Olfaction and Declarative Memory in Aging: A Meta-analysis

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Abstract

Olfactory and declarative memory performances are associated, as both functions are processed by overlapping medial-temporal and prefrontal structures and decline in older adults. While decline in olfactory identification may be related to a decline in declarative memory, the relationship between olfactory detection threshold and declarative memory remains unclear. In this meta-analysis, we assessed (1) the relationship between olfactory identification/detection threshold and verbal declarative memory in cognitively normal older adults, and (2) the effect of age on these relationships.

We included articles from PsychNet, PubMed, and Academic Search Complete according to the following criteria: 1) inclusion of cognitively normal older adults; 2) assessment of episodic or semantic memory; and 3) assessment of olfactory identification or detection threshold. Seventeen studies and 22 effect sizes were eligible and included in this meta-analysis.

Olfactory identification was associated with episodic (small effect size: $r = .19$; $k = 22$) and semantic memory (small effect size: $r = .16$; $k = 23$). Similarly, the olfactory detection threshold was associated with both episodic (small to medium effect size: $r = .25$; $k = 5$) and semantic memory (small effect size: $r = .17$; $k = 7$). Age was found to moderate the relationship between olfactory detection threshold and memory performance.

Both olfactory identification and detection threshold performances are associated with declarative memory in older adults, and age only moderates the relationship between olfactory detection threshold and declarative memory performances.

Keywords: Olfaction, Episodic Memory, Semantic Memory, Aging, Meta-Analysis.

INTRODUCTION

Olfactory function and declarative memory are associated in young and older adults (e.g. Hedner et al., 2010; Knight et al., 2020; Larsson et al., 2016; Lehrner, 1999). Compared to procedural memory, declarative memory is a long-term memory involving explicit, conscious storage, and retrieval of factual information or previous experiences (Ullman, 2004). Declarative memory encompasses episodic and semantic memory, which are two distinguishable concepts: episodic memory pertains to the memory of personally experienced events that occurred at specific times and places, while semantic memory refers to facts, concepts, and general knowledge (Tulving, 1972).

Olfaction is the sense by which odors are perceived. Most commonly, olfaction is assessed through odor identification and odor detection threshold tasks. Olfactory identification tasks measure the ability to identify or associate a target odor among different labels, while olfactory detection threshold tasks measure the lowest concentration of an odorant that can be detected reliably. Olfactory identification is often characterized as a "central" olfactory function because of its relation to higher cognitive functions such as executive function, and episodic and semantic memory (Dulay et al., 2008; Economou, 2003; Larsson, 2004). More specifically, some authors have conceptualized olfactory identification as a function involving semantic memory for olfactory stimuli, since odor identification relies on an individual's prior specific knowledge to properly label the target odor (Hedner et al., 2010; Larsson, 1997; Larsson et al., 2016; Schab, 1991).

Key structures supporting learning and retrieval of previously learned information (Gabrieli et al., 1997; Squire, 2004; Squire & Zola, 1996; Squire & Zola-Morgan, 1991) are also involved in the identification of olfactory stimuli (i.e., the hippocampus , the entorhinal and the parahippocampal cortex). On a structural level, the entorhinal cortex is part of the primary olfactory cortex, as it receives direct input from the olfactory bulb (Gottfried, 2010; Lundström et al., 2011), and the hippocampus receives olfactory information from entorhinal projections; only three synapses separate it from the peripheral receptive structures in the olfactory mucosa (Schwerdtfeger et al., 1990; Staubli et al., 1984, 1986). On a functional level, the hippocampus, parahippocampal and entorhinal cortex are activated during both olfactory stimulation (Steffener et al., 2021; Torske et al., 2021) and olfactory identification tasks (Kjelvik et al., 2012, 2021; Kose et al., 2021).

Olfactory detection threshold, in turn, has been suggested to reflect the functioning of the peripheral olfactory system (Hedner et al., 2010; Hummel et al., 2007; Moberg, 1999) since several pathologies affecting the peripheral olfactory system lead to decreased sensitivity for olfactory stimuli (Landis et al., 2005; Nordin & Brämerson, 2008; Patel et al., 2022). For instance, septal deviation (Pfaar et al., 2004) and allergic rhinitis (Stuck et al., 2003) are associated with a decreased sensitivity for olfactory stimuli without any alteration in the ability to identify these stimuli.

However, olfactory detection threshold and identification functions may not completely be independent, as olfactory detection threshold and identification performances are associated (Doty et al., 1984, 1994). This suggests that olfactory detection threshold function may involve some cognitive processes. This hypothesis is further supported by the common decline in olfactory detection threshold and memory in older adults (Dulay et al., 2008; Dulay & Murphy, 2002). Key structures to support this hypothesis are the hippocampal and prefrontal regions, as they are both vulnerable to the aging process (Bartsch & Wulff, 2015; Bettio et al., 2017), related to odor detection (Igarashi et al., 2014; Murphy et al., 2003; Potter & Butters, 1980; Steffener et al., 2021; Zhang et al., 2019), and memory functioning (Borders et al., 2022; Cabeza et al., 2002; Kesner & Hunsaker, 2010; Melrose et al., 2020; Sexton et al., 2010).

The association between olfaction and memory is of particular interest in older adults, since this population is at risk of developing olfactory and memory decline. A study involving more than 9000 participants showed that performance in both olfactory identification and detection threshold decline in adulthood and more severely from the age of 60 onwards (Oleszkiewicz et al., 2019). In healthy adults above 60 years of age, roughly 40% show olfactory impairment while a similar proportion exhibits some sort of memory decline (Dintica et al., 2019; Oleszkiewicz et al., 2019; Small, 2001). Even semantic memory, which is relatively preserved in aging, plateaus at around 60 years of age (Salthouse, 2019).

