

Running head: MEMORY FOR PUBLIC EVENTS IN aMCI AND AD

Memory for public events in Mild cognitive impairment and Alzheimer's disease: The  
importance of rehearsal

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Abstract

Ribot's law refers to the better preservation of remote memories compared with recent ones that presumably characterizes retrograde amnesia. Even if Ribot-type temporal gradient has been extensively studied in retrograde amnesia, particularly in Alzheimer's disease (AD), this pattern has not been consistently found. One explanation for these results may be that rehearsal frequency rather than remoteness accounts for the better preservation of these memories. Thus, the aim of present study was to address this question by studying retrograde semantic memory in subjects with amnesic Mild Cognitive Impairment (aMCI) (n = 20), mild AD (n = 20) and in healthy older controls (HC; n = 19). In order to evaluate the impact of repetition as well as the impact of remoteness, we used a test assessing memory for enduring and transient public events that occurred in the recent and remote past. Results show no clear temporal gradient across time periods (1960-1975; 1976-1990; 1991-2005; 2006-2011), but a better performance was observed in all three groups for enduring compared with transient events. Moreover, although deficits were globally found in both patients groups compared with HC, more specific analyses revealed that aMCI patients were only impaired on transient events while AD patients were impaired on both transient and enduring events. Exploratory analyses also revealed a tendency suggesting preservation of remote transient events in aMCI. These findings are discussed with regards to memory consolidation models.

Keywords

Alzheimer's disease, mild cognitive impairment, retrograde memory, semantic memory, famous public events, transient, enduring.

## Introduction

Retrograde memory refers to memories from the past, as opposed to anterograde memory which is the ability to learn new information. A unique and interesting way to assess retrograde memory is to use semantic memory tests that assess knowledge of public events. Indeed, memories of public events are unique in that they concern specific information and details associated with an event (semantic memory), in addition to being associated with a specific spatiotemporal context (the time and place the event occurred).

The two classical models on consolidation of long term memory, the Standard model [1, 2] and the Multiple trace theory [3-5], both assume that semantic retrograde memories are mediated by the medial temporal lobe (MTL) only for a limited period of time, after which they become increasingly reliant on neocortical structures; eventually, they can be retrieved without recruitment of the MTL. More specifically, the standard model of consolidation suggests that the MTL initially connects different neocortical sites in order to activate memory representations. As part of the normal brain activity, repeated co-activation gradually produces over time a long-lasting strengthening of the connectivity between neocortical regions. Eventually, memories thus become progressively independent from the MTL and rely exclusively on cortico-cortical connections [1, 2]. Similarly, the Multiple traces theory [3, 4] proposes that each new retrieval promotes re-encoding and produces the formation of multiple MTL-neocortical memory traces, with semantic information being mediated by the neocortex and unique autobiographical episodes being represented by the hippocampal complex [3]. Over time, remote memories are more often retrieved, become supported by more or stronger traces, thus acquiring more resistance to damage than recent memories. Thus, in the case of

MTL damage, both models predict that remotely acquired semantic memories will be better preserved than more recent ones. Accordingly, in Alzheimer's disease (AD) and in amnesic Mild Cognitive Impairment (aMCI), which is considered by many to be the prodromal stage of AD in which pathology is essentially limited to the MTL [6-8], semantic memory impairment should be more pronounced for recently acquired than for remotely acquired information .

Deficits in semantic memory have been extensively documented in AD using tests of famous people [9-13] and public events [13-23]. Studies have also demonstrated semantic impairment in aMCI using tests requiring the identification of famous people and famous buildings [11, 12, 24-29], as well as public events [15, 24, 27, 30-32]. However, the temporal gradient of these retrograde memory deficits has been much less investigated (i.e. does time passing promote better preservation of remote memories?), especially in aMCI, and the studies that have investigated the temporal gradient have produced mixed results.

