

HHS Public Access

J Int Neuropsychol Soc. Author manuscript; available in PMC 2020 July 01.

Published in final edited form as:

Author manuscript

J Int Neuropsychol Soc. 2020 July ; 26(6): 545–556. doi:10.1017/S1355617720000016.

False memories: The other side of forgetting

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Abstract

Objective: To measure caregiver and clinician perception of false memories in the lives of patients with memory loss due to Alzheimer's disease (AD) and Mild Cognitive Impairment (MCI) using a novel false memories questionnaire. Our hypotheses were that false memories are occurring as often as forgetting according to clinicians and family members.

Method: This prospective, questionnaire-based study consisting of 20 false memory questions paired with 20 forgetting questions, had two forms: one for clinicians and the other for family members of older subjects. 226 Clinicians and 150 family members of 49 patients with AD, 44 patients with mild cognitive impairment (MCI), and 57 healthy older controls (OCs) completed the questionnaire.

Results: False memories occurred nearly as often as forgetting according to clinicians and family members of patients with MCI and AD. Family members of OCs and patients with MCI had fewer false memories compared to those of the AD group. As MMSE scores decreased, the mean score increased for both forgetting and false memories. Among clinicians, correlations were observed between the dementia severity of patients seen with both forgetting and false memories questionnaire scores as well as with the impact of forgetting and false memories on daily life.

Conclusion: Patients with AD experience false memories almost as frequently as they do forgetting. Given how common false memories are in AD patients, additional work is needed to understand the clinical implications of these false memories on patients' daily lives. The novel false memories questionnaire developed may be a valuable tool.

Potential Conflicts of Interest: The authors have no conflicts of interest to declare.

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Keywords

alzheimer's disease; dementia; mild cognitive impairment; everyday function; memory and surveys

Introduction

Non-pharmacological techniques such as pill boxes and reminder notes can enable individuals with moderate or even severe amnesia due to stroke or encephalitis to live independently (Acevedo & Loewenstein, 2007). These memorial aids typically fail in patients with Alzheimer's disease (AD) due, in part, to an increased tendency to form false memories (Malone et al., 2018). False memories may occur in several forms. For example false memories may be related to events that never occurred or to events that are distorted or mis-remembered (Malone et al., 2018). It is possible that false memories have an equal or greater impact on function in the lives of patients with mild cognitive impairment (MCI) and AD dementia compared to forgetting itself. For example, elevated rates of false memories in AD patients increase the likelihood that patients will mis-remember having taken their medications or turned off the stove when they have not performed these activities.

Using experimental methods developed to examine false memory in healthy individuals (Cotel, Gallo, & Seamon, 2008; Devitt & Schacter, 2016; Norman & Schacter, 1997; Daniel L. Schacter, Israel, & Racine, 1999), we and others have examined false memories in patients with AD in laboratory settings. This work established that many AD patients' false memories were related to the fact that they could remember the general idea, meaning, or gist of an event, but not the specific details (Budson, Daffner, Desikan, & Schacter, 2000). Part of their difficulty with false memories was related to the fact that patients have an abnormal sense of familiarity for things that were actually new (Deason et al., 2017).

In the laboratory, patients with AD show higher rates of false memories than do healthy older adults and those with amnesia due to other causes, possibly related to an abnormal liberal response bias (Budson, Wolk, Chong, & Waring, 2006; Koutstaal, Verfaellie, & Schacter, 2001; D. L. Schacter, Verfaellie, Anes, & Racine, 1998; Snodgrass & Corwin, 1988). Furthermore, false memories among possible AD patients may be a more specific indicator of AD pathology than memory performance alone (Hildebrandt, Haldenwanger, & Eling, 2009a, 2009b). One longitudinal investigation of preclinical AD has shown that distorted and false memories may be useful clinically for identifying preclinical AD (Schmid, Taylor, Foldi, Berres, & Monsch, 2013).

Thus, false memories may have diagnostic and prognostic value for patients with memory disorders that can be used by their clinicians. In addition, it is generally accepted by the clinical and scientific community that disruption of memory impacts function in AD patients, and thus we believe that false memories are likely to have significant functional impact as well.

It is important to better understand the cognitive and physiologic basis of false memories in MCI and AD so that interventions can be developed to reduce false and distorted memories,

and thus help patients maintain function in daily life. Given the lack of a gold standard tool for assessing false memories in daily life, it was necessary to develop a questionnaire designed to measure the occurrence of false memories in the lives of patients with MCI and AD. Use of a false memories questionnaire may also improve our understanding of the basis of false memories that, in turn, may enable us to find ways to reduce false memories.

The present study set out to answer several main questions. First, how common are false memories in patients with AD, MCI, and older adults, when compared to forgetting? Second, what were clinicians' impressions of how common false memories are in patients with AD compared to forgetting? These questions motivated our two hypotheses.

First, we hypothesized that false memories are occurring as often as forgetting in AD patients, which led us to measure the occurrence of false memories and forgetting in the daily lives of older controls (OC), MCI and AD patients according to the views of family members and clinicians. Second, since awareness of false memories may be related to clinicians' experience level, we hypothesized that clinicians who have more contact with patients with MCI and AD would likely report that false memories are occurring as often as forgetting.

Methods

Family members.

150 family members of individuals with MCI (44 participants), AD dementia (49 participants), and healthy OCs (57 participants) were recruited from the Boston University Alzheimer's Disease Center and the Veterans Affairs Boston Healthcare System, both in Boston, MA. Patients met criteria for MCI or probable AD dementia as described by the National Institutes of Aging–Alzheimer's Association (Albert et al., 2011; McKhann et al., 2011). See Table 1 for Mini Mental State Examination (MMSE; (Folstein, Folstein, & McHugh, 1975) scores and demographics. Patients were assessed and diagnosed by a neurologist and/or neuropsychologist and were excluded for clinically significant depression, alcohol and drug use, prior stroke, traumatic brain injury, unstable medical condition, or other neurological disorder.

Clinicians.

226 clinicians who self-reported seeing patients with AD dementia as part of their practice were recruited for this study using flyers and direct recruitment following conference sessions by study staff members from four sources: 1) Harvard Dementia Update Course 2015 in Boston, MA; 2) Alzheimer's Association International Conference 2015 in Washington, DC; 3) Gerontological Society of America Annual Scientific Meeting 2015 in Orlando, FL; and 4) online through Survey Monkey. Demographic information for clinicians can be found in Table 2. This study was approved by the Institutional Review Board at Boston University School of Medicine and the Veterans Affairs Boston Healthcare System.