A decline in both olfactory and memory performances is also found in Alzheimer's disease. Indeed, decline in both declarative memory and olfactory function are among the first symptoms to appear in the progression of Alzheimer's disease, possibly as a result of the tau pathology accumulation, which first appears in the trans-entorhinal and hippocampal regions of the brain (Aschenbrenner et al., 2018; Braak & Braak, 1991; Hessen et al., 2015; Risacher et al., 2017; Weigand et al., 2021). In this context, it is noteworthy that olfactory impairment in Alzheimer's disease and in mild cognitive impairment is more pronounced for olfactory identification than for olfactory detection threshold (Rahayel et al., 2012; Roalf et al., 2017). Since memory impairment occurs early in the development of Alzheimer's disease, it has been hypothesized that impairment of higher cognitive processes may explain functional differences between olfactory identification and olfactory detection threshold (Rahayel et al., 2012). As a consequence, olfactory identification, as opposed to the olfactory detection threshold, is considered to be an early clinical marker of Alzheimer's disease (Jobin et al., 2021; Quarmley et al., 2016; Roalf et al., 2017).

In the same vein, decline in olfactory identification has been associated with a decline in declarative memory in cognitively normal older adults. More specifically, impaired olfactory identification, which was found to predict a general cognitive decline in healthy older adults (Olofsson et al., 2009; Sohrabi et al., 2012), appears to affect verbal episodic and semantic memory (Dintica et al., 2019; Swan & Carmelli, 2002). Similarly, older adults genotyped as apolipoprotein E-ε4 (APOE-ε4) carriers – a risk factor for Alzheimer's disease – were found to experience a decline in episodic memory over one to two decades, which was also associated with an impairment to identify olfactory stimuli (Olofsson et al., 2016). On the other hand, the age-related decline in olfactory detection threshold performance has been explained by anatomical and physiological changes to peripheral structures (such as nasal diseases, damages to the olfactory epithelium, ossification of the cribriform plate, and neurochemical changes) and central nervous structures (e.g., damage to olfactory cells receptor, and neuronal damages associated with neurodegenerative disease pathologies) (for reviews on this, see, Doty & Kamath, 2014; Olofsson et al., 2021), rather than changes in cognition or memory.

According to the literature, aging-associated decline in olfactory identification is associated with a decline in declarative memory, while the relationship between olfactory detection threshold and declarative memory remains unclear. Because the relationship between olfactory function and memory performance has not yet been evaluated systematically in older adults, this meta-analysis aimed to provide a comprehensive overview of (1) the relationship between olfactory identification/detection threshold and verbal declarative memory in cognitively normal older adults, and on (2) the potential effect of age on these relationships.

Methods

Eligibility criteria of the studies selected. To be eligible, studies had to examine the relation between (1) a memory score ((a) episodic or (b) semantic) and (2) an olfactory score ((a) identification or (b) detection threshold). Participants of selected studies had to be cognitively normal and aged >45 years and the mean age of participants >55 years. This criterion is based on previous studies showing that both memory and olfaction already started declining before the age of 55 (Oleszkiewicz et al., 2019; Salthouse, 2009, 2019). Studies involving participants with any condition that could affect cognition (i.e., psychiatric diagnoses and/or neurological conditions) or olfaction were excluded.

Outcome. Included studies had to measure verbal declarative memory. (a) Episodic memory measurements included (i) immediate and (ii) delayed recalls of word lists, as measured by the California Verbal Learning Test (CVLT, Delis et al., 2008), the Rey Auditory Verbal Learning Test (RAVLT, Schmidt, 1996) or the Hopkins Verbal Learning Test (HVLT, Benedict et al., 1998). Next, (b) semantic memory had to be measured by (i) categorical fluency tasks, as measures by the Delis-Kaplan Executive Function System Battery Tests (Delis et al., 2001), (ii) denomination, (iii) general knowledge, and (iv) vocabulary tasks, as evaluated through subtests from the Wechsler Adult Intelligence Scale (Wechsler, 2008). We did not include correlations from composite scores that included other olfactory or memory components.

Typically, (a) olfactory identification was evaluated by a validated behavioral test, e.g., the Sniffin'Sticks Identification Test (Hummel et al., 1997), the University of Pennsylvania Smell Identification Test (UPSIT, Doty et al., 1984), or any other common olfactory identification test. In short, olfactory identification tasks involve matching an odor to the right label among different choices. (b) Olfactory detection threshold was assessed using the Sniffin'Sticks Threshold Test (Hummel et al., 1997) or another equivalent test. Typically, threshold test procedures require the participant to choose between three stimuli that are presented sequentially. Among these stimuli, only one is odorous (target). The concentration of the target changes between trials (for a more detailed procedure description see Rumeau et al., 2016).

Search Strategy and Information Source. We searched for studies published up to January 1st, 2023. No studies were excluded from our meta-analysis based on their country of origin and only studies published in English were included. We searched for published studies in the following databases: PsychNet, PubMed, and Academic Search Complete (Ebsco). The following keywords were used in our search ("olfac*" OR "smell" OR "odor") AND ("memor*" OR "cogniti*") AND ("correlat*"). We also verified the presence of potential eligible studies in the references of eligible studies found in database extraction. After excluding duplicate studies, 1539 titles and abstracts were reviewed. Studies were excluded when they were off topic (e.g., animal studies, assessment of other sensory modalities, etc.), or when they qualified as reviews, case studies, qualitative papers, or if they only included clinical groups. Only direct correlations between a specific cognitive domain and a specific olfactory domain were eligible. Two hundred and twenty-eight studies were identified for a full-text examination (Figure 1).

Study selection. The eligibility of the studies was assessed by BJ and FRC according to the criteria mentioned above. Articles were included if they were approved by both BJ and FRC based on the risk of bias assessment (Munn et al., 2020).

