



THE UNIVERSITY *of* EDINBURGH

Edinburgh Research Explorer

Episodic future thinking in amnesic mild cognitive impairment

Citation for published version:

Gamboz, N, De Vito, S, Brandimonte, MA, Pappalardo, S, Galeone, F, Iavarone, A & Della Sala, S 2010, 'Episodic future thinking in amnesic mild cognitive impairment', *Neuropsychologia*, vol. 48, no. 7, pp. 2091-2097. <https://doi.org/10.1016/j.neuropsychologia.2010.03.030>

Digital Object Identifier (DOI):

[10.1016/j.neuropsychologia.2010.03.030](https://doi.org/10.1016/j.neuropsychologia.2010.03.030)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Peer reviewed version

Published In:

Neuropsychologia

Publisher Rights Statement:

This is an author's Accepted Manuscript of the following article: Gamboz, N., De Vito, S., Brandimonte, M. A., Pappalardo, S., Galeone, F., Iavarone, A. & Della Sala, S. 1 (2010) "Episodic future thinking in amnesic mild cognitive impairment", *Neuropsychologia*. 48, 7, p. 2091-2097. © The Authors. The final, definitive version is available at: <http://www.sciencedirect.com/science/article/pii/S0028393210001314>

General rights

Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.



Episodic future thinking in amnesic mild cognitive impairment

Nadia Gamboz^a
Stefania De Vito^{a, b}
Maria A. Brandimonte^a
Stella Pappalardo^c
Filomena Galeone^d
Alessandro Iavarone^{c, e}
Sergio Della Sala^b

^a Laboratory of Experimental Psychology, Suor Orsola Benincasa University, Via Suor Orsola 10, 80135 Naples, Italy

^b Human Cognitive Neuroscience, Psychology, University of Edinburgh, UK

^c Neurological and Stroke Unit, CTO Hospital, Naples, Italy

^d Laboratory of Neuropsychology of Aging, Department of Geriatrics, ASL, Napoli 1, Italy

^e Department of Relational Sciences, University of Naples Federico II, Naples, Italy

Abstract Results from behavioral studies of amnesic patients and neuroimaging studies of individuals with intact memory suggest that a brain system involving direct contributions from the medial temporal lobes supports both remembering the past and imagining the future (Episodic Future Thinking). In the present study, we investigated whether amnesic Mild Cognitive Impairment (aMCI) affects EFT. Amnesic MCI is a high-risk factor for Alzheimer's disease and is characterized by a selective impairment of episodic memory, likely reflecting hippocampal malfunctioning. The present study assessed, for the first time, whether the reduction of episodic specificity for past events, evident in aMCI patients, extends also to future events. We present data on 14 aMCI patients and 14 healthy controls, who mentally re-experienced and pre-experienced autobiographical episodes. Transcriptions were segmented into distinct details that were classified as either internal (episodic) or external (semantic). Results revealed that aMCI patients produced fewer episodic, event-specific details, and an increased number of semantic details for both past and future events, as compared to controls. These results are discussed with respect to the constructive episodic simulation hypothesis, which suggests that reminiscence and future thinking are the expression of the same neurocognitive system.

Keywords Future, Memory, Amnesia

1. Introduction

The ability to mentally travel forth in time has been differently referred to as prospection (Buckner & Carroll, 2007), proscopic chronesthesia (Tulving, 2002), or episodic future thinking (Atance & O'Neill, 2001).

In recent years, an increasing number of cognitive, neuropsychological, and neuroimaging studies have suggested that remembering the past and imagining the future rely on common psychological and neural processes. For instance, it has been shown that the phenomenal characteristics associated with both projecting oneself into the past or into the future are influenced by similar factors, such as the temporal distance from the present (D'Argembeau & van der Linden, 2004; see also Addis et al., 2008, D'Argembeau and van der Linden, 2006 and Spreng and Levine, 2006). Recent neuroimaging studies have

demonstrated that remembering past events and imagining novel scenarios that might happen in the future rely on a common network of neural regions (e.g., Addis et al., 2009a, Addis et al., 2007, Okuda et al., 2003 and Szpunar et al., 2007). This common network of prefrontal, medial temporal lobe, and posterior regions, including the posterior cingulate and retrosplenial cortex, is remarkably similar to the network involved in the retrieval of episodic memories of past autobiographical events (e.g., Cabeza and St Jacques, 2007 and Maguire, 2001). Most recently, this network of regions has been suggested to belong to an anatomically defined brain system (default network) that is activated when individuals engage in internally focused tasks including autobiographical memory retrieval, envisioning the future, and conceiving the perspectives of others (Buckner, Andrews-Hanna, & Schacter, 2008). There is also evidence that amnesic patients highly impaired on retrieving past events may be also impaired in imagining future autobiographical events (Hassabis et al., 2007, Klein and Loftus, 2002 and Tulving, 1985).