The Remote Memory Battery [33] is a test combining naming of famous faces and a public events questionnaire that was developed to investigate the temporal gradient. Using this test, a Ribot-type temporal gradient (TG) was found in AD, with better memory for remote compared with recent periods [21, 22, 34]. Similarly, the same Ribot TG was obtained in AD using tests of famous people [10] or public events only; however, this temporal gradient was very slight [16, 17, 35], or probably due to items selection since it was found in both AD and control groups [36]. To our knowledge, only two studies found a Ribot TG for memory about public events in aMCI patients specifically, and results were subtle. Indeed, in one study, this pattern was found only in half of the

patients [37]. In the other study, extensive retrograde amnesia covering four decades before the diagnosis was reported, whereas memories were better preserved for the most remote periods, i.e. 60 to 40 years before the diagnosis [31]. In contrast, other studies found a TG in AD patients limited to recent periods using tests of famous people [13] or tasks combining famous people and public events [38], pointing to the anterograde amnesia as a plausible explanation for the results. Moreover, completely opposite patterns have also been found in AD when combining famous people and famous public events, whereby better performance was observed for recent rather than for remote periods [14]. Finally, no particular TG was found in a few other studies assessing memory for public events in AD and aMCI [15, 18, 23, 39]. Overall, although retrograde memory has been widely investigated in the past fifty years, studies have yielded mixed findings concerning the temporal extent of the retrograde amnesia in AD and aMCI.

Recent studies offer an alternative explanation that may be helpful in conceptualizing differently consolidation, as well as the processes underlying retrograde amnesia in AD. That is, rather than being consolidated over time, memories may be strengthened through rehearsal [15, 20]. Indeed, beneficial effects of repetition on consolidation processes have been found in some studies assessing memory for public events in healthy subjects. For example, Koppel and colleagues showed a positive relationship between the accuracy of memories concerning the emergency landing of US Airways Flight 1549 off the coast of Manhattan in 2009 and the frequency with which participants reported having thought or spoken, as well as watched, read and listened to the media coverage about this event [40]. In another study, prior retrieval caused by repeated testing seemed to promote better recall for September 11<sup>th</sup> 2001 events [41].

In aMCI, Seidenberg and coworkers [28] found a better recall of semantic information concerning famous persons who became popular in the 1950's and were still well-known (enduring famous names) compared with those who rapidly went out of the public eye (transient famous names). In addition, no Ribot TG was found between recent and remote periods in regards to these famous names. Also, in a recent study, Müller and colleagues [20] specifically studied the effect of retrieval frequency on memory for public events in AD and aMCI patients. They found more detailed recall for contextual memories about events as well as more accurate dating of events and more vivid memories when retrieval frequency was judged as being high as opposed to medium or low. This favorable effect of retrieval frequency was observed across all time periods, yet a Ribot TG was also found in the recall of contextual memories. However, in these studies, aMCI and AD patients were pooled together, without examining performance of subgroups separately; therefore potential differences between patient groups are not known.

Thus, the general aim of this study was to compare the performance of aMCI patients with that of AD patients and healthy older controls (HC) on a test of memory for famous public events. More specifically, the aims of the present study were: i) to investigate semantic retrograde memory using a test of public events in order to clarify the pattern of performance across different time periods (temporal gradient); ii) to investigate the impact of repetition of the events. We hypothesized that none of the three groups would show a temporal gradient, but rather that repetition of events would have an impact on performance. More precisely, we predicted that repetition would favor a better preservation of memories for public events.

## Materials and Methods

### Participants

All participants included in our study were elderly native French speakers, who had lived at least the past 40 years in Quebec, Canada. Participants were tested individually during two sessions lasting approximately two and a half hours each, either at the Centre de recherche de l'Institut universitaire de gériatrie de Montréal (IUGM), the Notre-Dame Hospital (CHUM), or at home, depending on their preference. The research protocol was approved by the Research Ethics Board of IUGM and CHUM and all participants gave written informed consent before participation.