Questionnaire Development and Validity Analysis—The false memories questionnaire is a novel, 40-item questionnaire with two versions: a family member version and a clinician version (see Appendices A and B for the complete questionnaire). Items on

the questionnaire were largely designed to investigate forgetting and false memory in daily life, such as those concepts explored in the activities of daily living questionnaire (Lawton & Brody, 1969). In addition, two questions regarding function were added for clinicians. Each forgetting question was paired with a false memory question. For example, "How often do your patients/does your loved one forget to pay a bill?" was paired with "How often do your patients/does your loved one think they've paid a bill when they haven't?" These pairs were placed adjacent to each other on the questionnaire. For each question, family members and clinicians were provided with the following response options (assigned to numeric values): Often = 3, Sometimes = 2, Rarely = 1, Never = 0, and Don't Know (not scored).

The Clinician version started with questions regarding demographics, including medical specialty, years practicing, percentage of patients seen with MCI or AD dementia (item 3 of clinician questionnaire), how many patients with AD followed (item 4 of clinician questionnaire), and the average severity of the patients with AD. The questionnaires themselves were identical between the clinician and family member versions with the exception of the word "patient" in the clinician version replaced by the word "loved one" in the family member version and the addition of two questions in the clinician version regarding the impact of forgetting and false memories on patient function.

Confirmatory factor analyses (CFAs) were used to evaluate the dimensionality of each survey questionnaire. Item response theory (IRT) models were applied to each item question for purposes of item parameter estimation and evaluating test information functions for the false memory and forgetfulness questionnaires separately. One-dimensional IRT structures were parameterized with the two-parameter logistic model, which was applied to all 20-item questions with ordinal scores. A byproduct of IRT estimation is the ability to plot test information curves (TICs), which graphically represent the quality of measurement provided by an item question across the range of latent ability that underlies test takers' performance. The higher the TIC is at a given level of the construct, the smaller the standard error of measurement. Hence, TICs are directly related to the reliability of each of the two tasks, completion of the forgetting questions and false memory questions as shown in Figure 1.

Forgetting: All question items were at least moderately related to the latent construct of forgetting and they varied from 0.61 to 0.87. Item slopes varied widely (2.0 to 6.5) as shown in Figure 1A & C. Cronbach's alpha for forgetting questions for both clinicians and family members was very high (0.97).

False memory: All question items were at least moderately related to the latent construct of false memory and they varied from 0.63 to 0.87. Item slopes varied widely (1.9 to 5.8) as shown in Figure 1B & D. As with the Forgetting questionnaire, Cronbach's alpha for false memory questions for both clinicians and family members was very high (0.97) with similar but lower information coverage. The TIC shows that high information is especially concentrated in the middle of the latent construct with good coverage across different levels.

Overview of Data Analytic Strategy

<u>Clinician Data Analysis:</u> Clinician data was analyzed by first examining group differences for question type using ANOVA. Then we performed correlation and linear regression

analyses between co-variates related to clinician expertise and experience. These co-variates had the potential to modify clinician's perceptions of false memories and forgetting and their respective functional impact. Average forgetting and false memory scores were then analyzed using an ANCOVA including both co-variates, "% of patients seen" and "patient

Rationale for inclusion of clinician expertise and experience variables as co-variates in

severity" as expertise and experience variables that correlated with outcomes of interest.

clinician analysis: Clinician expertise and experience may play a large role on a clinician's reporting of both forgetting and false memories. Thus, we performed initial correlations between clinicians' responses to questions regarding percent of patients seen with Alzheimer's disease, mild cognitive impairment, and other dementias and memory disorders (question 3, clinician questionnaire), as well as the severity of AD patients seen (question 4, clinician questionnaire) with average forgetting and false memories scores, as well as with their perception of the impact of false memories and forgetting. These initial correlations, which showed a relationship between expertise and experience variables ("patients seen" and "patient severity") and outcomes of interest (see results section), led us to perform an ANCOVA to evaluate the effects of expertise and experience on the perception of false memories and forgetting. The question posed to clinicians that allowed calculation of the patient experience variable was, "What percentage of your patients with Alzheimer's disease show the following severity for each group: Very Mild-Mild, Moderate, and Severe." Given our hypothesis that false memories and forgetting would both vary with patient severity, it is important to factor in each clinician's experience with patients of various severities into our analyses.

Family Member Data Analysis: Average forgetting and false memory scores for each clinical group were analyzed using an ANCOVA controlling for age and education. Correlations were performed between MMSE scores and both average forgetting and average false memory scores. Finally, prevalence of both false memories and forgetting was calculated using two methods of converting false memory and forgetting scores for individuals to dichotomous results indicating either the presence or absence of forgetting and false memories in an individual. Two methods were used because one was overly conservative and one overly liberal in estimations of forgetting and false memories. Prevalence was then compared between groups using a Chi-squared test.

Don't Know Data Analysis: A repeated-measures ANOVA was performed between the percentage of "Don't Know" responses for clinicians for each question type (forgetting and false memories), and an analogous group by question type ANOVA was used to analyze the percentage of "Don't Know" responses for family members.

Results

Clinician Data

Analysis of clinicians' answers to the two functional questions, "How often do your patients forget information that is important to their function?" and "How often do your patients have distorted, confused, or false memories of information that is important to their function?"

showed a significant effect of question type (forgetting vs. false memory) ($F_{(1,220)}$ =31.627; p<.001; η^2 = .126), suggesting that forgetting (M=2.71, SE=.033) was perceived as more frequently impacting patients' function compared to false memories (M=2.49, SE=.043).

The first measure, "patients seen," was obtained from the question, "What percentage of patients with Alzheimer's disease, mild cognitive impairment, and other dementias do you see?" A four-point scale (1=0%-10%, 2=10%-25%, 3=25%-50%, 4=>50%) was used. The second measure, "patient severity," was obtained by computing a severity score from the answer to the question, "What percentage of your patients with Alzheimer's disease show the following severity". Clinicians were asked to report percentages for "Very mild – mild", "Moderate", and "Severe" severities. Severity score was computed as [(% Very mild – mild*1) + (% Moderate*2) + (% Severe*3)/300(Maximum score)].

Pearson bivariate correlation analyses were conducted between mean forgetting and false memories questions scores and expertise and experience variables computed above. "Patients seen" and "Patient severity" showed positive correlations with forgetting (r = .253, p = < .001; r = .224, p = < .001; respectively) and false memories average scores (r = .155, p = < .05; r = .183, p = < .01; respectively).