Risk of bias in individual studies. Risk of bias was evaluated for each selected study according to the Joanna Briggs Institute's Checklist for Analytical Cross-Sectional Studies (as recommended by Ma et al., 2020), addressing the possibility of bias in design, conduct and analysis. BJ and FRC evaluated each eligible study according to the inclusion criteria mentioned above. When disagreement emerged at this stage, the most conservative result was selected. A consensus was reached after pooling the results and no major disagreement emerged. No studies were excluded following this evaluation.

Analyses

We performed analyses using *Meta-Essentials* (Suurmond et al., 2017). We used Fisher's r-to-z transformation for each correlation coefficient to determine an effect size for each sample. Next, we calculated combined effect sizes. According to Cohen's guidelines, we interpreted $r = .10$, $r = .30$, and $r = .50$ as small, medium, and large effect sizes, respectively (Cohen, 2013). We used the more conservative random effects model to compute the significance level of the mean effect sizes for each study.

Risk of bias across studies. We qualified heterogeneity using Cochrane's Q-statistic and quantified the degree of heterogeneity using I^2 among effect sizes (Hedges & Olkin, 2014). We assumed heterogeneity if P_Q was significant at $p < .05$. When heterogeneity was assumed and the number of included studies per subgroup was sufficient as suggested (Fu et al., 2011; Higgins et al., 2019), we then tested the moderating effect of each measure of episodic memory (i.e. (i) immediate and (ii) delayed recalls of word lists) and semantic memory (i.e. (i) categorial fluency, (ii) denomination, (iii) general knowledge, and (iv) vocabulary).

Finally, we performed meta-regressions with age as a potential moderator for the relationships between olfactory identification and olfactory detection threshold and declarative memory performances.

We qualified publication bias using both visual inspection of funnel plots and Rosenthal's failsafe-N test that gives the number of potential unpublished studies that are required to turn the combined effect size statistically insignificant or to change the conclusions of the meta-analysis (Rosenthal, 1979).

Results

Correlations between olfactory identification and declarative memory. After analyzing full-text articles, twenty-two correlations between olfactory identification and episodic memory scores, and twenty-three correlations between olfactory identification and semantic memory scores, were included in the meta-analysis (Table 1). We present effect size correlations between olfactory identification and episodic and semantic memory in Figure 2. The analysis on olfactory identification and episodic memory scores revealed a significant small effect size (r = .19, 95% CI [.13, .25]; k = 22) that was significantly heterogeneous

(Q=50.69, P_Q<.001; I^2=58.58%). We further found significant small effect size correlations between olfactory identification scores and (i) immediate recall (*r* = .18, 95% CI [.10, .27]; *k* = 15) and (ii) delayed recall scores (*r* = .20, 95% CI [.09, .31]; *k* = 7).

The correlational analysis on olfactory identification and semantic memory scores revealed a significant small effect size (*r* = .16, 95% CI [0.09, 0.22]; *k* = 23) that was significantly heterogeneous (Q=134.27, P_Q<.001; I^2=83.61). We found significant correlations for (ii) denomination tests (*r* = .13, 95% CI [.02, 0.23]; *k* = 5; small effect size), (iii) general knowledge tests (*r* = .08, 95% CI [.04, .12]; *k* = 3; small effect size), and (iv) vocabulary (*r* = .22, 95% CI [0.14, 0.28]; *k* = 7), but not for i) categorical fluency tests (*r* = .15, 95% CI [-.09, .37]; *k* = 8).

Rosenthal's failsafe-N was 1302 for the correlation between olfactory identification and episodic memory, and 2054 for the correlation between olfactory identification and semantic memory, indicating no publication bias. Asymmetry at the bottom (left) of the funnel plot (Figure 3), which analyzes the relationship between olfactory identification and episodic memory, suggests an overrepresentation of a negative relationship between these two concepts and, therefore, a possible publication bias.

Correlations between olfactory detection threshold and declarative memory.

After analyzing full-text articles, five correlations between olfactory detection threshold and episodic memory scores and seven correlations between olfactory detection threshold and semantic memory scores included in the meta-analysis (Table 2). Figure 4 shows effect size correlations between olfactory detection threshold and episodic memory (left) and semantic memory (right). The analysis on olfactory detection threshold and episodic memory scores revealed a significant small-to-medium effect size (*r* = .25, 95% CI [.02, .45]; *k* = 5) that was homogenous (Q=8.48, P_Q=.08; I^2=52.81).

Next, the analysis on olfactory detection threshold and semantic memory scores revealed a significant small effect size (*r* = .17, 95% CI [.04, .29]; *k* = 7) that was homogenous (Q=8.33, P_Q=0.26; I^2=27.94). While most of the studies included a three-alternative forced-choice procedure to assess olfactory detection threshold, the one study (Dulay et al., 2005) that included a two-alternative forced-choice procedure showed a smaller effect size compared to the others (Table 2).

Rosenthal's failsafe-N was 33 for the correlation between olfactory detection threshold and episodic memory, and 25 for the correlation between olfactory detection threshold and semantic memory, indicating a potential publication bias. However, the generated funnel plot showed no major asymmetry, indicating no potential publication bias (Figure 3).

Age as a moderator

Meta-regressions showed that age was not a significant moderator of the relationship between olfactory identification and declarative memory performance in older adults. However, we found a significant moderator effect of age on the relationship between olfactory detection threshold and declarative memory performance, showing a higher relationship between olfactory detection threshold and memory scores in studies including participants with an older mean age (Figure 5).

Discussion

This meta-analysis assesses the relationship between olfactory and verbal declarative memory performance in a cognitively normal older adult population. We found that (1) olfactory identification and detection threshold are both significantly correlated with declarative memory in cognitively normal older adults, with comparable effect sizes; and (2) age moderates the relationship between olfactory detection threshold and declarative memory performances.