Nineteen (19) HC, 20 aMCI patients and 20 mild probable AD patients took part in our study. Twenty (20) HC were initially recruited, but one had to be subsequently excluded based on the neuropsychological assessment results. HC were recruited from a pool of volunteers enrolled at the Centre de recherche de l'IUGM and from various senior centers or associations. Patients were referred by physicians of the CHUM and IUGM.

Patients' diagnosis was established based on the National Institute on Aging-Alzheimer's Association (NIA-AA) recommendations. Thus, for aMCI diagnosis, most recent MCI core clinical criteria [6] were applied. Criteria for aMCI patients included: (a) objective evidence of memory impairment ( $> 1.5$  standard deviation below the mean of age and education-matched healthy participants on at least two standardised tests assessing anterograde memory), (b) the cognitive decline should not interfere with autonomy in activities of domestic and daily living, except for mild difficulties in complex activities such as financial management, and (c) the cognitive impairment

should not fulfill criteria for dementia. Criteria for AD diagnosis included: (a) meeting criteria for dementia, (b) having presented insidious onset of symptoms with (c) typical initially predominant amnesic presentation and (d) a clear-cut history of worsening of cognition [42]. Furthermore, AD patients had to be in an “early” stage of the disease to avoid floor effects on cognitive measures. Clinical diagnosis of patients was confirmed during consensus clinical meetings and based on the results of a detailed neuropsychological assessment. Exclusion criteria for HC and patients groups included a history of systemic or neurological disease (excluding AD), traumatic brain injury, psychiatric illness, history of alcoholism or drug abuse, untreated medical or metabolic condition and general anesthesia in the past six months. Normal cognitive functioning of HC was also confirmed during consensus meetings based on the results of an extensive neuropsychological assessment described in the next section.

### Neuropsychological assessment

All participants underwent a comprehensive neuropsychological assessment. Verbal anterograde memory was assessed with the RL/RI 16 which is a free/cued word recall test [43], a French version of the Rey Auditory Verbal Learning Test (RAVLT) [44], and a story recall test adapted from the Wechsler Memory Scale [45]. Visual anterograde memory was assessed using the Rey complex figure (ROCF) [46], the Brief Visuospatial Memory Test – Revised [47] and the DMS 48 visual recognition test [48]. Semantic memory was assessed with the Pyramids and Palm Trees Test [49] and the Information subtest of the Wechsler Adult Intelligence Scale-Third Edition [50]. In order to assess language, praxis, visuoperceptual and visuoconstructional skills, as well as attention and executive functions, we used a short 30-item version of the Boston Naming



Test [51], the letter (P) and category (animals) fluency tests, a test of praxis, the clock drawing test [52], the screening subtest of the Visual Object and Space Perception Battery [53], the Judgment of Line Orientation Test [54], the D-KEFS Color-Word Interference Test [55], the Trail Making Test and a test of cognitive estimation [56]. Moreover, the Montreal Cognitive Assessment [57-59] was also used as a general cognitive test to compare severity of cognitive decline between groups.

#### Memory assessment of public events

The PUB-40 [60] was used to assess memories of public events. This recently developed test comprises 40 4-forced choice questions concerning news events that received large media coverage in Quebec. Selected events were equally distributed across four time periods between 1960 and 2011, as determined by the moment at which they occurred (1960 to 1975; 1976 to 1990; 1991 to 2005; 2006 to 2011). Two types of events were included: 20 enduring and 20 transient events. Enduring events were those that remained under media coverage for a long period of time and that were recalled many times since their occurrence (for example, explosion of the Chernobyl nuclear power plant; terrorist attacks of September 11th). In contrast, transient events benefited from media coverage only for a short and circumscribed period of time and never drew public attention afterwards (for example, criminal charges against Russel Williams - a Colonel at Trenton military base; Super Bowl 2004 halftime show - controversy implicating Janet Jackson). The classification of chosen events (enduring vs transient) was confirmed in a previous study [60] - through a preliminary analysis and comparison of performance of healthy young and old adults - and was based on Mayes' guidelines for the construction and development of tests assessing remote memory [61]. Indeed, poor performance of

