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PRE-PRINT PUBLICATION

A meta-analysis of semantic memory in Mild Cognitive Impairment

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Abstract

Introduction: Accumulating evidence over the past decade suggests that semantic deficits represent a consistent feature of Mild Cognitive Impairment (MCI). A meta-analysis was performed to examine if semantic deficits are consistently found in patients with MCI.

Methods: Studies meeting all inclusion criteria were selected for the current meta-analysis. An effect size and a weight were calculated for each study. A random effect model was performed to assess the overall difference in semantic performances between MCI patients and healthy subjects.

Results: 22 studies (476 healthy participants, 476 MCI patients, mean MMSE of the MCI patients: 27.05 ± 0.58) were included in the meta-analysis. Results indicate that MCI patients systematically performed significantly worse than healthy matched controls in terms of overall semantic performance (mean effect size of 1.02; 95% CI [0.80; 1.24]).

Discussion: Semantic deficits are a key feature of MCI. Semantic tests should be incorporated in routine clinical assessments.

Keywords: semantic memory; naming; MCI; Alzheimer's disease; meta-analysis

1. Introduction

Semantic memory refers to general knowledge that we share about the world, its organization and its meaning. It includes for instance knowledge that we acquire and store over a lifetime about famous people, famous historical events, famous places, buildings and landmarks, and is expressed mainly via a linguistic coding system. It differs from episodic memory, which refers to life events that have been personally experienced and that are specifically coded in time and space (Tulving 1972). Semantic memory can be assessed through picture naming tasks (e.g., naming famous faces), picture and name matching tasks, and via questions probing semantic knowledge (e.g., generating information about famous persons). Semantic deficits are marked by degraded knowledge or difficulty in accessing this knowledge and can be evidenced using these tasks. Semantic deficits are also differentiable from lexical retrieval difficulties, which impair an individual's ability to specifically recall the names of objects, places and people (e.g., tip-of-the-tongue). Semantic memory remains stable or improves as we age, reflecting the accumulation of knowledge over the course of our lifetime. This contrasts with other domains of memory such as visuospatial and verbal working memory or episodic memory, which show a mild but continuous decline with ageing (Park et al. 2002).

The typical staging of cognitive deficits in Alzheimer's disease (AD) has been documented to affect episodic memory in the earliest stage, followed by semantic and attentional deficits, and later visuospatial and auditory-verbal short term memory deficits (Perry and Hodges 2000). An expression of this view is that the diagnostic criteria of amnesic Mild Cognitive Impairment (aMCI), considered to reflect the prodromal stage of AD since many of these individuals go on to develop AD (Tabert et al. 2006), include deficits on tests of episodic memory as the primary feature (Petersen 2003; Dubois et al. 2014). The assumption that episodic memory impairment is the hallmark of early AD has been challenged, however, and it has been proposed that deficits in context-free memory, which encompasses semantic

memory, may actually represent one of the earliest clinical signs of the disease (Didic et al. 2011). This view is based on the fact that in the early “transentorhinal stage” of the disease, neurofibrillary tangles (NFT) related to Tau pathology first develop in the subhippocampal region (perirhinal and entorhinal cortices). This region, which is functionally integrated into an anterior mesiotemporal network, has been shown to play a key role in context-free memory both in human and animal studies (Davies et al. 2004; Didic et al. 2011). Hodges and colleagues (Hodges et al. 2006) suggested that “*Amnesic MCI may not be an accurate concept unless semantic memory impairment is also considered as an integral core deficit*”. The view that semantic decline is found very early on in the AD process is corroborated by large epidemiological studies which suggested that the earliest cognitive changes in cognitively intact elderly individuals who will many years later go on to develop AD concern semantic memory (Amieva et al. 2008; Wilson et al. 2011). For instance, Wilson et al. (Wilson et al. 2011) have shown that the acceleration in cognitive decline in healthy elderly individuals who later developed dementia occurred slightly earlier for semantic memory (76 months before diagnosis) and for working memory than for episodic memory.

In the last decade, a number of studies have attempted to investigate semantic deficits in individuals with aMCI, who have a significant risk of conversion to dementia of the AD type in the following years (Tabert et al. 2006). Several studies demonstrated that individuals with aMCI are impaired on basic, commonly used, neuropsychological tests such as category fluency (Chasles et al. 2019) and picture naming tests (Balthazar et al. 2008). Other studies have shown that patients with aMCI are impaired on picture naming tasks of famous faces and famous monuments (Ahmed et al. 2008) and have degraded semantic knowledge about famous persons (Leyhe et al. 2010; Benoit et al. 2017; Barbeau et al. 2012) and famous historic events (Langlois et al. 2016; Leyhe et al. 2010; Barbeau et al. 2012). Similarly, one study showed that healthy carriers of the Presenilin-1 mutation performed worse than healthy controls when asked

to name faces of famous people (Arango-Lasprilla et al. 2007). Also, it has been shown that there is an absence of semantic priming effect for famous person knowledge in aMCI, indicating that semantic disturbances in aMCI reflect a central breakdown of semantic knowledge, in addition to semantic retrieval difficulties (Brambati et al. 2012).

Among the studies evaluating semantic knowledge in aMCI patients, several have shown that deficits in lexical retrieval (i.e., naming) and semantic knowledge were more important for famous people and historic events than for common objects and animals (Ahmed et al. 2008; Joubert et al. 2010). It has been suggested that the uniqueness and idiosyncratic nature of the former may be more vulnerable to semantic breakdown (Joubert et al. 2010; Joubert et al. 2008). The former tests are thus more sensitive in detecting semantic deficits in prodromal and early AD. In addition, aMCI patients have been shown to perform normally on commonly used picture naming tests of objects and animals such as the Boston Naming Test (BNT) when compared to AD patients (Balthazar et al. 2008). Finally, tests such as the BNT (Kaplan et al. 1983) and the DO80 (Deloche and Hannequin 1997) don't or poorly allow differentiating anomia due to a lexical retrieval impairment from a semantic impairment. Tests of verbal fluency and object naming indeed have the advantage of being quick to administer and hence are commonly used as part of routine neuropsychological assessments, but they are not pure measures of semantic memory and rely on multiple cognitive functions such as executive functions, processing speed, language and perception. When performance is impaired, it is often difficult to infer what underlying cognitive processes are affected. In sum, several tests reported as part of a routine neuropsychological assessment are often coarse or lack sensitivity to detect semantic changes in patients with MCI who do not match diagnostic criteria for dementia (Balthazar et al. 2008; Adlam et al. 2006; Joubert et al. 2010). For these reasons, we chose to focus in the current study on tests of famous people, famous public or

historical events, famous places or buildings, which are purer and more sensitive measures of semantic knowledge.