As expected, our meta-analytical results are in line with previous reports suggesting that olfactory identification and episodic memory are associated in older adults (Chen, Zhong, Mai, Peng, Zhang, et al., 2018; Devanand et al., 2019; Larsson et al., 2016; Seubert et al., 2020) and younger adults (Hedner et al., 2010). Patients suffering from diseases associated with episodic memory deficits, such as Alzheimer's disease, also typically exhibit olfactory identification dysfunction (Bahar-Fuchs et al., 2010; Park et al., 2018; Rahayel et al., 2012). Olfactory identification is the first observed olfactory deficit in Alzheimer's disease (Hedner et al., 2010; Murphy et al., 2003; Serby et al., 1991), and a lower olfactory identification score is associated with episodic memory decline in patients with Alzheimer’s disease (Knight et al., 2018).

Our results also support the notion of an association between olfactory identification and semantic memory. This link is not surprising as olfactory identification requires labelling a specific odor, which relies on one's semantic knowledge (Larsson, 1997; Schab, 1991). However, the association is characterized by a small effect size. This result might support a model of an olfactory memory as being separate from – although influenced by – verbal declarative memory (Larsson et al., 2016), an idea initially suggested by Herz & Engen (1996). Larsson et al. (2016) suggested various hypotheses to explain the differences between olfactory memory and memory for other sensory stimuli, such as differences with respect to the neuroanatomical organization of olfactory imagery capacity (Arshamian & Larsson, 2014) and the olfactory-language network (Olofsson et al., 2014). Indeed, connections between the piriform cortex and the cortical regions associated with semantic networks are more direct although less elaborate, compared to other sensory modalities. This difference could lead to a lack of olfactory feature analysis, a poor translation of odor objects to lexical representations, and a cumulative deterioration of signal quality over different processing stages from odor input to odor identification (Herz, 2005; Olofsson et al., 2013, 2014; Olofsson & Gottfried, 2015).

Next, our results showed a significant association between olfactory detection threshold and declarative memory scores with a small effect size, suggesting that olfactory detection threshold procedures involve mnesic processes (Dulay et al., 2008). Two possible hypotheses can be put forward to explain these results. One hypothesis (1) relies on the procedure for assessing olfactory detection threshold. Typically (e.g., Sniffin' Sticks olfactory threshold test, Hummel et al., 1997), olfactory threshold tests are based on alternative forced-choice procedures consisting in distinguishing between stimulations with and without odors (target vs. non-target) in random temporal order. In other words, the participant must remember and compare each stimulus before identifying the target among two or three non-targets. Thus, to pass the test, one solution is to use a cognitive strategy based on the ability to detect non-targets and thus guess the stimulation that is the target. Interestingly, one study from the present meta-analysis (Dulay et al., 2005) included a two-alternative forced choices method instead of a three-alternative forced choices method, and showed smaller effect sizes, which could suggest a lower cognitive load compared to a three-alternative forced choices method.

Furthermore, the use of alternative olfactory detection tests designed to have minimal memory or cognitive impact (Doty & Laing, 2015) could test this first hypothesis. Signal detection tests are good candidates, as they are based on a non-forced choice procedure (i.e. participants are asked to determine whether the stimulus presented is detectable or not, without having to directly compare it with another one previously presented, e.g. Doty et al., 1981) and account for the subject's response criterion in reporting the detection of an odor or not (liberalism vs. conservatism) (Doty et al., 1981; Doty & Laing, 2015). In the present meta-analysis, however, none of the included studies used a signal detection test to assess olfactory threshold detection. Future studies involving patients with cognitive disorders should keep that potential bias in mind when assessing the olfactory detection threshold in these populations.

The positive association between olfactory detection threshold and declarative memory performances may alternatively be explained by (2) the effect of age on brain regions that are common to both declarative memory and olfaction (Baltes & Lindenberger, 1997; Dulay & Murphy, 2002). Aging effects on hippocampal and prefrontal regions (Bartsch & Wulff, 2015;

Bettio et al., 2017) could play a mediator role in the relationship between olfactory detection threshold and declarative memory performance, as both regions are involved in odor detection (Igarashi et al., 2014; Murphy et al., 2003; Potter & Butters, 1980; Steffener et al., 2021; Zhang et al., 2019) and memory functioning (Borders et al., 2022; Cabeza et al., 2002; Melrose et al., 2020; Sexton et al., 2010). Future neuroimaging studies should evaluate the potential mediating effect of hippocampal and prefrontal cortex volume on the relationship between odor detection threshold and declarative memory.

Meta-regressions showed that age moderates the relationship between olfactory detection threshold and memory performance in older adults, as the relationship is stronger in advanced age. The effect of age on the relationship can be explained by the fact that these two capacities are especially weakened by the aging process. Normative data suggest that olfactory detection thresholds are most sensitive to aging compared to other olfactory functions (Hummel et al., 2007; Oleszkiewicz et al., 2019). The same phenomenon is found with memory, as episodic memory is the type of long-term memory that is the most sensitive to aging, while semantic memory is mostly preserved (Nyberg et al., 2003, 2012; Rönnlund et al., 2005). Again, age-related damages to medial-temporal lobe structures have been associated with both worse declarative memory and olfactory detection threshold performance in healthy older adults. More specifically, levels of Tau and β-amyloid aggregations in the brain are associated with atrophy of medial temporal lobe structures and worse declarative memory in cognitively normal older adults compared to young adults (Marks et al., 2017), while olfactory detection threshold performance has been associated with a smaller volume of the hippocampus and other medial temporal structures, such as the amygdala and the entorhinal cortex, in healthy older adults (Murphy et al., 2003).