"Patients seen" and "Patients severity" also explained a significant proportion of variance of forgetting $R^2 = .096$, $F_{(2, 223)} = 11.866$, p < .001 and false memories $R^2 = .048$, $F_{(2, 222)} = 5.621$, p < .005, predicting clinicians' perception of forgetting and false memories ($\beta = .218$, $t_{(223)} = 3.37$, p < .001; $\beta = .182$, $t_{(223)} = 2.81$, p < .005; respectively). "Patient severity" predicted false memories ($\beta = .159$, $t_{(218)} = 2.38$, p < .05) and "Patients seen" was nearly significant ($\beta = .123$, $t_{(222)} = 1.85$, p = .06). This analysis suggests that, similar to the analysis of the two functional questions, when taking expertise and experience into account, clinicians' perceptions of the frequency of forgetting and false memories did not differ and that expertise and experience influences clinicians' rating of the frequency of both false memories and forgetting.

When we included the expertise and experience variables ("patients seen" and "patient severity") as covariates in the global questions analysis, the main effect of question Type (forgetting vs. false memory) was not significant, $F_{(1, 218)} = 7.87$, p = .319, $\eta^2 = .005$. Both "Patients seen" and "patient severity" showed a positive correlation with clinician's perception of the impact of forgetting on function (r = .277, p < .001; r = .298, p < .001; respectively) and the impact of false memories on function (r = .210, p < .005; r = .189, p < .005; respectively). This result suggests that clinician expertise and experience modifies clinicians' perceptions of the functional impact of forgetting and false memories and that when accounting for expertise and experience, clinicians rate forgetting and false memories as impacting function at the same frequency.

The mean scores for the 20 forgetting and 20 false memory questions were then analyzed including "Patients seen" and "Patient severity" as covariates. When performing an ANCOVA including "Patients seen" alone as a co-variate, the main effect of question type forgetting (M = 2.35; SE = .026) vs. false memory (M = 2.19; SE = .031) was not significant $F_{(1, 222)} = .723$, p = .40, $\eta^2 = .003$. When performing an ANCOVA including "Patient

severity" alone as a covariate, there was a main effect of question type, forgetting vs. false memory, $F_{(1, 222)} = 6.805$, p = 0.01, $\eta^2 = .03$. Finally, while performing an ANCOVA using both co-variates, the main effect of question type forgetting vs. false memory was not significant $F_{(1, 222)} = .662$, p = .417, $\eta^2 = .003$, although it was significant using an ANOVA not controlling for "Patients seen" and "Patient severity," $F_{(1, 224)} = 53.964$, p < .001, $\eta^2 = .194$.

Family Member Data

Mean scores for the forgetting and false memory questions for each of the family member groups can be seen in Figure 2. Mean scores were analyzed using a 3 (group: OC, MCI, AD) X 2 (question type: forgetting, false memory) ANCOVA including age and education as covariates. One AD subject and one MCI subject did not have age and education recorded and were excluded from these analyses. A main effect of group was observed ($F_{(2, 143)} = 34.67$, p < .001, $\eta^2 = .326$). When comparing the estimated marginal means, family members of OCs reported less forgetting and fewer false memories combined (M = .66; SE = .087) compared to patients with AD (M = 1.69; SE = .093; p < 0.001). Patients with AD (M = 1.69; SE = .093; p < 0.001). Patients with AD (M = 1.69; SE = .093; p < 0.001). Neither a main effect of question type or group X question type interaction were observed (F < 1, p > .1).

We also analyzed Mean scores using a 3 (group: OC, MCI, AD) X 2 (question type: forgetting, false memory) ANOVA without including age and education as covariates. A main effect of group was observed ($F_{(2, 147)} = 52.04$, p < .001, $\eta^2 = .415$). When comparing the estimated marginal means, AD patients had greater forgetting and false memory scores (M =1.8, SE = .091) compared to the MCI group (M=0.87; SE=.096 p <.0001) and compared to OCs (M= 0.57, SE = 0.08; p<.0001). A main effect of question type was also observed, ($F_{(2, 147)} = 68.832$, p < .001, $\eta^2 = .319$), (Mean forgetting=1.19, SE=.056; Mean false memories =0.97, SE= .05). A group X question type interaction was not observed (F < 1, p > .1).

Finally, Pearson bivariate partial correlations between MMSE scores and each average question type score, correcting for age and education yielded correlations between MMSE score and both average forgetting (r = -.456, p < .001) and false memory (r = -.441, p < .001), see Figure 3. These results indicated that as MMSE scores decreased, both forgetting and false memories increased.

Prevalence

Prevalence of false memories and forgetting were calculated for OC, MCI, and AD subjects using two methods as described below. The first, more conservative method, used average questionnaire responses 3 (Often) and 2 (Sometimes) translated into the binary value 1, and responses 1 (Rarely) and 0 (Never) were translated into the binary value 0. Having assigned every subject to either a 1 (presence of false memories/forgetting) or 0 (absence of false memories/forgetting), the prevalence was calculated by dividing the number of subjects that experienced false memories/forgetting (binary score of 1) by the total number of subjects.

Using this initial method, there was a higher prevalence of forgetting for the AD group compared to MCI ($\chi^2 = 18.095$; p < .001) and OC ($\chi^2 = 38.484$; p < .001), and a marginally significant trend for MCI compared to OC ($\chi^2 = 3.653$; p = .056). A higher prevalence of false memories was found for AD compared to MCI ($\chi^2 = 22.874$; p < .001) and OC ($\chi^2 = 27.264$; p < .001); no difference was found between MCI and OC ($\chi^2 = .002$; p = .966). No differences were found between forgetting and false memories prevalence within groups for AD ($\chi^2 = 2.724$; p = .101) or OC ($\chi^2 = .435$; p = .510), but the MCI group showed more forgetting than false memories ($\chi^2 = 5.388$; p < .020) (Table 1).

Given that the rate of forgetting in the AD group was 69% and thus lower than would be expected clinically, it is likely that this conservative method may underestimate the true rates of false memory and forgetting as rare answers were counted as representing the absence of false memories and forgetting.

Thus, we performed a secondary analysis of prevalence using more liberal criteria for the presence of forgetting and false memories where we calculated the binary value of presence versus absence of false memories and forgetting using the answers 3 (often), 2 (sometimes), and 1 (rarely) as criteria for presence of false memories and forgetting, and only the answer choice 0 (never) as consistent with absence of false memories or forgetting. Using these methods, we re-calculated the prevalence of forgetting and false memories between the three groups (see Table 1).

Using the second, more liberal method, there was a higher prevalence of forgetting for the AD group compared to MCI ($\chi^2 = 5.74$; p < .05) and OC ($\chi^2 = 30.57$; p < .001), and MCI compared to OC ($\chi^2 = 11.93$; p < .001). A higher prevalence of false memories was found for AD compared to MCI ($\chi^2 = 8.98$; p < .005) and OC ($\chi^2 = 34.52$; p < .001); MCI and OC ($\chi^2 = 9.08$; p < .005). No differences were found between forgetting and false memories prevalence within groups using this method AD ($\chi^2 = 1.37$; p = .24), MCI ($\chi^2 = 2.71$; p = 0.10), and OC ($\chi^2 = 1.78$; p = 0.18) (Table 1). See Table 1 for prevalence using both methods for each group.