Neuroimaging studies of semantic breakdown in aMCI are scarce. One study showed correlations between semantic knowledge and a ventral mesiotemporal pathway including perirhinal/entorhinal areas and the anterior hippocampus (Barbeau et al. 2012). A positive correlation between connectivity of the anterior temporal network and a semantic memory task was found using resting state fMRI (Gour et al. 2011). A recent study also showed that semantic performance during MEG recording was associated with a pattern of functional hyperactivation in aMCI participants relative to controls within key regions of the semantic network (Pineault et al. 2018). This included the anterior temporal lobe (ATL), which has been associated with amodal semantic processing, and the prefrontal cortex and posterior middle temporal gyrus, which are associated with semantic executive processes (Ralph et al. 2017). Although more neuroimaging studies are needed, these results highlight abnormal patterns of brain function in MCI that extend beyond the hippocampal formation within regions that are critical for semantic memory.

In summary, there has been controversy regarding the staging of memory deficits in prodromal AD. It has generally been considered that the episodic memory impairment is the hallmark of the disease, such as evidenced by current diagnostic criteria of aMCI, but there is mounting evidence that semantic deficits are a key and early feature of aMCI. Therefore, the aim of the current study was to conduct a meta-analysis of existing studies of semantic memory in aMCI in order to determine if semantic impairment is a consistent feature of aMCI. In other words, are semantic deficits in aMCI consistently found in reported studies and what is the magnitude of the effect size? A second objective was to determine whether aMCI patients are impaired both on Free recall and Facilitated recall semantic tasks, as an impairment on Facilitated recall semantic tasks may suggest a central, or “true,” semantic impairment

(Brambati et al. 2012), unrelated to executive-based semantic deficit. Free recall (effortful) naming tasks (e.g. “What is the name of this famous person?”) and semantic tasks (e.g. “What does Chernobyl evoke to you?”) require the self-initiated free retrieval and generation of lexical and semantic knowledge, respectively, while Facilitated recall (less effortful) semantic tasks (e.g. “select the appropriate response among the following four choices”) offer a maximum of contextual information and exert fewer demands on retrieval processes. Results of this meta-analysis may have clinical implications. They may contribute to reconsidering what tests should define a standard neuropsychological assessment in the context of abnormal cognitive aging. The inclusion of semantic tests may represent a useful addition to the assessment of older individuals who may be in the very early stages of AD.

2. Material and methods

This meta-analysis was conducted following the guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Shamseer et al. 2015). Python version 3.6 and R version 3.5 were used for all statistical analyses and plots.

2.1. Criteria for inclusion

Four inclusion criteria were used to include a study in this meta-analysis:

1. *The study had to report results about a group of MCI patients.* The definition of MCI in studies corresponded to published and accepted criteria (Albert et al. 2011; Petersen 2004; Petersen et al. 2001; Petersen et al. 1999). Of the 22 selected studies, 20 used the criteria of amnesic MCI. One study (Gardini et al. 2015) included both amnesic and non-amnesic MCI patients but most patients in this study were actually amnesic MCI (18/21). Another study (Smith et al, 2013) did not specify MCI subtype, but used the inclusion criteria of Albert et al. 2011, which specifically

refer to MCI due to AD. Diagnostic criteria for the different studies are provided in Table 1.

2. *The study had to report results about a healthy control group that was equivalent to the MCI group in terms of demographic variables such as age and education.* This criterion was necessary to calculate an effect size.
3. *The study had to report semantic tasks about unique entities.* Among the studies evaluating semantic knowledge in MCI patients, we selected only those that investigated naming or specific knowledge about unique entities such as famous people, famous public or historical events, famous places or buildings. Studies of verbal fluency or naming common objects were not included in the present meta-analysis. Names of the tests are reported in Table 1.
4. *The study had to provide the necessary data to calculate an effect size (means and standard deviations for both the patients and healthy controls).* Sometimes the effect size could be extrapolated from available data. When not available, the authors of the study were systematically contacted by email to obtain missing information. If they did not reply, the study was excluded from the analyses.

2.2. Search strategy

We searched for publications specifically evaluating semantic memory in MCI patients. Databases of peer-reviewed literature were systematically searched on PubMed and GoogleScholar for manuscripts in the English language published from 1990 to 2019. The primary search criteria included “Alzheimer” or “Alzheimer’s Disease” or “MCI” and were secondarily connected with the term “Semantic” or “Semantic memory” or “Semantics”. This search yielded a large number of articles. Titles and/or abstract were thus reviewed to refine the number of potentially interesting articles. Following this step, the inclusion criteria were

assessed for each study by carefully reading the Methods and Results sections of each article. In addition, the own personal databases of articles on semantic memory in aMCI patients gathered by four authors of this study (all experts of the field) were systematically screened by three of the authors to ensure that no study had been omitted during the initial search process. As a final step, if an article met the search criteria, all references of the selected articles at this stage were examined one-by-one by the authors to make sure that no study had been omitted.

2.3. Effect size calculation

For each comparison, we calculated an effect size using Hedge's g (Hedges and Olkin 1985). This effect size allows for standardization of units and comparison among studies using different units or semantic tests. We chose Hedge's g over Cohen's d and Glass's Delta, because its result takes into account the size of each of the two samples. Moreover, its value is more penalized for small samples (<50). The 95% CI of each effect size was also calculated. Forest plots were used to present the result for each study and the overall result.

2.4. Data extraction

Results on semantic tasks were entered into a spreadsheet. Global (mean) performance was first considered. When several tasks were used in the same study, we calculated the overall effect size and confidence interval for this study (Borenstein et al. 2009). This overall effect size is the average of each effect size calculated individually on each task.

Then, when available, each task was further categorized and labelled based on the following classification:

- *Naming*: self-initiated lexical retrieval of names from pictures (e.g., famous persons, famous public events, etc.).