Our study has certain limitations. First, there was heterogeneity regarding tests that were included. With regards to the olfactory tests, a majority of included correlations were performed using validated tests such as the Sniffin' Sticks Test (Hummel et al., 1997, 2007), the University of Pennsylvania Smell Identification Test (UPSIT, Doty et al., 1984), the Scandinavian Odor-Identification Test (Nordin et al., 1998), and the 12-item Cross-Cultural Smell Identification Test (Doty et al., 1996), while others used equivalent experimental tests. Similarly, regarding memory tests, we only included similar and comparable tests (episodic memory: free immediate and delayed recalls of word list learning; semantic memory: categorial fluency, denomination, general knowledge, and vocabulary tasks). When heterogeneity was found in different effect sizes, we analyzed correlation effect sizes for each subcategory of memory tests. Further, this meta-analysis does not include other cognitive domains that may influence olfactory scores, such as working memory (Hedner et al., 2010; Dulay et al., 2008; Tonacci et al., 2017). Another limitation is the small number of studies included that assessed the relationship between olfactory detection threshold and declarative memory (k = 5 for episodic memory; k = 7 for semantic memory). Therefore, our results must be interpreted carefully. Finally, by design, this study only included studies with linear correlation effect sizes between olfactory and memory performance in cognitively normal older adults. Other studies may have included data relating to olfactory and memory performance in this population, but did not show correlational effect sizes, which prevented us from including them in the present meta-analysis.

Conclusion

Olfactory identification and olfactory detection threshold are related to declarative memory in cognitively normal older adults. These results suggest that both olfactory performances are related to verbal declarative memory but remain distinct from it. Finally, age moderates the association between olfactory detection threshold and memory performance.

Conflict of interest

The authors declare no conflict of interest.

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Data availability

This meta-analysis used accessible data from different published studies. This study was not preregistered.

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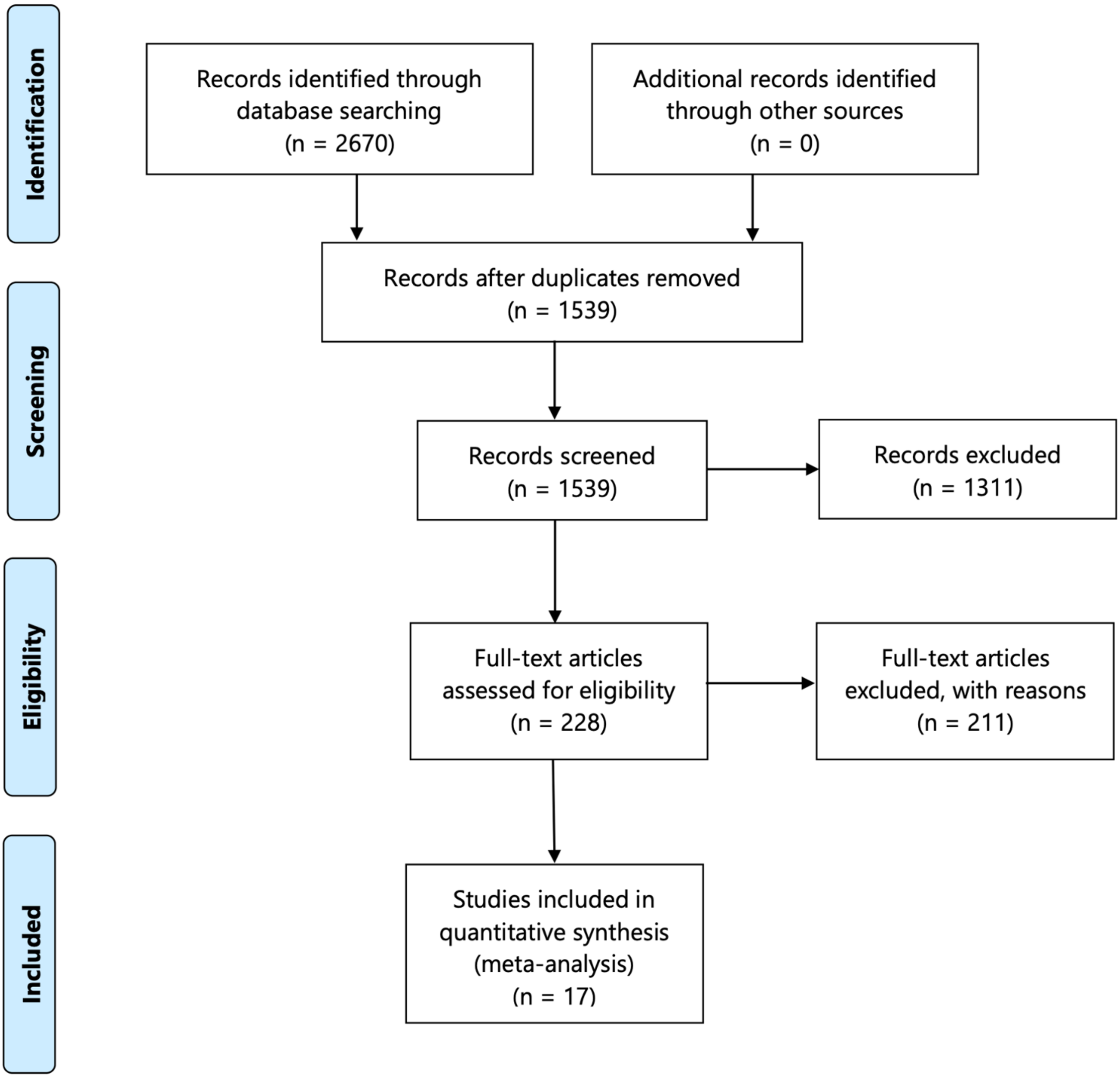

Figure 1. PRISMA flowchart illustrating the selection of the studies.