younger healthy subjects at recognizing remote events strongly suggests that these events have never been presented in the media after their initial occurrence (transient events), whereas good performance of younger controls indicates that they have been presented in the media long after their initial occurrence, thus leading to their learning (enduring events). In addition, in this study, the level of difficulty was equated between enduring and transient events across all time periods using performance of older participants (for further details on the method, see Langlois et al. 2015). Each of the 40 questions was presented individually on an 8 ½ x 11 booklet page. First, participants had to read aloud two examples of questions and the associated 4 multiple-choice responses in order to rule out reading difficulties. Afterward, they could choose to read the items silently or ask the examiner to read aloud for them. For each question, participant had unlimited time to select one of the choices or to take a guess when necessary. One point was awarded for each correct response, resulting in a maximum of 40 points. Responses were recorded by the examiner on a separate scoring sheet.

In addition to the PUB-40, we explored media exposure and interests of participants for various domains covered in the news. We inquired about weekly frequency of news exposure via television, radio, newspapers and internet, as well as reading and TV/movie habits concerning historical documentaries or annual reviews. Finally, we noted the level of interest of each participant for global news, economy, politics, environment, arts and sports on a 5-points scale.

Statistical analysis

SPSS (version 22) was used to perform data analysis. Level of statistical significance was set at  $p < 0.05$ . Normality of the distribution was confirmed with Kolmogorov-Smirnov test. Different analyses were performed to evaluate groups' characteristics and performances on the PUB-40. Firstly, differences between groups in demographic data were assessed using chi-square test for gender, and analysis of variance (ANOVA) for age, years of education, number of years living in Quebec, MoCA scores, as well as media exposure and habits. When required, post-hoc analyses were conducted with Tukey's test. Secondly, a mixed between-within subjects repeated measures ANOVA was conducted in order to examine the main effects and interactions between group performances (HC, aMCI, AD), across the four time periods (1960 to 1975; 1976 to 1990; 1991-2005; 2006-2011), and regarding both enduring and transient events. Since many comparisons were made for post-hoc analyses, the more conservative Scheffe's test was chosen. We also examined the performance patterns of the three groups across time periods for each type of event separately. Thus, separate multivariate repeated measures ANOVAs along with Scheffe's post-hoc analyses were conducted on both enduring and transient events. In addition, exploratory non-parametric analyses were carried out to investigate specific differences between groups for each time period. Indeed, for each event type and time period, separate Mann-Whitney U tests were performed to examine differences between groups (HC vs aMCI; aMCI vs AD; AD vs HC). Finally, the relationship between performance on the PUB-40 and participants' characteristics, as well as with standard anterograde and retrograde memory tasks were investigated with Pearson correlations.

## Results

### Participant's characteristics

As expected, we found no group difference in terms of age ( $F [2, 56] = 1.5, p = 0.24$ ), years of education ( $F [2, 56] = 2.0, p = 0.15$ ), number of years in Quebec ( $F [2, 55] = .94, p = .40$ ), nor in terms of the proportion of men and women ( $X^2 [2, n = 59] = 0.12, p = 0.94$ ). Weekly news exposure was also similar across groups for television, radio, newspaper and internet media ( $F [2, 56] = 2.3, p = 0.11$ ). As expected, a significant difference in MoCA scores was found between groups ( $F [2, 56] = 56.03, p < 0.0005, \eta^2 = 0.67$ ). Demographic characteristics of participants are presented in Table 1.