- *Free recall of semantic information:* self-initiated recall of semantic information about famous persons, famous public events, etc. (without cues).
- *Facilitated recall of semantic information:* cued recall of semantic information about famous persons, famous public events, etc. or multiple-choice questions.

2.5. Random-effects model

A random-effects model was calculated following Borenstein’s guidelines (Borenstein et al. 2009). The parameter τ^2 (Tau squared) is the between-study variance, meaning that if we somehow knew the true effect size for each study and computed the variance of these effect sizes (across an infinite number of studies), this variance would be τ^2 . To compute the random-effects model, we calculated both the within-study variances and the τ^2 since the study’s total variance is calculated using these two parameters. A $\tau^2 > 1$ suggests the presence of substantial statistical heterogeneity (van Loon et al. 2018). Therefore, the closer τ^2 is to 0 the better. Each random variable of the model was weighted in inverse proportion to its variance:

$$w = \frac{1}{(V_y + \tau^2)}$$

With w = weight of a given study; V_y = within-study variance and τ^2 = between-studies variance.

The results obtained using Borenstein’s method were verified and compared to those obtained with the R “metafor” package (Viechtbauer 2010) for multi-level meta-analysis. The parameter “studies” was considered as a random-effect because one study could contain several tests. Both methods showed the exact same overall effect size, 95% CI and τ^2 .

A P value <0.05 was considered as statistically significant throughout this study.

2.6. Fail-safe N estimation

While a meta-analysis yields a mathematically accurate synthesis of the studies included, if these studies are a biased sample of all relevant studies, then the mean effect computed by the meta-analysis might reflect this bias. Since studies reporting positive results (i.e., significant differences between conditions) are more likely to find their way into a meta-analysis, this bias is likely to be reflected in the meta-analysis as well. This issue is generally known as the publication bias, or “file drawer” problem. To address this, we calculated an estimation of how many studies with a null effect would be necessary to invalidate our results, i.e., to show that no difference existed between MCI and healthy control participants, using Rosenthal’s method (Rosenthal 1979; Orwin 1983). The greater is this estimated number of studies, the more reliable are the results of the meta-analysis (Borenstein et al. 2009).

3. Results

A total of 747 studies had in their title the words corresponding to the search criteria (selection diagram in *Figure 1*). After reading the titles and abstracts as well as adding the relevant articles gathered by the authors of this meta-analysis, 85 appeared relevant to the goal of the present study and were investigated in detail to verify if they met the inclusion criteria. Out of these 85 references, 60 did not pass the inclusion criteria and were therefore excluded from the meta-analysis (i.e., basic or nonspecific semantic tests = 39, absence of MCI participants in the study = 16, literature review with no participants = 5). Of the 25 remaining studies, 3 could not be considered because the information provided in the article did not allow calculating an effect size and the authors did not respond to our request for further information. Thus, 22 studies respected the inclusion criteria and were hence analyzed in our study (details in *Table 1*). These 22 studies lead to the inclusion of 952 participants (476 healthy participants [251F/131M; 94 not reported] and 476 MCI patients [221F/189M; 66 not reported]; mean

MMSE of MCI patients = 27.05 ± 0.58 , n = 358; mean MOCA of MCI patients = 25.96 ± 0.08 , n = 40; MCI patients without MMSE or MOCA, n = 78).

[Insert Table 1 about here]