Table 1

Olfactory Identification and Memory Correlations

Study	Participants characterization	n	Mean Age (SD)	Olfactory Test	Memory Test	Effect size
(Bailie, 2009)	Aged 55 and over, from skilled nursing homes, independent living facilities, and senior citizen support groups.	45	75.76 (10.30)	Multiple Intensity Odor Identification Test	CVLT BNT CF	.40 .25 .67
(Chen, et al., 2018)	Evaluated by two psychiatrists, including a comprehensive neuropsychological assessment.	154	67.63 (8.5)	Sniffin' Sticks	AVLT LMT CF	.22 .10 .09
(Cozac et al., 2017)	Participants screened by neuropsychologist and neurologist.	21	67.5 (N/A)	Sniffin' Sticks	SVCF	-.08
(Devanand et al., 2019)	Intact cognition after a neuropsychological assesement.	92	77.55 (4.49)	UPSIT	SRT	Total Immediate Recall = .27 Delayed Recall = .16
(Dulay et al., 2005)	- Older adults from living retirement communities. - Exclusion of participants with known neurologic or psychiatric conditions. - DRS-2 > 131	80	77.08 (8.50) (Full-Sample)	UPSIT	CVLT-II Short-Form	.01
(Hedner et al., 2010)	All participant were in good health and underwent a detailed ear–nose–throat (ENT) examination.	170	57.2 (13.8)	Sniffin' Sticks	16 Concrete Nouns Test	.21
(Larsson, 2004)	Population based study. MMSE score > 24 and absence of subjective olfactory disorder.	1906	67.5 (N/A)	SOIT	CF Vocabulary	.15 .31
(Larsson et al., 2016)	Population based study including geriatric, neurological, and psychiatric assessments; and neuropsychological testing.	2280	71.46 (9.68)	Sniffin' Sticks	16 Unrelated Nouns Test Vocabulary GK Vocabulary	Free Odor Identification = .26 Total Odor Identification = .25 Free Odor Identification = .19 Total Odor Identification = .21 Free Odor Identification = .09 Total Odor Identification = .07 Free Odor Identification = .19 Total Odor Identification = .21
(Liu et al., 2022)	Evalation made by at least two neurologists with expertise in dementia, a neuropsychologist, and a geriatric psychiatrist.	189	67.29 (7.49)	Sniffin' Sticks	AVLT (RAVLT) BNT Verbal Fluency Test	Short-term delayed recall = .30 Long-term delayed recall = .20 0.16 0.13
(Makowska et al., 2011)	MMSE > 27.	30	72.33 (6.29)	PST	ADAS-COG Cognitive Subscale – Word Recall	Absolute Identification = -.43 Forced Choice = -.40
(Seubert et al., 2020)	MMSE > 24.	422	69.73 (8.76)	Sniffin' Sticks	30-Item Vocabulary Test Free Recall 30-Item Vocabulary Test Synonyms	0.14 0.21
(Wehling et al., 2010)	No neurological or psychiatric disorders, head trauma, or other	136	61.7 (7.8)	SOIT	CVLT	Cued Odor Identification: Total Learning = .18 Long Delay Free Recall = .26

	significant medical conditions. Normosmia assessed by an olfactory detection test.				Vocabulary (WASI)	Free Odor Identification: Total Learning = .26 Long Delay Free Recall = .29 Cued Odor Identification = .02 Free Odor Identification = .19
(Zhang et al., 2022)	Assessed by two neuropsychiatrists, one neuropsychologist, and one psychiatrist.	105	67.30 (6.5)	Sniffin' Sticks	AVLT (RAVLT) Animal Verbal Fluency Test	.11 -.25

Note. BNT: Boston Naming Test; CC-SIT: Cross-Cultural Smell Identification Test; CF: Category Fluency; GKQ: General Knowledge; LMT: Logical Memory Test; MMSE: Mini-Mental State Evaluation; N/A: Not available; PST: Pocket Smell Test; RAVLT: Rey Auditory Verbal Learning Test; SOIT: Scandinavian Odor Identification Test; SRT: Selective Reminding Test; SVCF: Semantic Verbal Categorial Fluency; UPSIT: University of Pennsylvania Smell Identification Test; WASI: Wechsler Abbreviated Scale of Intelligence.

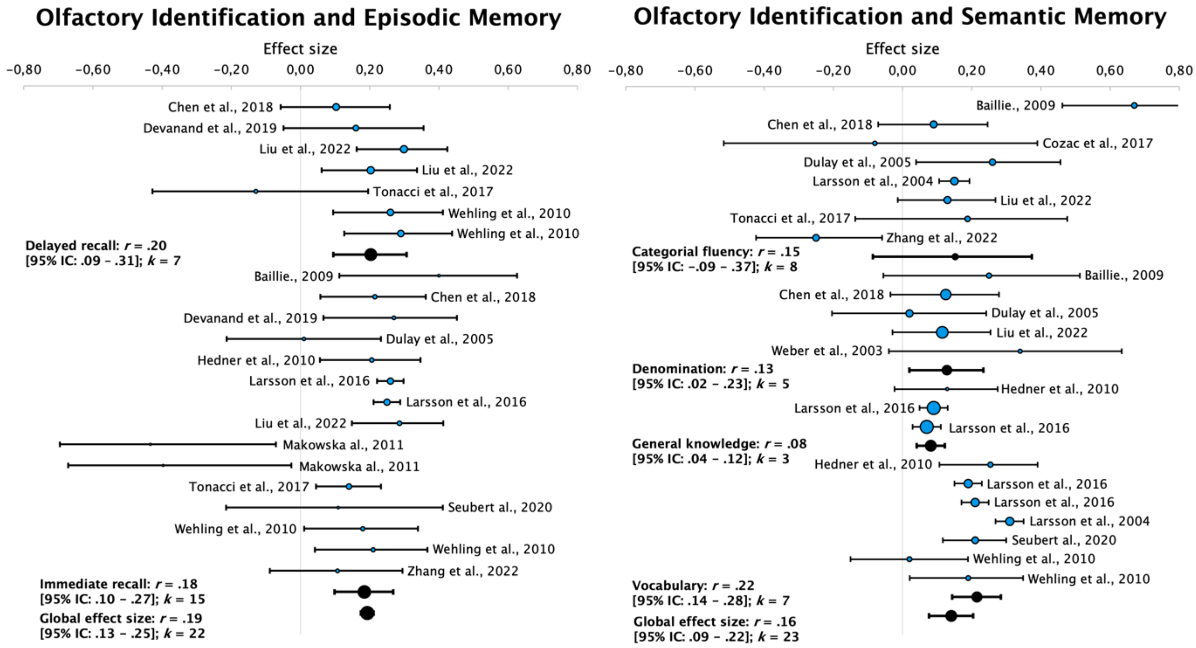

Figure 2. Forest plot of effect sizes for the correlations between olfactory identification and episodic memory (left) and semantic memory (right). Error bars represent 95% CIs.