Don't Know Response Analysis

Finally, in order to investigate whether false memories may be under-recognized by family members and clinicians, we analyzed the mean percentage of "Don't Know" responses for each group (all family member groups and clinicians) by question type. "Don't Know" is different from missed items because it is a specific choice that participants could choose (see Appendix B, family member questionnaire). This "Don't Know" response analysis did not include any questions left unanswered so as not to confound these responses with inadvertently skipped answers.

Clinicians

A repeated-measures ANOVA was performed between the percentage of Don't Know responses for forgetting and false memory questions, which revealed a main effect of question type ($F_{(1, 225)}=37.402$, p<.001, $\eta^2 = .142$), such that the mean percentage of Don't Know responses for false memories questions (M=11.2%, SE= 0.011) was significantly

higher than the mean percentage of Don't Know responses for forgetting questions (M=7.2%, SE=0.008). (See Figure 4A).

Family members

A 3 (group: OC, MCI, AD) X 2 (question type: forgetting, false memories) repeatedmeasures ANOVA was used to analyze the mean percentage of Don't Know responses for family members. A main effect of question type was observed ($F_{(1, 147)}$ =42.606, *p*<.001, η^2 = .225), such that the mean percentage of Don't Know responses for false memory questions (M=7.5%, SE= 0.011) was significantly higher than the mean percentage of Don't Know responses for forgetting questions (M=4.2%, SE=0.008).

A group X question type interaction was observed ($F_{(2, 147)}=4.169$, p<.05, $\eta^2 = .054$). The mean percentage of Don't Know responses for family members of AD patients for the false memories questions (M=9.4%, SE=0.017) was significantly higher than the mean percentage of Don't Know responses for the forgetting questions (M=4.3%, SE=0.013; p<0.001), as they were for the MCI patients: false memory questions (M=8.1%, SE=0.018), forgetting questions (M=5.0%, SE=0.014; p<0.05). No significant difference was observed for the Don't Know responses in the OC group between false memories (M=5.0%, SE=0.016) and forgetting responses (M=3.3%, SE=0.012; p=0.310). No main effect of group type was observed for the Don't Know responses ($F_{(2, 147)}=1.088$, p=.339, $\eta^2 = .015$). (See Figure 4B).

Discussion

This is the first study to our knowledge that measured clinician and family member perceptions of false memories and their frequency in the daily life of memory patients. To test our hypotheses that false memories were occurring as often as forgetting, we developed a questionnaire given the lack of gold standard or other validated instrument for the measurement of false memories in daily life. Contrary to our hypothesis, we found that patients with AD, MCI, and OCs all experience false memories less frequently than they do forgetting, as reported by both family members and clinicians. However, when correcting for the number of dementia patients seen and their severity, there was no difference in the average forgetting and average false memory score reported by the clinicians. Furthermore, our analysis of "Don't Know" responses suggests that false memories may be underreported by both clinicians and family members. Lastly, even taking our primary results at face value, prevalence calculations using family member data found that false memories in the AD and MCI groups were quite high—almost as high as forgetting. False memories were also present to some degree in OCs, consistent with prior findings (Daniel L. Schacter et al., 1999). To our knowledge, this is the first report of the estimated prevalence of false memories in the daily life of older adults as well as in patients with MCI and AD.

Using both the clinician and family member data, we found that the degree of false memories among MCI and AD patients correlated strongly with the severity of their cognitive impairments. Specifically, MMSE scores correlated with family member average forgetting and false memory scores and, among clinicians, measures of clinical severity correlated with average forgetting and false memory scores. Given that MMSE scores have

been shown to correlate with function in daily life (Tekin, Fairbanks, O'Connor, Rosenberg, & Cummings, 2001), our finding that false memories correlate with MMSE has potential bearing on the impact of false memories in daily life. Our results also indicated that clinicians who see more AD patients and/or a higher percentage of more impaired patients report a greater impact of forgetting and false memories on the daily lives of their patients. In fact, when accounting for clinicians' expertise and experience with AD patients, clinicians tend to think forgetting and false memories impact patients' lives at equivalent rates. Taken together, the clinician results also showed that clinicians' expertise and experience plays a crucial role in their perception of false memories. Future studies could directly compare false memories questionnaire results to detailed measures of activities of daily living, in order to further investigate the impact of false memories in the daily lives of patients with AD and MCI.

Correcting for age and education between OC and AD groups can lead to inherent bias in some circumstances (Miller & Chapman, 2001) therefore we performed an ANOVA comparing average forgetting and false memory scores between patient groups not controlling for age and education. ANOVA results of average forgetting and false memories scores between patient groups and question type, not controlling for age and education, there is a main effect of question type and forgetting scores are greater than false memory scores. Of note, both forgetting and false memories have been reported to be highly associated with healthy aging as well as Alzheimer's disease (Balota, Watson, Duchek, & Ferraro, 1999; Norman & Schacter, 1997; Tun, Wingfield, Rosen, & Blanchard, 1998). Demographics for the three cohorts (Table 1) show that the AD group was older and less educated than the OC group and furthermore, that the MCI group was also less educated than the OC group, but more educated than the AD group. These findings are in keeping with previous literature that older and less educated individuals are at greater risk of AD (Alzheimer's Association Facts and Figures, 2019). Furthermore, age is independently associated with increases in false memories (Norman & Schacter, 1997). Using an analysis which does not account for age and its potential impact on forgetting and false memories introduces potential confounding as it is difficult to determine if our dependent variable of interest, incidences of forgetting and false memories, are in fact elevated in older cohorts due to normal aging or due to the increased incidence of MCI and AD that also occurs with aging and may independently affect rates of both forgetting and false memories. Since our cohorts differed in age and education, we felt it most appropriate to use an ANCOVA accounting for age and educational differences between cohorts when analyzing group differences in forgetting and false memory scores.

Therefore, although we report an additional analysis using ANOVA without the effect of age and education included, we believe that it is most appropriate to interpret and discuss data related to our initial ANCOVA analysis using age and education and co-variates. Therefore, the average forgetting and false memory scores may be interpreted as follows: forgetting and false memory scores are either equal (ANCOVA) or forgetting scores are somewhat larger than false memory scores (ANOVA) (1.19 vs. 0.97). In either case, although the difference in the ANOVA is significant, the numerical values are similar, suggesting that false memories are being perceived as occurring nearly as frequently as forgetting. Thus, researchers, pharmaceutical companies designing clinical trials, and clinicians should consider the

existence of false memories as an additional clinical symptom that occurs frequently in patients with Alzheimer's disease.