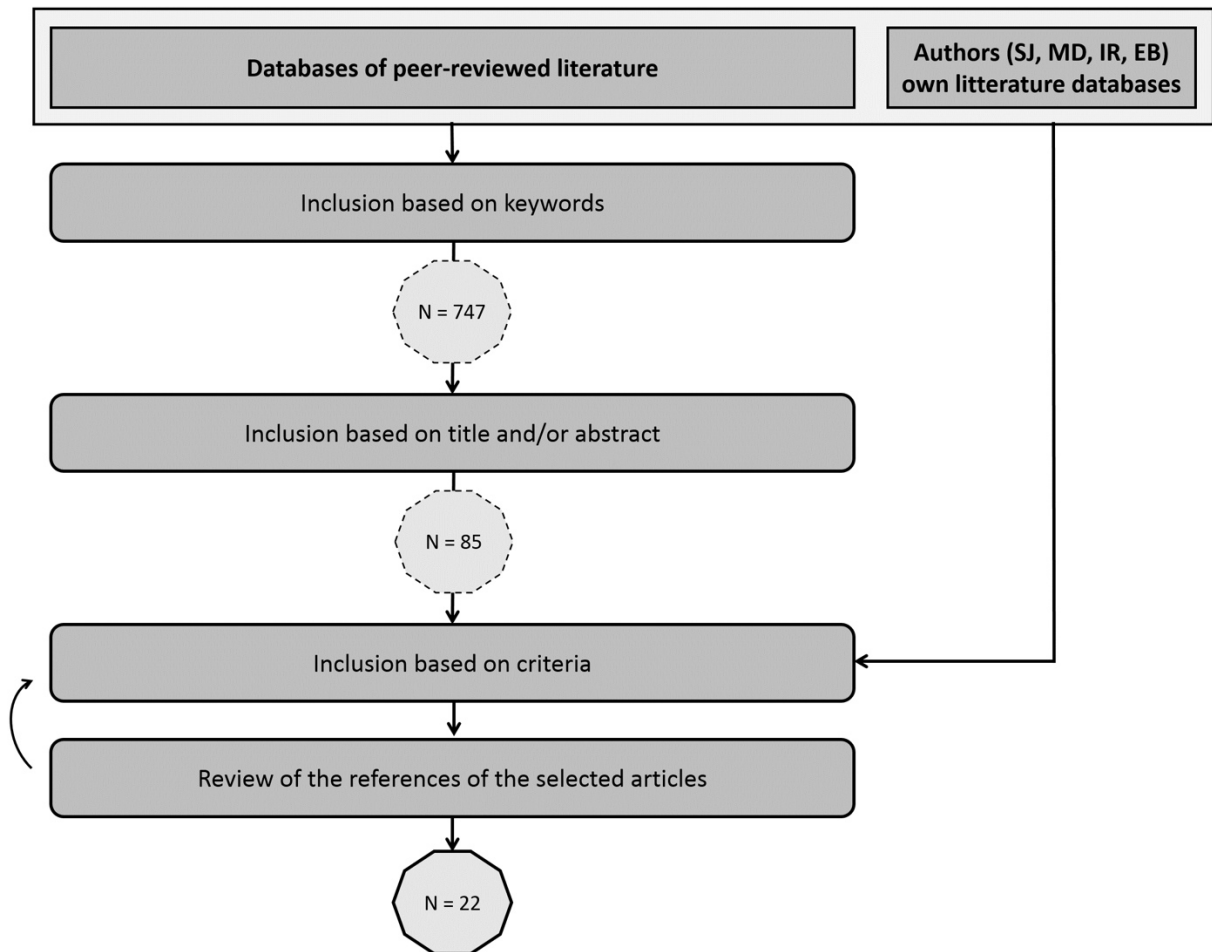


Figure 1. Diagram of study inclusion. 747 study titles contained at least two keywords of interest. Reading these titles and abstracts, 85 studies could fit the topic of interest. Following the review of the Methods and Results sections, 22 studies finally met all inclusion criteria.

Some studies included several semantic memory tests/tasks that met the inclusion criteria. Thus, a total of 64 tasks comparing the performance of aMCI patients to healthy subjects were part of the 22 studies. A mean effect size and variability were calculated for each study, with the “study” parameter being considered as a random variability factor to take into account the fact that one study could involve several tasks. Two studies had same groups (Benoit et al. 2017; Langlois et al. 2016) but this was controlled in the statistical model since this parameter was considered as a random variable. The effect size indicated better semantic performance in healthy elderly groups than in MCI groups in every study. These results, plotted in *Figure 2*, are represented in descending order of weight. The random-effects model, considering all effect sizes, within-studies variance, weight and total between-study variance, confirmed the previous observation ($p < 0.001$, overall $d = 1.02$, 95% CI of $d [0.80; 1.24]$, $\tau^2 = 0.16$, red diamond at the bottom of *Figure 2*). The fail-safe N , calculated using Rosenthal’s method (Rosenthal, 1979), was 1730, indicating that 1730 studies showing no difference between patients and control subjects would be needed to invalidate current findings. Finally, one study (Smith et al., 2013) used the Albert et al. (2011) MCI due to AD criteria but did not explicitly mention MCI subtype, so we ran the analyses excluding this study as an additional measure, but this did not change the results (the overall d changed from 1.02 to 1.04).

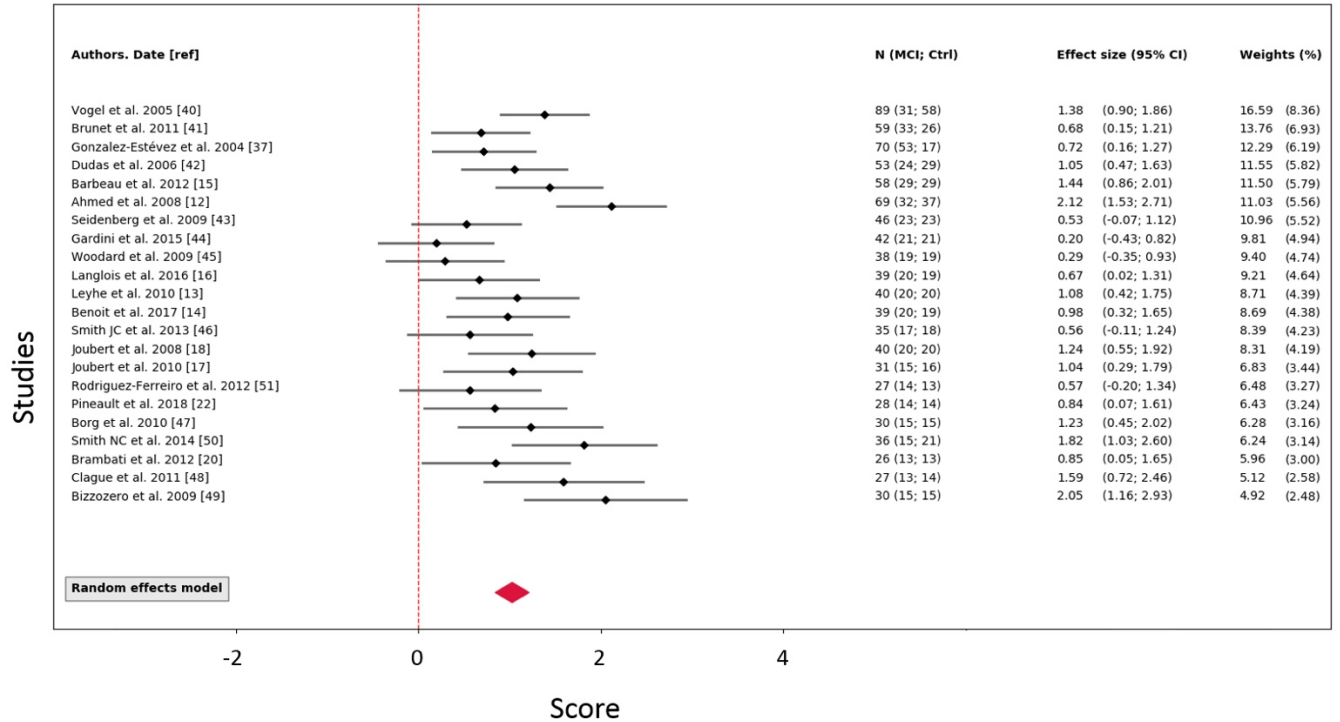


Figure 2. Forest plot showing the overall effect size +/- 95% confidence interval for each study in terms of semantic performance. The studies are ordered in decreasing size of weight. A position to the right of the red vertical line indicates better performance of the control subjects on semantic tests. The red diamond at the bottom of the figure shows the random-effects model estimate which can be considered as the mean effect size +/- 95% CI among all studies. Ctrl: control subjects. CI: confidence interval. N: number of subjects.