Table 2

Olfactory Detection Threshold and Memory Correlations

Study	Participants characterization	n	Mean Age (SD)	Olfactory Test	Memory Test	Effect size
(Bailie, 2009)	Aged 55 and over, from skilled nursing homes, independent living facilities, and senior citizen support groups.	45	75.76 (10.30)	Four Odor Threshold Tests for *N*-Butanol (3-AFC)	CVLT BNT CF	0.54 0.20 0.46
(Dulay et al., 2005)	- Older adults from living retirement communities. - Exclusion of participants with known neurologic or psychiatric conditions. - DRS-2 > 131	80	77.08 (8.50) (Full-Sample)	PEAT (2-AFC)	CVLT-II Short-Form BNT Short-Form CF	0.12 0.04 0.02
(Hedner et al., 2010)	All participant were in good health and underwent a detailed ear–nose–throat (ENT) examination.	170	57.2 (13.8)	Sniffin' Sticks (3-AFC)	16 Concrete Nouns Test GK Vocabulary	0.13 0.15 0.23
(Tonacci et al., 2017)	Neuropsychological assessment was performed	41	73.5 (4.3)	Sniffin' Sticks (3-AFC)	RAVLT GK	Immediate Recall = 0.26 Delayed Recall = 0.27 0.14

Note. AFC: alternative forced choice; BNT: Boston Naming Test; CF: Category Fluency; CVLT: California Verbal Learning Test; DRS-2: Dementia Rating Scale 2; GK: General Knowledge; PEAT: Two Alternative Forced-choice Phenyl Ethyl Alcohol Threshold; RAVLT: Rey Auditory Verbal Learning Test.

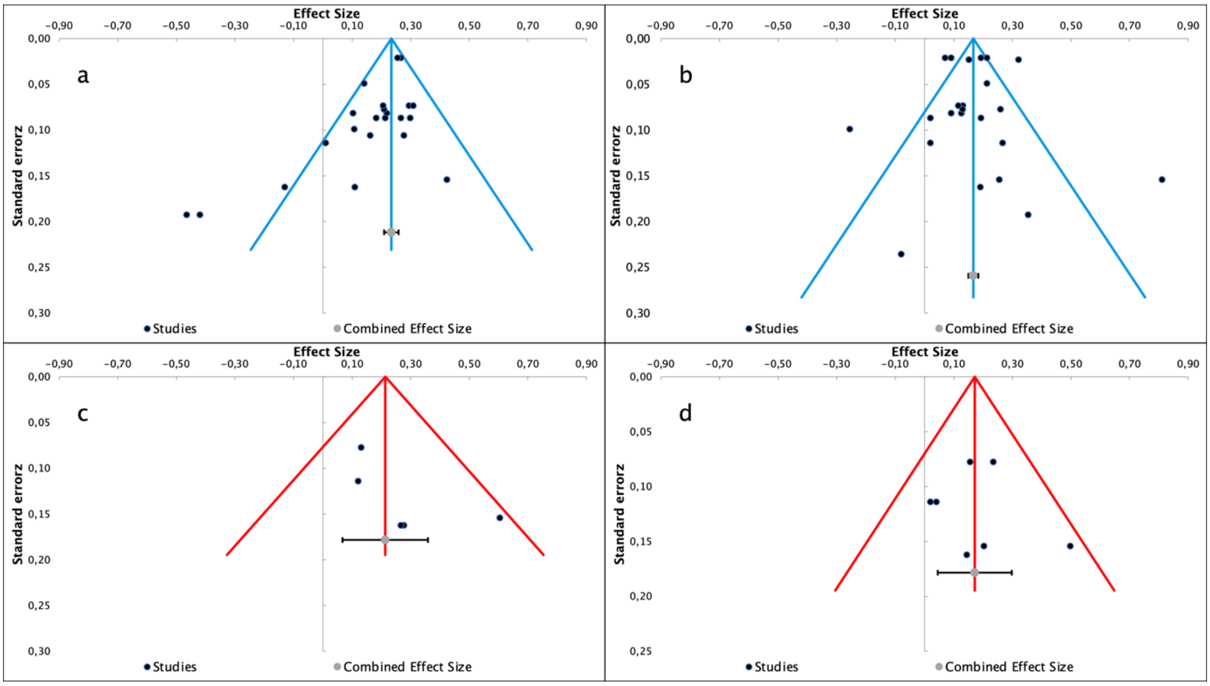

Figure 3. Funnel plot of standard errors z of effect sizes for each meta-analysis. a) represents the funnel plot of the relationship between olfactory identification and episodic memory; b) olfactory identification and semantic memory; c) olfactory detection threshold and episodic memory; d) olfactory detection threshold and semantic memory. Error bars represent 95% CIs.