There are no currently used guidelines, gold standards, or generally accepted questionnaires to help clinicians detect false memories. This lack of tools to measure false memories in current clinical practice may lead less experienced clinicians to underestimate or ignore false memories during assessment. We hope the questionnaire developed here provides a starting point to measure false memories in AD and MCI. Our validity analyses indicate that both the false memory and forgetting parts of our questionnaire were related to the latent construct of each question type, given that the information response curve for each question type was high, with good coverage across the range of abilities within the patient population, as shown in Figure 1.

It should be noted that this is a questionnaire-based study and thus subject to reporting limitations of a second-party observer. It is therefore possible that the true frequency and prevalence of false memories among patients with MCI and AD is being under recognized as there is currently no gold standard method of assessing the true frequency of false memories in daily life. Future ecological studies aimed at investigating the true incidence of false memories in daily life will be useful in conjunction with our newly developed questionnaire.

We used two methods to calculate the prevalence of false memories and forgetting in our population. Using the more liberal calculation method for prevalence, as expected, we found high rates of both forgetting and false memories, with the AD group approaching 96% forgetting and almost as much (90%) false memory. The OC group, showed forgetting at nearly 46%, and false memories occurring in approximately one-third. These high rates are likely attributable to the fact that even healthy older adults experience many instances of forgetting and false memories. Using the conservative calculation method resulted in comparatively lower prevalence of both forgetting and false memories across groups compared to the liberal method. While conservative method for the OC group showed lower baseline rates of forgetting (10.53%) and false memories (7.02%), the AD group approached only 69.39% forgetting, which is below the rate of forgetting one would expect based on clinical observation of AD patients. Thus, each method for calculating prevalence may be over- or under-estimating the true prevalence, and the conservative method is potentially advantageous in that likely reflects more of the pathologic instances of forgetting and false memories and less of the baseline rate of each behavior that can occur with normal aging and the liberal method is potentially useful as well as it tends to reflect the clinically seen rates of forgetting in the AD group, and thus may be a more accurate representation of false memory prevalence in the AD group.

The Don't Know analysis revealed that both clinicians and family members of AD and MCI patients made more Don't Know responses for false memory questions compared to forgetting questions. Clinicians and family members are thus less certain about how often their patients and loved ones are having false memories compared to how certain they are about how often they are forgetting, given that Don't Know responses were higher for false

memory questions than for forgetting questions for both groups. This result suggests that false memories are likely under-recognized and under-reported.

In regards to the relative impact of forgetting versus false memories on function when accounting for our expertise and experience measures ('patients seen' and 'patient severity' in clinician data, respectively), perceived functional impact of false memories and forgetting was indistinguishable. False memories may have an equal or greater functional impact compared to forgetting in AD and MCI, but as shown in the "Don't Know" analysis, due to under-reporting our results could be underestimating the impact of false memories on daily life. Even if false memories have less impact on function than forgetting, we would argue strongly that does not mean they should be ignored. With 5.8 million Americans with Alzheimer's disease being attended to by more than 16 million caregivers over 18.5 billion hours (association, 2019) even a small increase in our understanding of these patients' impairments could make a large impact on people's lives. Thus, the development of questionnaires to measure False memories in daily life is important.

The false memories questionnaire developed, similar to other instruments commonly used in the AD population, is a caregiver-reported instrument. Although caregiver-reported instruments may have drawbacks, such as variability related to how well the caregiver knows the patients, we believe that it is better than a self-reported questionnaire for the following reasons. Previous studies have shown an absence of relationship between subjective memory complaints and objective impairment in patients with AD, likely due to poor insight (Jungwirth et al., 2004). These findings are also supported by the results of other studies of patients with dementia that show a higher correlation between clinical outcomes and caregiver-reported quality of life (QOL) compared to self-reported QOL (Jungwirth et al., 2004; Lenehan, Klekociuk, & Summers, 2012). It is likely that self-report measures of false memories would suffer from the same biases due to lack of insight when used for self-report. However, it is possible that those with MCI, given their earlier stage of disease, may have retained awareness and may be able to self-report about episodes of false memories. This is an area of possible exploration for future studies.

This study measured clinicians' impression of patient function but not family members' impressions of function. We plan to examine family members' impression of patient function in future studies.

This study did not explicitly address different types of false memories: events that occurred in altered form versus events that never occurred. However, the questionnaire covers topics related to misremembering and memory distortions in questions 8, 12, and 14 (see Appendix for complete questionnaire) while other questions are related to memory for events that did not happen.

Furthermore, as this study was questionnaire-based, it did not address whether patients truly had false memories; future studies could perhaps use continuously recording cameras to track an individual's actual actions and measure their reported true memories, false memories, and forgetting against this objective standard. In addition, we did not measure

family member exposure to or time with patients—a relevant variable we plan to collect in future work as it could influence family members' perceptions of false memories.

In summary, knowledge of false memories in AD and MCI groups may be clinically important. Others have previously noted that memory distortions among AD patients result in behavioral disturbances that may impair ability to live independently (Borson & Raskind, 1997). It has also been suggested that the degree of measured false memories is a more specific indicator of AD pathology than memory performance alone (Hildebrandt et al., 2009a). We have shown that although false memories are less prevalent than forgetting in AD and MCI patients, they are nearly as common as forgetting. The false memories questionnaire created as part of this study may be helpful as a clinical and research tool to measure false memories in daily life.

Acknowledgements:

This work was supported by the National Institutes of Health (grant number P30-AG013846, A.B.) and also from the United States Department of Veterans Affairs, Merit Review Award (grant number, CX000736, A.B.)

Appendix A.: False Memories Questionnaire for Clinicians

Understanding Clinician Impressions of Memory Impairments: A Survey Study

Thank you in advance for your interest in filling out this survey. The purpose of this survey is to obtain your impression of different types of memory deficits that patients with Alzheimer's disease and other dementias experience in day-to-day life. Questions in this survey will ask you about different memory problems your patients or their caregivers may report having and frequency of their occurrence. You will be asked to answer each question as best as possible. This survey is voluntary and should only take about 10 minutes of your time. All responses will be anonymous. Thank you for your participation in this survey. If you have any questions, you may contact our laboratory at 857-364-4554 or e-mail us at ctcnbrainlab@gmail.com.