In light of such findings, it has been proposed that the constructive nature of episodic memory allows one to draw on the past and to flexibly extract and re-combine elements of previous experiences (Buckner and Carroll, 2007, Hassabis and Maguire, 2007 and Schacter and Addis, 2007). This conceptualization is often referred to as the constructive episodic simulation hypothesis (Schacter & Addis, 2007).

One key outstanding issue that still needs to be clarified concerns the precise relationship between future-event simulation and episodic memory in patients suffering from episodic memory impairments. As mentioned above, in the neuropsychological literature, two amnesic patients suffering from total loss of episodic memory, K.C. (Tulving, 1985) and D.B. (Klein & Loftus, 2002), were described as being highly impaired on both retrieving past and imagining future autobiographical events. K.C. suffered from an extensive brain damage, affecting medial temporal, prefrontal and other brain regions, while little information was provided concerning the location of D.B.'s lesion. Most recently, Hassabis et al. (2007) have found that imagined experiences of five patients with amnesia deriving from bilateral hippocampal damage were deficient in spatial coherence, relative to controls, resulting in their constructions being fragmented and lacking in richness. In this study, however, participants were not specifically requested to construct scenes pertaining to future events, therefore leaving open the possibility that patients with hippocampal damage suffer from a more general event simulation deficit in constructing novel scenes, irrespective of time period (Schacter, Addis, & Buckner, 2008). Therefore, these studies do not allow one to draw precise conclusions concerning the basis for the patients' future events simulation deficit and its relation to their episodic memory problems. The idea that thinking of the future is closely related to retrospective memory received strong support by recent evidence indicating that healthy older adults (Addis et al., 2008) and patients with Alzheimer's disease (AD; Addis, Sacchetti, Ally, Budson, & Schacter, 2009) show impairments, although different in severity, in autobiographical memory as well as in future-event simulation.

As far as healthy aging is concerned, studies on autobiographical memory have demonstrated that, compared to young people, older adults tend to recollect fewer details about happenings, locations, perceptions, and thoughts, whereas they produce an equivalent, or larger, number of semantic details that are not connected to any particular time or place (e.g., Levine et al., 2002 and Piolino et al., 2002). These specific age-related differences in the qualities of autobiographical recollections have been accounted for within recent models of autobiographical memory (e.g., Conway, 2001 and Conway and Pleydell-Pearce, 2000). Such models distinguish between the episodic component of autobiographical memory, providing lower level event-specific sensory and perceptual episodic information, which is affected by healthy aging, from the semantic component of autobiographical memory, containing a more abstract autobiographical knowledge base and the conceptual self, which is preserved in healthy aging. Recently, Addis et al. (2008) demonstrated that the age-related reduction of episodic specificity, evident for past events, extends also to future events. In particular, when probed to generate autobiographical events from the past and the future, older adults produced fewer internal-episodic details and more external-non-episodic details, as

assessed by the scoring procedure of Levine et al.'s (2002) Autobiographical Interview. Furthermore, the number of internal event-specific details and external semantic details were correlated across past and future events, and the number of internal details for both past and future events correlated significantly with a measure of relational memory (paired-associate learning) that is known to be dependent on the hippocampus (Giovanello, Schnyer, & Verfaellie, 2004). This pattern of results suggests that both retrieving past and imagining future detailed autobiographical events rely on relational memory, i.e., the ability to re-combine and integrate details from various episodic memories. The pattern of decreased internal and increased external details for past and future events likely reflects an increased reliance on external semantic details when people are unable to generate internal-episodic details (Addis et al., 2008).

With respect to AD, in addition to episodic memory problems, which are the hallmark and the earliest manifestation of this neurodegenerative disease, there are also major semantic memory dysfunctions (e.g., Chertkow and Bub, 1990 and Hodges and Patterson, 1995). This conjoined pattern of deficits, which is clearly detectable by traditional laboratory and neuropsychological tests, also affects the content of autobiographical memory. In general, there have been several studies, using a variety of methods, showing a deficit in the retrieval of autobiographical memories with a shallow temporal gradient indicating more successful retrieval of earlier memories (e.g., Hou et al., 2005, Ivanoiu et al., 2006, Kopelman et al., 1989, Nestor et al., 2002, Piolino et al., 2002 and Snowden et al., 1996). As far as the integrity of the episodic and semantic components of autobiographical memory is concerned, most studies documented some level of impairment in one or both types of memory. However, results of recent studies that used different memory tests, such as the Autobiographical Memory Questionnaire of Kopelman, Wilson, and Baddeley (1990) and the Autobiographical Interview of Levine et al. (2002), converged in showing severe deficits in AD patients in both the episodic and semantic component of autobiographical memory (e.g., Ivanoiu et al., 2006 and Leyhe et al., 2009).