As mentioned in the Methods section, semantic tasks were further classified into three categories (naming, free recall of semantic information-FrR, facilitated recall of semantic information-FaR). This classification allowed to assess the impact of the nature of the task (retrieval of semantic knowledge vs. lexical retrieval of a name) and the difficulty of the task (Free recall/effortful vs. Facilitated recall/less effortful) on effect size. The results presented in Figure 3 indicate that MCI participants performed worse than healthy subjects even on facilitated recall tasks (effect sizes compared to a mean of 0 using a univariate t test, $t = 8.81$, $df = 34$, $p < 0.001$). Analyses based on a Linear Mixed Model (64 observations, 22 groups,

fixed effects: conditions [Naming, FrR, FaR], random effects: studies [1 to 22]) also indicated that MCI participants were impaired to a greater extent on free recall ($t = 3.27, p < 0.01$) and on naming tasks ($t = 3.025, p < 0.01$) than on facilitated recall tasks (details in Table 2). No significant difference was observed between free recall and naming.

[Insert Table 2 about here]

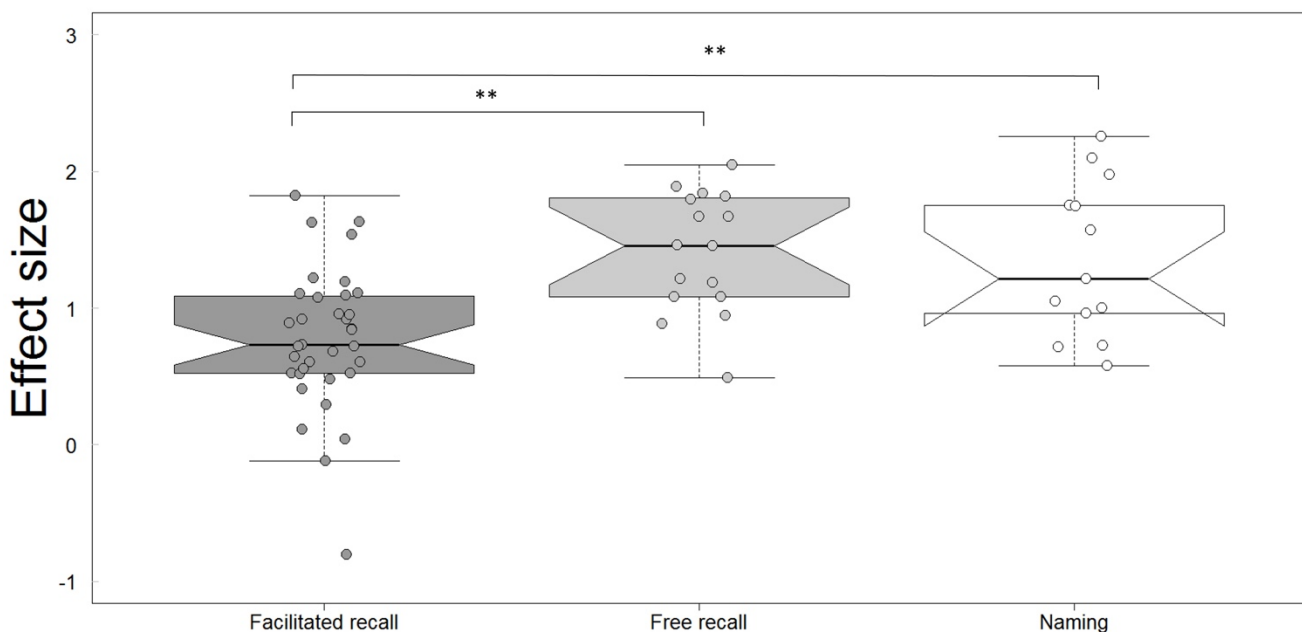


Figure 3. Comparison of the effect size across the different types of tasks: facilitated recall of semantic information (cued recall or multiple-choice questions), free recall of semantic information and naming single entities. Participants performed worse than healthy subjects on all conditions, including facilitated recall. Free recall and naming's effect size were also larger than for facilitated recall. Each dot represents the effect size for one task. Since one study can be composed of several tasks, there are more dots than studies. The oblique lines going up and down from each horizontal median line represent the nonparametric 95% confidence interval (notch = TRUE in R). On the 3rd boxplot, the lower limit of this interval exceeds the 1st quartile. ** $p < 0.01$.

4. Discussion

Twenty-two studies were included in the current meta-analysis following stringent selection criteria. Results show a mean effect size of 1.02 (95% CI [0.80; 1.24]) indicating that aMCI participants perform significantly worse in terms of overall semantic performance when compared to healthy age- and education-matched controls. This corresponds to a large to very large effect size (Cohen 1988; Sawilowsky 2009). The effect size was > 0 for each of the 22 studies, indicating that this effect was found systematically across all studies. In addition, it was found that 185 studies showing no difference between controls and aMCI would be needed to invalidate these results. Results of this meta-analysis thus support the view of a semantic impairment in individuals with aMCI.

Further analyses also revealed that aMCI individuals were significantly impaired on Free recall (effortful) semantic tasks (self-initiated free retrieval and generation of semantic knowledge, ex. “What does Chernobyl evoke to you?”) and naming tasks (ex. “What is the name of this famous person?”). However, aMCI patients were also impaired on Facilitated recall (less effortful) semantic tasks (ex. “Select the appropriate response among the following four choices”). These results support the view that semantic deficits in MCI may result both from central semantic disturbances, i.e., a degradation of semantic knowledge and from difficulties in semantic executive processes required to retrieve, manipulate and generate semantic knowledge (Joubert et al. 2010; Brambati et al. 2012).

Amnesic MCI is considered by many authors to reflect a prodromal stage of AD (Dubois and Albert 2004) because a significant proportion of aMCI individuals develop AD over the years, especially those with deficits in multiple cognitive domains (Tabert et al. 2006). Over the years, clinical research criteria have progressively incorporated the use of biomarkers for

the study of “MCI due to AD” (Albert et al. 2011). To our knowledge, none of the selected studies in the current meta-analysis had A β or Tau biomarkers of AD in MCI participants, but this represents a very interesting research perspective in future studies. For instance, a recent study by Loewenstein et al. (Loewenstein et al. 2018), showed that a test of semantic interference, the LASSI-L, was able to successfully discriminate between amyloid-positive and amyloid-negative participants with MCI, suggesting that this test may represent a specific cognitive test able to distinguish cases with AD (Loewenstein et al. 2018).