- 1. What best describes your medical specialty or profession? (check the box that is the most appropriate, or fill in the blank below)
 - Geriatrician
 - Internal Medicine / Primary Care Neurologist
 - Neuropsychologist
 - Nurse
 - Nurse Practitioner
 - Physician Assistant
 - Psychiatrist
 - Psychologist

- Social Worker
- Other (please list): ______
- 2. How many years have you been in practice? _____years
- **3.** What percentage of patients with Alzheimer's disease, mild cognitive impairment, and other dementias and memory disorders do you see?
 - >50%
 - 25-50%
 - 10-25%
 - 0-10%
- 4. How many patients with Alzheimer's disease do you currently follow?
- 5. What percentage of your patients with Alzheimer's disease show the following severity (please fill in the blanks with the appropriate percentage)?
 - Very Mild Mild _____
 - Moderate _____
 - Severe _____

Instructions for attached questionnaire

For the following questionnaire, you will be asked to provide an impression of memory problems your patients may experience for everyday activities. You are asked to provide your impressions for all the patients you have seen, not one specific patient. For each question, please check off the appropriate box *if you have observed that specific memory problem with a patient yourself, if your patients have reported any of the following memory problems, or their families or caregivers have reported any of these memory problems.* Please try to answer every question. If you do not know the answer to the question, please check of the box "Do not know."

How often do your patients forget information that is important for their function?

- Often
- Sometimes
- Rarely
- Never
- Do not know

How often do your patients have distorted, confused, or false memories for information that is important for their function?

- Often
- Sometimes

- Rarely
- Never
- Do not know

1(Adow often do your patients forget to pay a bill? • Often • Sometimes • Rarely • Never • Do not know	 1(B)ow often do your patients think they've paid a bill when they haven't? Often Sometimes Rarely Never Do not know
2(Abow often do your patients misplace things? Often Sometimes Rarely Never Do not know 	2(B)ow often do your patients think they know where something is but are mistaken? • Often • Sometimes • Rarely • Never • Do not know
 3(Abow often do your patients forget important numbers they should know well (e.g. their phone number, social security number, or address)? Often Sometimes Rarely Never Do not know 	 3(B) ow often do your patients misremember a number they should know well (e.g. remember the wrong phone number, social security number, or address)? Often Sometimes Rarely Never Do not know
 4(Al)ow often do your patients forget the name of someone they know well? Often Sometimes Rarely Never Do not know 	 4(B)ow often do your patients recall an incorrect name when trying to remember the name of someone they know well? Often Sometimes Rarely Never Do not know
 5(Abow often do your patients forget to bring something with them that they need? Often Sometimes Rarely Never Do not know 	 5(B) ow often do your patients think they've brought something with them that they need when they actually haven't? Often Sometimes Rarely Never Do not know

6(Ab) woften do your patients forget that a friend or relative has recently visited them?	6(B) ow often do your patients think a friend or relative has recently visited when they haven't?
• Often	• Often
• Sometimes	Sometimes
• Rarely	• Rarely
• Never	• Never
• Do not know	Do not know
7(Abow often do your patients forget to change their clothes?	7(B) ow often do your patients think they have changed their clothes when they haven't?
• Often	• Often
• Sometimes	Sometimes
Rarely	Rarely
• Never	• Never
Do not know	Do not know
8(Ab) woften do your patients forget information about their families? For example, how many children, grandchildren, or siblings they have or what their names are?	8(B)ow often do your patients misremember information about their families? For example, incorrectly remember how many children, grandchildren, or siblings they have or what their names are?
• Often	Often
• Sometimes	Sometimes
• Rarely	
• Never	Rarely
Do not know	• Never
	Do not know
9(Al) ow often do your patients forget to eat a meal?	9(B) ow often do your patients think they have eaten a meal when they haven't?
• Often	• Often
• Sometimes	Sometimes
Rarely	Rarely
• Never	• Never
• Do not know	Do not know
10(A) often do your patients forget to complete	How often do your nationts think they have
an errand?	How often do your patients think they have completed an errand when they haven't?
Often	
	completed an errand when they haven't?
• Often	completed an errand when they haven't?Often
OftenSometimes	completed an errand when they haven't? Often Sometimes
OftenSometimesRarely	completed an errand when they haven't? Often Sometimes Rarely
 Often Sometimes Rarely Never 	completed an errand when they haven't? Often Sometimes Rarely Never
Often Sometimes Rarely Never Do not know	completed an errand when they haven't?
Often Sometimes Rarely Never Do not know Illebow often do your patients forget to take their medication?	 completed an errand when they haven't? Often Sometimes Rarely Never Do not know 11(B)w often do your patients think they have taken their medication when they haven't?
 Often Sometimes Rarely Never Do not know 11140w often to your patients forget to take their medication? Often 	completed an errand when they haven't?

Do not know	Do not know
12(A)w often do your patients forget a birthday or an anniversary that they used to know?Often	12(B) w often do your patients misremember an important date they used to know? For example, they incorrectly remember a birthday or anniversary to be on a different date than it actually is?
• Sometimes	• Often
• Rarely	• Sometimes
• Never	• Rarely
Do not know	• Never
	Do not know
13(A) w often do your patients forget to buy something they need?	13(B) w often do your patients buy the wrong item or avoid buying something because they think they've already bought it?
• Often	• Often
Sometimes	Sometimes
Rarely	Rarely
• Never	• Never
Do not know	Do not know
14(Ab) often do your patients forget to pass on a message?	14(B) w often do your patients incorrectly remember part or all of a message when passing it on?
• Often	• Often
• Sometimes	Sometimes
• Rarely	• Rarely
• Never	• Never
Do not know	Do not know
15(Ax) often do your patients forget all or part of a recent conversation?	15(B) w often do your patients incorrectly remember part or all of a recent conversation?
• Often	• Often
• Sometimes	• Sometimes
Rarely	• Rarely
• Never	• Never
Do not know	Do not know
16 (A)), often do your patients forget what they ate at a recent meal?	16(B) w often do your patients think that they ate something at a recent meal that they did not eat?
• Often	• Often
Sometimes	Sometimes
Rarely	Rarely
• Never	• Never
Do not know	Do not know
17(A) w often do your patients forget what activities they did in recent days? For example, did not remember they went to the grocery store or post office?	17(B) w often do your patients think they did activities in recent days that they did not do? For example, thought they went to the grocery store or post office when they did not?
• Often	• Often