[INSERT TABLE 1 HERE]

### Comparison of group performance on the PUB-40 across time periods for the two types of events

Results revealed a main effect of group on the PUB-40 ( $F [2, 56] = 23.14, p < 0.0005$ , partial  $\eta^2 = 0.45$ ). Specifically, responses of participants in the HC group were more accurate than those in the aMCI ( $p < 0.01$ ) and AD patient groups ( $p < 0.0005$ ), the latter two groups also differing significantly between each other (aMCI scores  $>$  AD scores,  $p < 0.005$ ). Concerning the time periods, a main effect following a quadratic tendency revealed lower performances in the most remote time period (1960-1975) compared with both intermediate time periods (1976-1990,  $p < 0.001$  and 1991-2005,  $p < 0.005$ ) and marginally with the most recent one (2006-2011,  $p = 0.053$ ). Furthermore, we found a main effect of the type of events, with better performances for enduring than for transient events. No significant interaction was found (groups X type of events X time

periods,  $p = 0.42$ ; groups X time periods,  $p = 0.57$ ; groups X type of events,  $p = 0.11$ ), suggesting that the three groups showed similar patterns of performance on the PUB-40 across time periods and event types.

In addition, we explored performance for enduring and transient events separately in order to compare groups for each of these aspects of retrograde memory. In regard to questions about enduring events, a main effect was found for the group ( $F [2, 56] = 23.22, p < 0.0005$ ) and period variables ( $F [3, 54] = 4.49, p < 0.01$ ). HC and aMCI showed similar levels of performance, which were significantly higher than those of the AD group ( $p < 0.0005$ ). Across periods, a quadratic tendency ( $p = 0.001$ ) showed lower performance for the most remote period (1960-1975) compared with the two following periods (1976-1990 and 1991-2005). No significant interaction was found between the group and period variables. For questions about transient events, the main effect of group ( $F [2, 56] = 16.79, p < 0.0005$ ) remained significant, but the performance of the aMCI group was marginally different from that of the AD group ( $p = 0.06$ ), and both patient groups were significantly impaired compared with HC (aMCI vs HC:  $p = 0.005$ , AD vs HC:  $p < 0.0005$ ). No main effect of period ( $p = 0.21$ ) nor interaction ( $p = 0.19$ ) effect was found. Figure 1 presents results for the three groups on both enduring and transient events subscales.

[INSERT FIGURE 1 HERE]

Exploratory analyses were carried out to examine differences between groups, specifically within time period and for both event types. For enduring events, aMCI patients' performance was equivalent to that of HC ( $p = 0.11$  to  $p = 0.24$ ), and significantly better than that of AD patients ( $p < 0.001$  to  $p < 0.01$ ) across all time

periods, the only exception being the most recent time period for which the difference between the MCI and AD groups did not reach significance ( $p = 0.08$ ). For transient events, aMCI performance did not differ from that of HC for the most remote time period ( $p = 0.16$ ); however, for all subsequent time periods, MCI patients had a significantly lower performance than HC (all  $p \leq 0.05$ ). Moreover, aMCI and AD patients showed an equivalent performance on all time periods, except the 1991-2005 period ( $p < 0.05$ ). Finally, AD patients performed worse than HC across all time periods, both for transient and enduring events ( $p < 0.000$  to  $p < 0.01$ ). Results are presented in Table 2.

[INSERT TABLE 2 HERE]

#### Relationship between performance on the PUB-40 and participants' characteristics

We investigated the relationship between performances on the PUB-40 and general cognitive functioning, as measured with the MoCA, in both patients groups (aMCI and AD). Results indicated that higher levels of general cognitive status were associated with better performances on the PUB-40 global scale ( $r = 0.44$ ,  $n = 40$ ,  $p < 0.005$ ), as well as on each subscale (enduring:  $r = 0.46$ ,  $n = 40$ ,  $p < 0.005$ , transient:  $r = 0.36$ ,  $n = 40$ ,  $p < 0.05$ ). When introducing MoCA scores as a covariable to control for cognitive status, age showed no significant relationship with global performance on the PUB-40 ( $r = -0.22$ ,  $n = 59$ ,  $p = 0.09$ ), enduring events ( $r = -0.15$ ,  $n = 59$ ,  $p = 0.27$ ) and transient events ( $r = -0.25$ ,  $n = 59$ ,  $p = 0.06$ ) subscales. However, years of education did show a positive relationship with global performance on the PUB-40 ( $r = 0.34$ ,  $n = 59$ ,  $p < 0.05$ ) and with enduring events subscale ( $r = 0.51$ ,  $n = 59$ ,  $p < 0.0005$ ), but not with transient event subscale ( $r = 0.16$ ,  $n = 59$ ,  $p = 0.27$ ). Performance on the PUB-40 was not