One limitation of the current study, however, is that all the studies included in the current analyses were cross-sectional. To our knowledge, no study has yet specifically investigated the long-term progression of semantic deficits in MCI to determine whether semantic impairment in MCI may contribute to improving prognosis and help predict later decline to AD. However, one longitudinal study suggests that MCI patients who subsequently develop AD differ from non-converters on tasks that assess semantic memory at baseline (Didic et al. 2013). Only one study showed that MCI patients who had converted to AD after a 2-year follow-up performed significantly more poorly on a famous faces identification task at baseline than MCI non-converters and healthy controls (Estevez-Gonzalez et al. 2004). Future studies will need to examine more closely if those MCI individuals with semantic deficits are more likely to develop AD at follow-up. This will help to determine if semantic tests show an added value to episodic memory tests in the assessment of MCI. Finally, in most studies, it was not known whether amnesic MCI individuals were single domain or multiple domains. However, single domain MCI is uncommon compared to multiple domain aMCI (Hodges et al. 2006), and previous studies have shown that single domain aMCI, multiple domains aMCI and early AD likely represent three severity points along the continuum between normal aging and AD (Brambati et al. 2009).

Interestingly, impaired episodic memory can be related to a number of other conditions (ex. depression, thyroid dysfunction, polypharmacy) and situational factors (ex. fatigue, stress, depression, anxiety, negative stereotypes (Adam et al. 2013)). This is in line with the fact that a proportion of MCI individuals remain stable or even revert to normal at follow-up. In contrast, semantic memory is the only memory system that does not decline, and even improves, over the course of normal aging (Nilsson 2003), reflecting the accumulation of knowledge over the lifespan. The assessment of semantic memory is also much less susceptible to the situational factors described above. Therefore, the unique contribution of the current study to neuropsychology of MCI is that it shows that semantic tests may be helpful in improving the early identification of individuals who will later develop AD and may contribute to refining differential diagnosis between normal cognitive aging and early signs of AD. The clinical implications of this study are that we should reconsider what tests should define a standard neuropsychological assessment in the context of abnormal cognitive aging. The inclusion of semantic tests may represent a useful addition to the assessment of older individuals who may be in the very early stages of AD. Ideally, we hope that this may contribute to a revision of the diagnostic criteria of aMCI by consensus groups by considering the inclusion of semantic deficits. From a more fundamental point of view, memory impairment in aMCI may be best characterized as “declarative”, i.e., encompassing both episodic *and* semantic memory, rather than just episodic. Future studies will also need to determine which of the currently available semantic tests are most sensitive in detecting impairment and which ones are best in predicting future conversion to dementia. Cognitive tests remain the preferred tools in the assessment and diagnosis of neurocognitive disorders in the elderly because they are easily accessible and non-invasive.

In conclusion, results of the current meta-analysis reveal that semantic deficits are regularly found in MCI. In line with large epidemiological studies (Amieva et al. 2008; Wilson

et al. 2011) and with studies of familial AD (Arango-Lasprilla et al. 2007), semantic decline may represent one of the earliest and most consistent features of cognitive decline in prodromal AD. This calls to specifically test this hypothesis and for the systematic inclusion of tests assessing semantic skills in the neuropsychological assessment of early AD.

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Table 1. Characteristics of the 22 studies included in the meta-analysis. CS = control subject; N = naming; FrR = Free recall; FaR = facilitated recall; SD = standard deviation; edu = years of education.

| <i>Authors Year of publication</i> | <i>Semantic task</i> | <i>Diagnostic criteria</i> | <i>MCI mean age (±SD)</i> | <i>Controls mean age (±SD)</i> | <i>MCI group size</i> | <i>MCI mean edu</i> | <i>Controls mean edu</i> | <i>MCI - test mean score</i> | <i>MCI - test SD</i> | <i>Controls sample size</i> | <i>Controls - test mean score</i> | <i>Controls - test SD</i> | <i>Effect size (Hedge's g)</i> |
|--|--------------------------|--------------------------------|---------------------------------------|--|-------------------------------|-----------------------------|----------------------------------|--|--------------------------|-------------------------------------|---|-------------------------------|--|
| (Ahmed et al. 2008) | N | Petersen (2004) | 69.5 ± | 66.8 ± | 32 | 12.8 | 13.8 | 15.9 | 5 | 37 | 24.7 | 2.6 | 2.257 |
| | N | | 8.2 | 5.5 | | | | 14 | 5.1 | | 22.2 | 3.1 | |
| (Barbeau et al. 2012) | N | Petersen (2001) | 68.9 ± 6.6 | 68.8 ± 6.4 | 29 | 13.17 | 12.41 | 23.59 | 7.61 | 29 | 34.34 | 4.24 | 1.745 |
| | FrR | | | | | | | 32.83 | 5.6 | | 37.65 | 2.91 | 1.08 |
| | FrR | | | | | | | 13.86 | 5.91 | | 22.48 | 4.29 | 1.669 |
| | FrR | | | | | | | 11.96 | 4.75 | | 16.54 | 3.65 | 1.081 |
| | FrR | | | | | | | 8.39 | 4.84 | | 14.93 | 4.09 | 1.46 |
| | FaR | | | | | | | 8.64 | 1.7 | | 9.79 | 0.5 | 0.918 |
| | FrR | | | | | | | 5.93 | 3.45 | | 12.68 | 3.87 | 1.841 |
| | FrR | | | | | | | 3.71 | 1.54 | | 6.32 | 2.02 | 1.669 |
| | FrR | 13.86 | 5.91 | 22.48 | 4.29 | | | | | | | | |
| (Benoit et al. 2017) | FaR | Albert et al. (2011) | 76.9 ± | 73.9 ± | 20 | 14.5 | 14.6 | 81 | 13.19 | 19 | 93.02 | 7 | 1.078 |
| | FrR | 6.5 | 8.5 | 16.1 | | | | 4.9 | 20.6 | | 4.8 | 0.885 | |
| (Bizzozero et al. 2009) | FrR | Petersen (1999) | 75.3 ± | 74.6 ± | 15 | 9.3 | 9.3 | 51.26 | 35.23 | 15 | 121.46 | 28.89 | 2.048 |
| (Borg et al. 2010) | FrR | Petersen (2004) | 74.3 ± | 75.8 ± | 15 | 11.3 | 11.1 | 0.54 | 0.13 | 15 | 0.75 | 0.07 | 1.890 |
| | FaR | | | | | | | 0.88 | 0.08 | | 0.94 | 0.04 | 0.892 |
| | FrR | | | | | | | 0.52 | 0.16 | | 0.68 | 0.08 | 1.189 |
| | FaR | | | | | | | 0.8 | 0.16 | | 0.92 | 0.05 | 0.952 |
| (Brambati et al. 2012) | FaR | Petersen (2001) | 72.7 ± | 72.6 ± | 13 | 14.7 | 12.2 | 1.09 | 6.2 | 13 | 6.67 | 6.04 | 0.848 |
| | | | 4.9 | 6.2 | | | | | | | | | |
| (Brunet et al. 2011) | FaR | Petersen (2004) | 72.3 ± | 72.7 ± | 33 | 13 | 13.2 | 79.6 | 10.8 | 26 | 85.9 | 6.75 | 0.681 |
| | | | 6.1 | 5.3 | | | | | | | | | |
| (Clague et al. 2011) | N | Petersen (2004) | 66.7 ± | 64.3 ± | 13 | 13.1 | 13.3 | 16.43 | 10.485 | 14 | 47.355 | 16.19 | 2.1 |
| | N | | | | | | | 22.88 | 10.46 | | 34.19 | 10.635 | 1 |
| | FrR | | | | | | | 31.645 | 8.44 | | 44.5 | 4.49 | 1.8 |
| | FaR | | | | | | | 123.5 | 10.95 | | 138.07 | 4.845 | 1.628 |
| | FaR | | | | | | | 130.895 | 8.65 | | 141.57 | 1.67 | 1.63 |
| | FaR | | | | | | | 35.485 | 5.775 | | 44.645 | 3.385 | 1.824 |
| | FaR | | | | | | | 37.105 | 5.56 | | 44.645 | 3.145 | 1.574 |
| | FaR | | | | | | | 43.375 | 4.53 | | 47.57 | 0.945 | 1.219 |
| (Dudas et al. 2005) | N | Petersen (2001) | 68.2 ± 8 | 63.8 ± 8.3 | 24 | 11.8 | 12.4 | 9.5 | 5.5 | 29 | 15 | 5 | 1.051 |
| (Estevez-Gonzalez et al. 2004) | N | Petersen (2001) | 75 ± 6.4 | 74.7 ± 5.5 | 53 | NA | NA | 43.9 | 14.9 | 17 | 54.6 | 15.1 | 0.676 |