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Sometimes	Sometimes
• Rarely	• Rarely
• Never	• Never
• Do not know	Do not know
18(A)w often do your patients forget what they did to celebrate important events in the past year? For example, forget what they did for birthdays, Thanksgiving, an anniversary, etc?	18(B) w often do your patients incorrectly remember what they did to celebrate important events in the past year? For example, misremember what they did for birthdays, Thanksgiving, etc?
• Often	• Often
• Sometimes	Sometimes
• Rarely	Rarely
• Never	• Never
• Do not know	• Do not know
 19(%)w often do your patients forget to shower? Often Sometimes Rarely Never Do not know 	 19(B)w often do your patients think they have showered when they haven't? Often Sometimes Rarely Never Do not know
20(Ac) w often do your patients forget routes while driving or walking that they used to know well?	20(B) w often do your patients think they remember a route they used to know well, but their memory of the route is incorrect?
• Often	• Often
• Sometimes	Sometimes
• Rarely	Rarely
• Never	• Never
Do not know	Do not know

Appendix B.: False Memories Questionnaire for Family Members

1(Allow often does your loved one forget to pay a bill?	1(B) w often does your loved one think they've paid a bill when they haven't?
• Often	• Often
Sometimes	• Sometimes
• Rarely	• Rarely
• Never	• Never
Do not know	Do not know
2(A) w often does your loved one misplace things?	2(B) ow often does your loved one think they know where something is but are mistaken?
• Often	• Often
• Sometimes	• Sometimes
Rarely	Rarely

• Never	• Never
Do not know	Do not know
3(Abow often does your loved one forget important numbers they should know well (e.g. their phone number, social security number, or address)?	3(B) ow often does your loved one misremember a number they should know well (e.g. remember the wrong phone number, social security number, or address)?
• Often	• Often
• Sometimes	Sometimes
• Rarely	• Rarely
• Never	• Never
Do not know	Do not know
4(Ab) w often does your loved one forget the name of someone they know well?	4(B) ow often does your loved one recall an incorrect name when trying to remember the name of someone they know well?
• Often	Often
• Sometimes	Sometimes
• Rarely	Sometimes Rarely
• Never	Never
Do not know	Do not know
5(Abow often does your loved one forget to bring something with them that they need?	5(B) ow often does your loved one think they've brought something with them that they need when they actually haven't?
• Often	Often
• Sometimes	Sometimes
• Rarely	Rarely
• Never	Never
Do not know	Do not know
6(Alpow often does your loved one forget that a friend or relative has recently visited them?	6(B) w often does your loved one think a friend or relative has recently visited when they haven't?
• Often	• Often
Sometimes	Sometimes
Rarely	Rarely
• Never	• Never
• Do not know	Do not know
7(Ab) w often does your loved one forget to change their clothes?	7(B) ow often does your loved one think they have changed their clothes when they haven't?
• Often	• Often
Sometimes	• Sometimes
• Rarely	• Rarely
• Never	• Never
Do not know	Do not know
8(Ab) woften does your loved one forget information about their families? For example, how many children, grandchildren, or siblings they have or what their names are?	8(B) ow often does your loved one misremember information about their families? For example, incorrectly remember how many children,

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ot	

• Often	grandchildren, or siblings they have or what their
Sometimes	names are?
	• Often
• Rarely	• Sometimes
• Never	Rarely
Do not know	• Never
	Do not know
9(Allow often does your loved one forget to eat a meal?	9(B) w often does your loved one think they have eaten a meal when they haven't?
• Often	• Often
• Sometimes	• Sometimes
• Rarely	• Rarely
• Never	• Never
• Do not know	Do not know
10(A) often does your loved one forget to complete an errand?	10(B) w often does your loved one think they have completed an errand when they haven't?
• Often	• Often
• Sometimes	Sometimes
• Rarely	• Rarely
• Never	• Never
Do not know	Do not know
11(Ao) w often does your loved one forget to take their medication?	11(B) w often does your loved one think they have taken their medication when they haven't?
• Often	• Often
• Sometimes	Sometimes
• Rarely	Rarely
• Never	• Never
• Do not know	Do not know
12(Ho) w often does your loved one forget a birthday or an anniversary that they used to know?	12(B)w often does your loved one misremember an important date they used to know? For example, they incorrectly remember a birthday or
• Often	anniversary to be on a different date than it actually is?
Sometimes	• Often
Rarely	Sometimes
Never	
Do not know	Rarely Never
	Do not know
13(A) often does your loved one forget to buy something they need?	13(B) w often does your loved one buy the wrong item or avoid buying something because they think they've already bought it?
• Often	
• Sometimes	• Often
• Rarely	Sometimes
• Never	Rarely
	• Never

Do not know	• Do not know
14(Ao) often does your loved one forget to pass on a message?	14(B) w often does your loved one incorrectly remember part or all of a message when passing it
• Often	on?
• Sometimes	• Often
• Rarely	• Sometimes
• Never	• Rarely
Do not know	• Never
	Do not know
15(A) , w often does your loved one forget all or part of a recent conversation?	15(B) often does your loved one incorrectly remember part or all of a recent conversation?
• Often	• Often
• Sometimes	Sometimes
• Rarely	• Rarely
• Never	• Never
Do not know	Do not know
16(A) often does your loved one forget what they ate at a recent meal?	16(B) w often does your loved one think that they ate something at a recent meal that they did not eat?
• Often	• Often
Sometimes	Sometimes
• Rarely	• Rarely
• Never	• Never
Do not know	Do not know
17(10) often does your loved one forget what activities they did in recent days? For example, did not remember they went to the grocery store or post office?	17(B) w often does your loved one think they did activities in recent days that they did not do? For example, thought they went to the grocery store or post office when they did not?
• Often	• Often
• Sometimes	Sometimes
• Rarely	Rarely
• Never	• Never
Do not know	Do not know
18(A) w often does your loved one forget what they did to celebrate important events in the past year? For example, forget what they did for birthdays, Thanksgiving, an anniversary, etc?	18(B) w often does your loved one incorrectly remember what they did to celebrate important events in the past year? For example, misremember what they did for birthdays, Thanksgiving, etc?
• Often	• Often
Sometimes	• Sometimes
	• Rarely
Rarely	• Never
Never	Do not know
Do not know	
19(A) often does your loved one forget to shower?	19(B) w often does your loved one think they have showered when they haven't?
• Often	• Often

 Sometimes Rarely Never Do not know 	 Sometimes Rarely Never Do not know
 20(Ho)w often does your loved one forget routes while driving or walking that they used to know well? Often Sometimes Rarely Never Do not know 	 20(B)w often does your loved one think they remember a route they used to know well, but their memory of the route is incorrect? Often Sometimes Rarely Never Do not know

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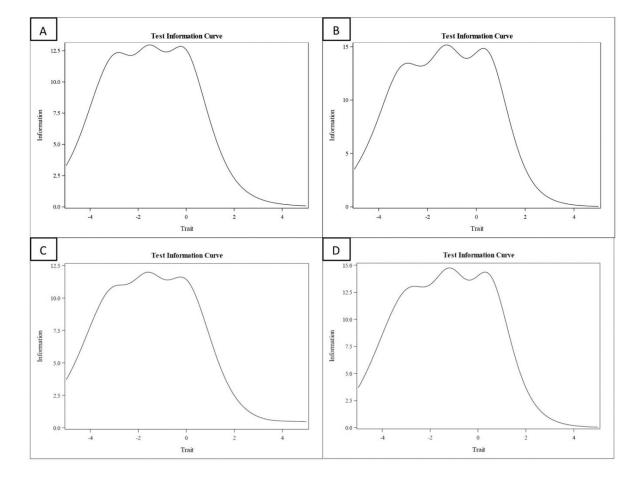


Figure 1.