significantly related to media exposure for global score ( $r = 0.19, n = 59, p = 0.16$ ), enduring score ( $r = 0.16, n = 59, p = 0.24$ ) or transient score ( $r = 0.19, n = 59, p = 0.14$ ) subscales.

Relationship between memory for public events and standard episodic and semantic memory tasks in patients groups

As shown in Table 3, even though we controlled for education, a significant relationship was found in patients between performance on the PUB-40 (total scale as well as enduring and transient events subscales) and standard measures of semantic memory (information subtest of the WAIS-IV and the Pyramids and Palm Trees Test), but not with anterograde episodic memory tasks (words list learning and story recall). Moreover, results indicate that performance for the most recent time period was not significantly correlated with tests of anterograde memory.

[INSERT TABLE 3 HERE]

## Discussion

In the present study, we investigated semantic knowledge about public events in aMCI and AD patients groups as a function of time period and nature of events (transient vs. enduring). Specifically, we wanted to test the hypothesis that repetition rather than time course allowed a better preservation of semantic retrograde memory. In order to test this assumption, we used a test including questions about public events that occurred in the recent and distant past and that either quickly fell out of the public's eye (transient events) or were repeatedly recalled by the media (enduring events).

First of all, our general finding that both aMCI and AD groups showed impaired memory for public events compared with HC, and that AD patients performed worse than MCI patients, is consistent with previous studies [13-24, 27, 30, 31]. Results of the present study suggest that the severity of the semantic memory impairment may be linked to the extent of temporal lobe damage, since the neurodegenerative process is thought to be more restricted to this area in aMCI than in early AD [62-66].

Secondly, we found that all three groups (HC, aMCI and AD) showed a similar pattern of performance across the four time periods. Surprisingly, the three groups' overall performance was lower for questions relating to the most remote time period. We found only one other study in which this pattern was found; this study used a test combining questions about public events and famous persons [14]. As in our own study, lower performance on remote items was also observed in HC, which leads us to believe that this may reflect inherent properties of the items. Indeed, despite the attempts made during the elaboration of the PUB-40 to have equivalent level of difficulty across all time periods, items for the 1960-1975 period may still be harder.

Thirdly, all three groups showed a better performance for enduring events than for transient ones, suggesting that frequently repeated memories are better preserved, regardless of the time period at which they were acquired. This finding is consistent with the beneficial effect of repetition demonstrated in other studies assessing semantic memory in young adults [40, 41] and aMCI [28]. This result is also similar to results reported by Müller et al. in aMCI and AD patients which showed that better performance was associated with greater self-reported retrieval frequency of historic events[20].



Furthermore, whereas AD patients were impaired on both transient and enduring events, aMCI patients showed preserved memory for frequently rehearsed public events (enduring), but impaired memory for transient events. Also, results of additional exploratory analyses suggest that aMCI patients may show a semantic memory loss that is temporally graded for transient public events that did not benefit from frequent rehearsal.

Finally, we carefully quantified participants' media exposure to ensure that all groups had equivalent and substantial degree of media exposure to the stimuli in the PUB-40. Therefore, we are confident that the patterns of retrograde memory observed reflect true patterns of memory loss, rather than a lack of knowledge about these events.