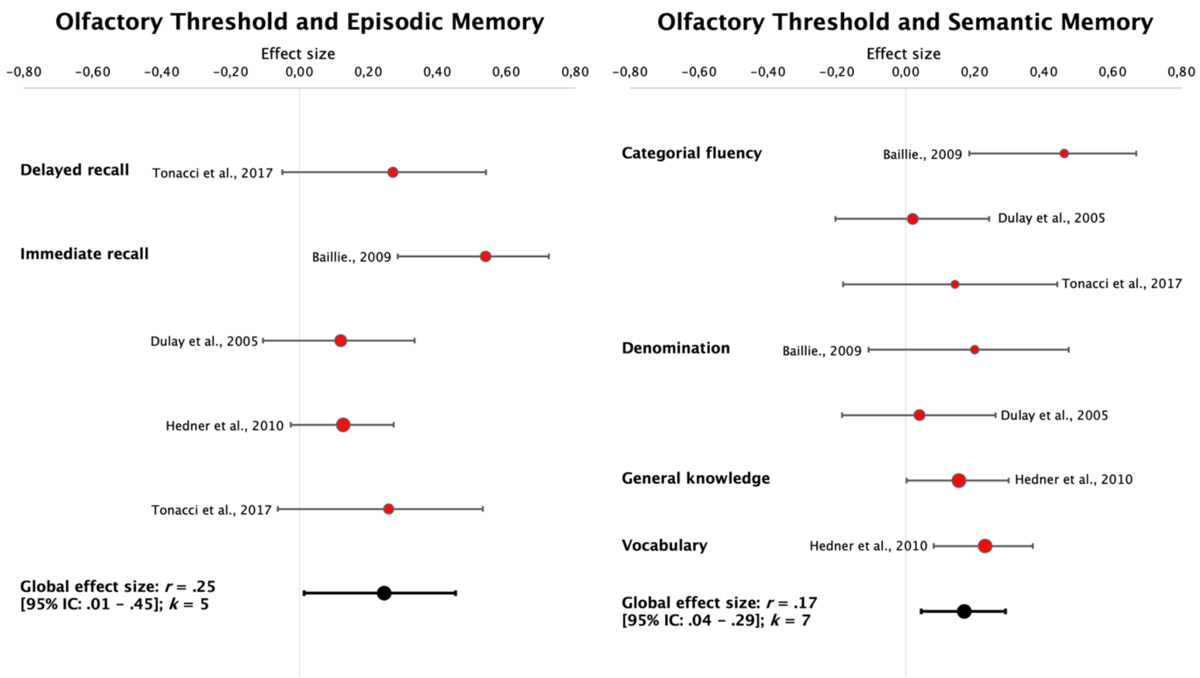

Figure 4. Forest plot of effect sizes for the correlations between olfactory detection threshold and episodic memory (left) and semantic memory (right). Error bars represent 95% CIs.

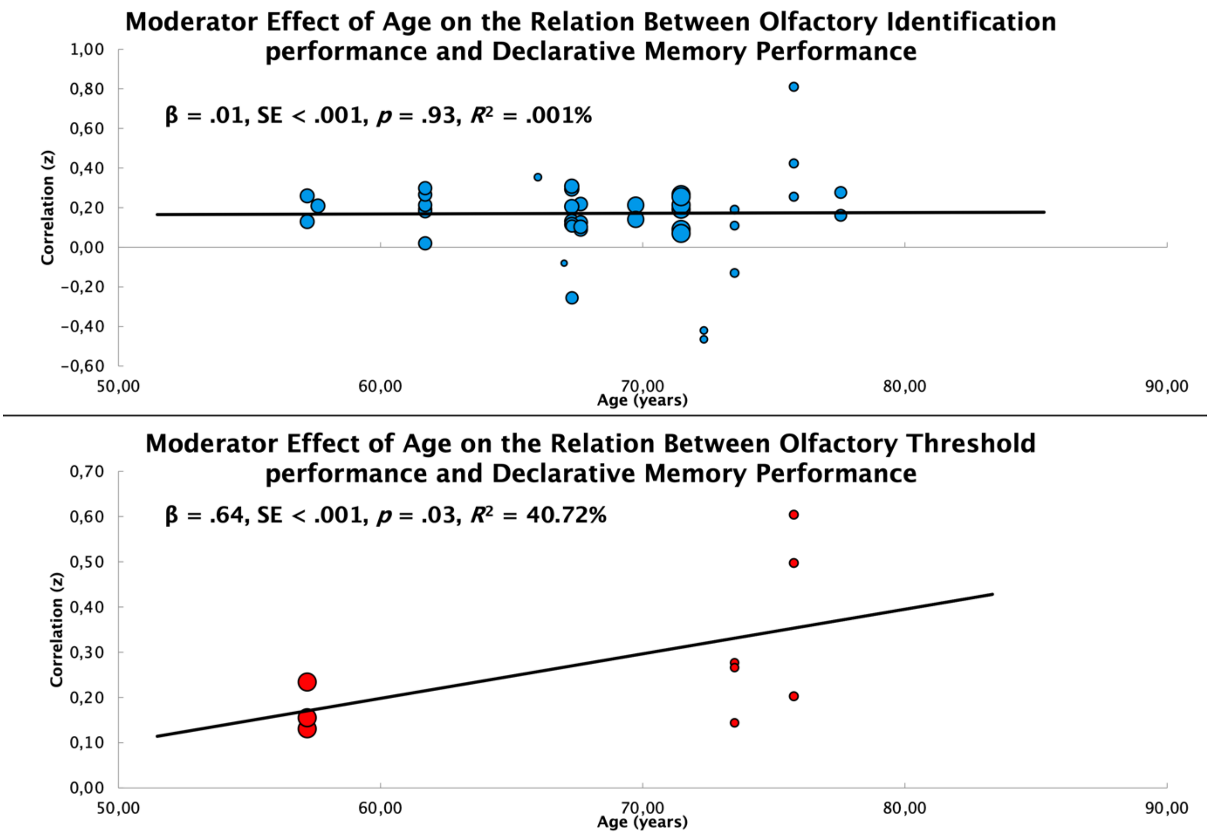

Figure 5. Meta-regressions evaluating the moderator effect of age on the relationship between olfactory capacities and declarative memory. The analyses were completed with studies whose information was available (two studies missing).