A. Test information curve for clinician forgetting questions B. Test information curve for clinician false memory questions. C. Test information curve for family member forgetting questions. D. Test information curve for family member false memory questions.

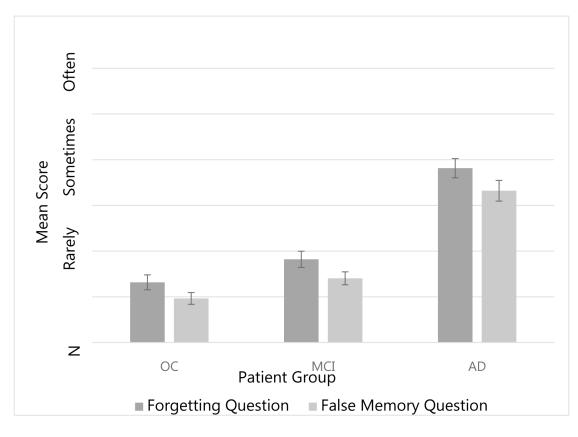


Figure 2.

Mean Memory Question scores by patient group for family member data

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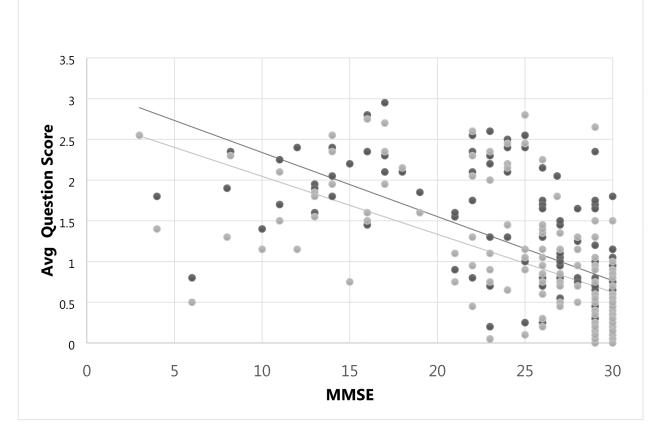


Figure 3.

Scatterplot of correlation between MMSE and average forgetting score (dark grey) and average false memory score (light grey) for family member data. 0=Never, 1=Rarely, 2=Sometimes, 3=Often

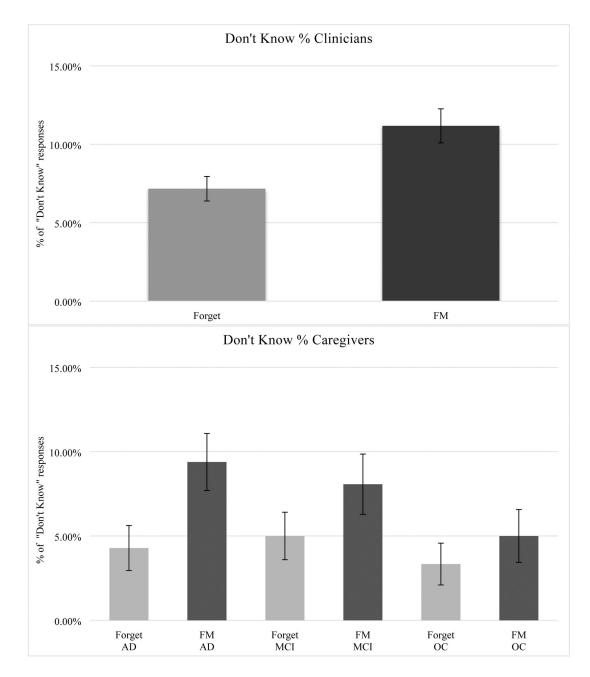


Figure 4.

Mean difference between don't know responses for forgetting and false memories questions (A) given by clinicians and (B) in the AD, OC and MCI caregiver groups.

Family member data: Demographic and prevalence information from associated patients

J Int Neuropsychol Soc. Author manuscript; available in PMC 2020 July 01.

 $_{p<.01}^{*}$

 $\dot{\tau}_{p < .001}$

 $^{**(c)}$ conservative and

 $\boldsymbol{\mathcal{O}}$ liberal estimates of forgetting prevalence, see methods for more details.

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Demographic information for clinicians

Profession	Years in Practice (SD)	Number of Clinicians that see >50% AD, MCI and other	Number of Clinicians that see 25-50% AD, MCI and other	Number of Clinicians that see 10-25% AD, MCI and other	Number of Clinicians that see 0- 10% AD, MCI and other	Mean Number of AD Patients Followed	Mean % of patients followed with very mild to mild AD	Mean % of patients followed with moderate AD	Mean % of patients followed with severe AD
Neurologist(N=43)	17.81 (11.26)	dementias	dementias	dementias	dementias 4	(SD) 216.62 (265.86)	39.53%	40.35%	18.81%
Geriatrician(N=41)	20.85 (10.73)	24	10	9	1	94.14 (103.73)	33.23%	42.33%	24.76%
Nurse(N= 34)	20.92 (11.01)	23	9	ю	2	242.29 (625.47)	29.76%	40.88%	27.37%
Psychiatrist(N= 25)	21.52 (12.17)	7	8	ю	7	68.77 (115.24)	32.95%	42.50%	21.31%
Neuropsychologist(N=23)	13.59 (10.88)	17	4	2	0	87.27 (101.76)	50.70%	38.75%	11.44%
Social Worker(N=21)	16.60 (12.29)	17	2	2	0	61.45 (95.12)	35.27%	40.83%	21.76%
Psychologist(N=17)	16.33 (11.63)	6	S	2	1	52.33 (53.13)	48.81%	31.25%	21.00%
*Other(N=12)	15.08 (13.80)	6	1	1	1	35.60 (45.90)	33.41%	39.66%	27.72%
Internal Medicine(N=10)	22.88 (12.27)	1	3	5	1	46.88 (36.14)	36.66%	43.88%	19.44%
Total / Mean(N= 226)	18.70 (11.62)	129	49	31	17	124.78 (275.89)	21.15%	16.19%	15.35%