Among the two main theories on long term consolidation, the Multiple traces theory (MTT) [4, 5] appears to be more in line with our findings, although not entirely. Indeed, according to this theory, frequently retrieved memories are supported by multiple memory traces and thus are more resistant to brain damage. This view is consistent with our global finding that all groups showed a better performance on frequently rehearsed enduring events compared with rarely repeated transient events. Also, the MTT considers that remote semantic memories are supported by more or stronger memory traces, and thus are more resistant to brain damage than recent ones. In the current study, Mann-Whitney U tests for each time period showed that memory for remote transient events was comparable in aMCI and controls. However, this effect is unlikely to be due to the fact that the most distant events were more likely to be rehearsed than recent ones, since the underlying selection criteria of transient events was that they quickly went out of the public eye, remained in the media for a very short period of time and were not later

recalled, at least not on a large scale. Therefore, they had a very low probability of being repeated after their initial occurrence. Consequently, these results may be more difficult to explain according to the MTT. In sum, results of this study suggest that a slight temporal gradient may characterize aMCI's retrograde semantic memory loss, but only for transient events. Therefore, the passage of time, rather than rehearsal per se, may play a distinct yet mild role on long-term consolidation processes. However, more studies will be needed in order to clarify the role of time passing on rarely rehearsed memories related to public event.

Furthermore, the MTT refers to a process of *semantization* in which semantic knowledge about events is separated from the episode where it has been acquired [3]. Indeed, in each new situation, common re-experienced information is extracted and integrated into pre-existing semantic knowledge mediated by the neocortex, whereas memory traces associated with unique autobiographical episodes are distributed in the hippocampal complex. Accordingly, memories about rarely repeated transient public events may not be *semantized*, relying on the hippocampal complex. On the other hand, enduring events benefit from *semantization* through frequent rehearsal and may thus gradually rely upon neocortical sites; at some point, knowledge becomes independent from the hippocampal complex. This is consistent with the recently proposed hypothesis that frequently retrieved memories become independent of the hippocampal complex [15, 20, 67], as well as with our finding that aMCI patients, who are presumed to have damage more confined to the MTL [6-8, 65], showed impaired memory for transient events but spared memory for enduring event.

There are some limitations to our study that need to be mentioned. First, it would have been interesting to know when the memory impairment began for each patient and to explore whether performance varied as a function of when the public event occurred, prior or after the onset of memory deficits. This data would help to contextualize performance and clarify if results for the most recent time periods were reflecting retrograde amnesia, rather than anterograde amnesia or a combination of both retrograde and anterograde amnesia. But, it is very difficult to determine at which specific point in time the memory decline began, making this endeavour difficult. In the current study, however, the absence of correlation between patients' performance on the PUB-40 and standard measures of anterograde memory, more specifically for the most recent time period, leads us to believe that the memory deficits observed for the most recent period is not associated with the anterograde memory impairment. Likewise, the lack of biomarkers for aMCI patients should be underlined. Indeed, we do not have biomarker evidence indicating that our aMCI patients are in fact in the prodromal stage of AD. Lastly, the status of enduring and transient events remains at least partly subjective, even if it was defined following pre-existing guidelines such as those proposed by Mayes and colleagues [61]. Also, especially for recent events, we cannot rule out the possibility that an event classified as transient may become enduring, for example if a movie based on this event is eventually made.

A better understanding of retrograde memory is of outstanding importance in the early detection of AD, since anterograde memory deficits that characterize aMCI cannot be used to distinguish patients who will develop AD from those who will not. Indeed, anterograde memory deficits can be found in treatable conditions such as depressive state

[68] or nutritional deficiencies [69]. However, some recent studies suggest that semantic memory deficits could help to identify which aMCI patients will eventually progress to AD [12, 26, 27]. Hence, sensitive retrograde memory tests assessing memories that did not benefit from rehearsal, such as transient events, may be useful in a clinical setting to target mild semantic deficits.