| | | | | | | | | | | | | | |
|----------------------------------|-----|---------------|----------|-----------|----|------|------|-------|-------|----|-------|-------|--------|
| (Gardini et al. 2015) | N | | | | | 9.19 | 11.7 | 11.62 | 5.45 | | 19.86 | 7.4 | 1.214 |
| | FaR | Petersen | 70.6 ± | 69.7 ± | 21 | | | 13.62 | 5.12 | 21 | 8.71 | 6.51 | -0.803 |
| | FrR | (2001) | 4.6 | 4.8 | | | | 12.1 | 8.57 | | 16.29 | 7.76 | 0.491 |
| | FaR | | | | | | | 12.29 | 5.85 | | 11.51 | 6.33 | -0.123 |
| (Joubert et al. 2008) | N | Petersen | 73.3 ± | 73.2 ± 11 | 20 | 11.1 | 10.8 | 64.3 | 20.8 | 20 | 77.3 | 12.3 | 0.727 |
| | N | (2001) | 7.1 | | | | | 55.7 | 18.5 | | 82.7 | 9.6 | 1.75 |
| (Joubert et al. 2010) | N | Petersen | 73.7 ± | 72.4 ± | 15 | 12.8 | 13.9 | 49.8 | 25.2 | 16 | 76.3 | 26.5 | 0.965 |
| | FaR | (2001) | 6.3 | 7.1 | | | | 75.7 | 9.7 | | 86.5 | 8.7 | 1.106 |
| (Langlois et al. 2016) | FaR | | | | | | | 3.8 | 1.15 | | 4.32 | 0.89 | |
| | FaR | | | | | | | 4.25 | 1.12 | | 4.74 | 0.56 | 0.481 |
| | FaR | | | | | | | 4.3 | 0.8 | | 4.74 | 0.56 | 0.524 |
| | FaR | Albert et al. | 77 ± 6.5 | 74 ± 8.5 | 20 | 15 | 15 | 3.85 | 1.18 | 19 | 4.47 | 0.7 | 0.605 |
| | FaR | (2011) | | | | | | 3.15 | 1.18 | | 3.74 | 0.99 | 0.606 |
| | FaR | | | | | | | 3.25 | 1.45 | | 4.31 | 0.76 | 0.516 |
| | FaR | | | | | | | 3.25 | 1.55 | | 4.47 | 0.7 | 0.867 |
| | FaR | | | | | | | 3.4 | 1.7 | | 4.42 | 0.77 | 0.731 |
| (Leyhe et al. 2010) | FaR | | | | | | | 74.75 | 23.78 | | 95.25 | 8.67 | 1.094 |
| | FrR | Petersen | 72.6 ± | 71.6 ± | 20 | 10.2 | 11.8 | 5.04 | 2.59 | 20 | 7.29 | 1.91 | 0.945 |
| | FrR | (1999) | 6.8 | 6.5 | | | | 5.14 | 2.72 | | 8.14 | 1.93 | 1.215 |
| (Pineault et al. 2018) | FaR | Petersen | 75.4 ± | 73.7 ± | 14 | 15.6 | 15 | 71 | 7.4 | 14 | 79 | 10.2 | 0.84 |
| | FaR | (2001) | 7.1 | 5.8 | | | | | | | | | |
| (Rodriguez-Ferreiro et al. 2012) | N | Petersen | 75 ± 6.4 | 74.7 ± | 14 | 7.4 | 7.2 | 31 | 16.7 | | 41 | 15.5 | 0.578 |
| | FaR | (2001) | | 5.5 | | | | 89 | 8.3 | 13 | 93 | 4.4 | 0.556 |
| (Seidenberg et al. 2009) | FaR | | | | | | | 0.75 | 0.23 | | 0.89 | 0.13 | 0.207 |
| | FaR | | | | | | | 0.92 | 0.13 | | 0.97 | 0.6 | 0.11 |
| | FaR | Petersen | 75.6 ± | 75.3 ± | 23 | 14.4 | 14.7 | 0.95 | 0.8 | 23 | 0.98 | 0.5 | 0.0432 |
| | FaR | (2001) | 5.6 | 4.7 | | | | 2.16 | 0.93 | | 2.68 | 0.97 | 0.526 |
| | FaR | | | | | | | 2.3 | 1.11 | | 3.05 | 1.12 | 0.647 |
| | FaR | | | | | | | 2.94 | 1.34 | | 4.44 | 1.25 | 1.113 |
| (J. C. Smith et al. 2013) | FaR | Albert et al. | 78.7 ± | 76 ± 7.3 | 17 | 15.5 | 16.6 | 80.2 | 16.4 | 18 | 87.1 | 15.8 | 0.407 |
| | FaR | (2011) | 7.5 | | | | | 83.2 | 18.6 | | 93.7 | 6.8 | 0.72 |
| (C. N. Smith 2014) | FrR | Petersen | 78.7 ± | 76.3 ± | 15 | 15.3 | 15.3 | 33.2 | 4.1 | 21 | 39.7 | 2.8 | 1.82 |
| | FrR | (2001) | 1.5 | 1.6 | | | | | | | | | |
| (Vogel et al. 2005) | N | Petersen | 75.9 ± | 74.1 ± | 31 | 11.1 | 11.6 | 13.19 | 4.23 | 31 | 18.09 | 2.334 | 1.434 |
| | FaR | (2001) | 6.1 | 4.9 | | | | 16.77 | 2.986 | | 19.26 | 1.396 | 1.068 |
| (Woodard et al. 2009) | FaR | Petersen | 75.4 ± | 75.1 ± | 19 | 14.1 | 14.0 | 87.4 | 14.6 | 19 | 90.9 | 7.1 | 0.291 |
| | FaR | (2001) | 6.9 | 5.9 | | | | | | | | | |

