false alarm rate from familiarity *post hoc* before calculating the effect size

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Table 4

Demographics of the healthy aging, aMCI, and AD studies included in the recollection and familiarity effect size analysis

		Age		Education		MMSE	
	n	**Mean**	**Range**	**Mean**	**Range**	**Mean**	**Range**
Healthy Aging Studies							
Young Adults	1080	21.47	18.90–30.00	14.55	12.80–18.30	–	–
Older Adults	1195	71.14	60.61–77.00	15.29	11.20–18.10	–	–
aMCI Studies							
Healthy Controls	239	71.92	66.90–77.3	15.18	12.90–16.20	29.02	27.10–29.60
aMCI Patients	181	73.14	66.10–77.3	15.23	12.90–16.90	27.61	25.50–28.50
AD Studies							
Healthy Controls	87	71.85	68.60–77.30	14.01	9.83–16.70	29.35	28.80–29.70
AD Patients	52	75.93	74.57–77.80	13.21	8.86–16.60	22.23	17.00–24.90

The means and ranges for age and education are based on studies that provided this data. For the healthy aging studies, one study did not report years of education for both young and older adults, one study did not report age or education for young adults, and three studies did not report education for older adults. The MMSE values were not reported for one AD study

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