In summary, our study provides strong evidence that repetition allows better preservation of memories for past public events, no matter the remoteness of these memories. This finding suggests that rehearsal may strengthen the memory trace more efficiently than the simple passage of time. This study challenges the widely accepted view that semantic retrograde memory is characterized by a Ribot-type temporal gradient, although future studies should focus on further understanding memory for transient events in aMCI. Moreover, our findings, based on the separate analysis of aMCI and AD patients, suggest that memories of transient events are first altered in aMCI, followed by memories of both transient and enduring events later in the disease. Our study, however, is cross-sectional in nature, and future longitudinal studies will allow to further elucidate this question. Future studies using structural or functional neuroimaging methods should also investigate the neural correlates of memories for enduring and transient public events. In these studies, it would also be interesting to determine, for instance, if neural correlates of deficits for famous public events are more righty-lateralized in aMCI and AD, as suggested by patients with the right temporal variant frontotemporal lobar degeneration who may be more particularly prone to being impaired on tests of unique entities [70, 71].

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Table 1

*Group characteristics*

	Groups			<i>p</i> -values
	HC	aMCI	AD	
<i>n</i>	19	20	20	
Age in years	74 (8.5)	77 (6.5)	78 (6.0)	<i>p</i> = 0.24
Years of education	15 (3.7)	15 (4.4)	12 (4.6)	<i>p</i> = 0.15
Sex (M/F)	6/13	6/14	7/13	<i>p</i> = 0.94
MoCA	28 (1.4)	26 (2.4)	20 (3.1)	HC > aMCI > AD*

*Notes.* Values are expressed in mean (standard deviation). \*  $p < 0.0005$ . HC, Healthy controls; aMCI, amnesic mild cognitive impairment; AD, probable Alzheimer's disease; *n*, number of subjects; M/F, male/female; MoCA, Montreal Cognitive Assessment (scores include the suggested adjustment of one additional point for subject who completed 12 years or less of education).

Table 2

*Results of exploratory analysis using Mann-Whitney U tests*

Enduring events			
Time periods	HC vs aMCI	aMCI vs AD	AD vs HC
1960-1975	$p = 0.18$	$p < 0.01$	$p < 0.00$
1976-1990	$p = 0.24$	$p < 0.00$	$p < 0.00$
1991-2005	$p = 0.11$	$p < 0.00$	$p < 0.00$
2006-2011	$p = 0.13$	$p = 0.08$	$p < 0.00$
Transient events			
Time periods	HC vs aMCI	aMCI vs AD	AD vs HC
1960-1975	$p = 0.16$	$p = 0.13$	$p < 0.00$
1976-1990	$p < 0.01$	$p = 0.37$	$p < 0.00$
1991-2005	$p < 0.01$	$p < 0.05$	$p < 0.00$
2006-2011	$p = 0.05$	$p = 0.07$	$p < 0.00$

*Notes.* Results indicate p-values. HC, Healthy controls; aMCI, amnesic mild cognitive impairment; AD, probable Alzheimer's disease.



Table 3

*Relation between performance on the PUB-40 scales and standard semantic and episodic memory tasks in aMCI and AD patients*

Standard episodic and semantic memory tasks	Performance on the PUB-40			
	Total PUB-40	Enduring events	Transient events	2006-2011
PPTT	0.51**	0.41*	0.53**	0.44**
Information (WAIS-III)	0.64**	0.54**	0.64**	0.50**
Story immediate recall	0.13	0.22	0.05	0.16
Story delayed recall	0.02	-0.01	0.04	0.05
RAVLT immediate recall	-0.01	0.04	-0.04	0.07
RAVLT delayed recall	-0.00	0.10	-0.08	0.01

*Notes.* Results indicate *p*-values of partial correlations with number of years of education introduced as covariable. *n* = 40. PPTT = Pyramids and Palm Trees Test. Information = Information subtest of the Wechsler Adults Intelligence Scale-Third Edition. RAVLT = Rey Auditory Verbal Learning Test. Significance (2 tailed) \* *p* < .05. \*\* *p* < .01.

Figure 1. PUB-40 performance across time periods in healthy control subjects (HC), amnesic Mild cognitive impairment patients (aMCI) and probable Alzheimer's disease patients (AD) for 1) enduring events and 2) transient events. Values indicate mean percentage of correct responses on the 40 multiple-choices questions (chance level = 25%). Error bars indicate standard errors.