Table 2. Linear mixed effects model summary table. Number of observations (semantic tests): 64, number of groups (studies): 22. AIC = 86.1; BIC = 96.9; logLik = -38.1; deviance = 76.1; df resid = 59. FaR: Facilitated Recall; FrR: Free recall; N: Naming.

| | FaR | | | | | N | | | | |
|----------------------------|-----------------|-------------------|-----------------|----------------|----------------|-----------------|-------------------|-----------------|----------------|----------------|
| Random effects | Variance | | Std. Dev | | | Variance | | Std. Dev | | |
| Studies (Intercept) | 0.1289 | | 0.3591 | | | 0.1289 | | 0.3591 | | |
| Residual | 0.1348 | | 0.3672 | | | 0.1348 | | 0.3672 | | |
| Fixed effects | Estimate | Std. Error | df | t value | p value | Estimate | Std. Error | df | t value | p value |
| Intercept | 0.8132 | 0.11 | 30.43 | 7.32 | 3.48e-8 *** | 1.2649 | 0.1414 | 47.82 | 8.943 | 8.87e-12 *** |
| FrR | 0.4730 | 0.15 | 57.8 | 3.27 | 0.0019 ** | 0.0213 | 0.1751 | 60.19 | 0.122 | 0.9037 |
| FaR | - | - | - | - | - | -0.4517 | 0.1493 | 59.87 | -3.025 | 0.0036 ** |
| N | 0.4517 | 0.1493 | 59.87 | 3.04 | 0.0036 ** | - | - | - | - | - |

Supplementary Table 1

| Authors | Country | Semantic Test/Task name |
|--------------------------------|----------------|--|
| Ahmed et al. 2008 | UK | Graded Buildings Test Graded Faces Test |
| Barbeau et al. 2012 | France | Naming famous faces Person Identification Person information QAD Short-Eve FR Short-Eve MCQ Short-Eve CQ Short-Eve Dote WAIS-III Information |
| Benoit et al. 2017 | Canada | POP-40 Test of famous persons WAIS-III Information |
| Bizzozero et al. 2009 | Italy | Media-mediated memory test |
| Borg et al. 2010 | France | Test of famous names: Morphological free recall (MFR) Test of famous names: Morphological recognition (MR) Test of famous names: Semantic questions (SQ) Test of famous names: Semantics recognition (SR) |
| Brambati et al. 2012 | Canada | Famous names semantic priming task |
| Brunet et al. 2011 | Canada | Semantic Memory Test for Famous Persons |
| Clague et al. 2011 | UK | Person fluency Person naming Person information Total face sorting Total name sorting Two choices associative (faces) Two choices associative (names) Name to face matching |
| Dudas et al. 2006 | UK | Face Place Test |
| Gardini et al. 2015 | Italy | Famous people free recall - Naming Famous people with cue - Naming Famous people free recall - Semantic informations Famous people with cue - Semantic informations |
| Estévez-Gonzalez et al. 2004 | Spain | Task of Famous Face Identification |
| Joubert et al. 2008 | France | Test of famous people Test of famous public events |
| Joubert et al. 2010 | Canada | Naming famous people Semantic facts about famous people |
| Langlois et al. 2016 | Canada | PUB-40 Famous public events: Enduring 60-75 PUB-40 Famous public events: Enduring 76-90 PUB-40 Famous public events: Enduring 91-2005 PUB-40 Famous public events: Enduring 2006-11 PUB-40 Famous public events: Transient 60-75 PUB-40 Famous public events: Transient 76-90 PUB-40 Famous public events: Transient 91-2005 PUB-40 Famous public events: Transient 2006-11 |
| Leyhe et al. 2010 | Germany | Recognition of famous events Dating famous events Context about famous events |
| Pineault et al. 2018 | Canada | Famous faces categorization |
| Rodriguez-Ferreiro et al. 2012 | Spain | Famous people knowledge and naming Faces - Words matching |
| Seidenberg et al. 2009 | USA | Recognition of famous names: recent Recognition of famous names: remote Recognition of famous names: enduring Semantic knowledge of famous names: recent Semantic knowledge of famous names: remote Semantic knowledge of famous names: enduring |
| Smith JC et al. 2013 | USA | Forced task - famous or not famous Forced task - famous or not famous |
| Smith NC et al. 2014 | USA | Free recall of famous events |
| Vogel et al. 2005 | Denmark | DMST subset: Naming famous faces DMST subset: Person Identification |
| Woodard et al. 2009 | USA | Semantic information about famous people |