In a very recent study, Addis, Sacchetti, et al. (2009) tested the ability of AD patients and age-matched controls to generate past and future autobiographical events. Results showed that AD patients exhibited deficits in both remembering past events and simulating future events, generating fewer internal and external episodic details (as estimated by the scoring procedure of the Autobiographical Interview) than healthy older controls. In line with the results of Addis et al. (2008), the internal and external detail scores were strongly correlated across past and future events. The authors attributed the semantic autobiographical deficit evident in AD (for both past and future events) to the progression of the atrophy of the hippocampus, beyond the medial temporal regions to larger portions of the neocortex supporting semantic memory (Leyhe et al., 2009). The results of Addis, Sacchetti, et al.'s (2009) study therefore suggest a close association between future thinking and retrospective memory. However, mild AD patients participating in this study may have been impaired on cognitive functions other than episodic memory that may have contributed – to some extent – to their future-event simulation deficits. Neuropsychological testing indeed revealed some impairment in executive functioning (as assessed by the Trial Making Test-Part B). The supposed symmetry of past and future episodic deficits should be further investigated in populations affected by selective memory impairment.

The aim of the current study is to assess the relation between past and future thinking in patients suffering from amnesic Mild Cognitive Impairment (aMCI). The term MCI has become widely used to describe a condition in old people whose memory and/or other cognitive abilities are below the normal level, but who do not meet the accepted criteria for dementia. Clinically, different subtypes of MCI have been recognized, with the amnesic subtype having an elevated risk of progressing to Alzheimer's Disease (AD; rate of conversion to AD is 10–15% per year; Gauthier et al., 2006, Petersen and Negash, 2008 and Petersen et al., 2001). Amnesic MCI is characterized by a selective and isolated impairment of episodic memory, while the other cognitive functions and the ability to deal with daily living activities are relatively preserved. Patients with aMCI typically show atrophy of the hippocampus and other medial temporal lobe regions (e.g., Jack et al., 2000 and Killiany et al., 2002). The isolated impairment of episodic memory, due to hippocampal malfunctioning, renders aMCI a clinical condition particularly suitable for a direct

assessment of the relation between past and future thinking. If, as suggested by the constructive episodic simulation hypothesis, people use episodic memory to imagine future autobiographical events, and as aMCI is considered to be a transitional stage between healthy aging and AD, and given that both these extremes of the aging process show some form of impairment in autobiographical memory as well as episodic future thinking, aMCI patients should show an impairment in autobiographical memory and episodic future thinking somehow intermediate to that of normal aging and AD. In this respect, it is important to note that there is some evidence showing that autobiographical memory is indeed impaired in aMCI. For example, using the Autobiographical Interview (Levine et al., 2002), Murphy, Troyer, Levine, and Moscovitch (2008), found that, although aMCI and healthy controls generated protocols of similar length, the aMCI group produced fewer episodic, event-specific details and an increased number of semantic details in their recollections, as compared to controls. This pattern of reduced episodic but elevated semantic autobiographical memory in aMCI as compared to healthy controls magnifies finding with healthy older adults relative to younger adults for past events.

The present study, which for the first time assesses episodic future thinking in aMCI, will help track the course of the deficit in past and future thinking, thus providing potentially important information on the relation between these two supposedly associated cognitive processes.

2. Methods

2.1. Participants

Fourteen old adults affected by aMCI and 14 healthy controls participated in this experiment.

The participants with aMCI were selected from a larger panel at the Laboratory of Neuropsychology of Aging of the Department of Geriatrics (ASL Napoli 1). The diagnosis of aMCI was reached according to the criteria proposed by Petersen et al. (1999), including (a) exclusion criteria for dementia (DSM-IV, APA, 1994); (b) memory complaints documented by the patient or by a collateral source; (c) a performance of at least 1.5 standard deviations below age and education matched controls on at least one of the measures assessing episodic memory included in the Mental Deterioration Battery (MDB – Carlesimo, Caltagirone, & Gainotti, 1996); (d) no evidence of significant deficits in other cognitive domains explored by means of the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975; Italian norms in Measso et al., 1993), the MDB (Carlesimo et al., 1996), and the Frontal Assessment Battery (FAB – Dubois, Slachevsky, Litvan, & Pillon, 2000; Italian norms in Iavarone et al., 2004); (e) a score of at least 26 on the MMSE; (f) no evidence of difficulties in everyday activities; (g) no history of stroke or other cerebrovascular disease; (h) no evidence of metabolic, endocrine, or nutritional deficiencies.

Healthy older adults were members of different, non-academic, local associations. Individuals assuming psychoactive pharmacological treatment able to alter normal memory skills, with a history of neurological and psychiatric disorders and the elderly with a score less than 26 on the MMSE were excluded from the study. There were no significant differences (all p s > .05) between aMCI and controls on demographic variables related to age (aMCI, $M = 74.7$, $SD = 7.4$; controls, $M = 73.5$, $SD = 8.0$), education (aMCI, $M = 12.8$, $SD = 5.1$; controls, $M = 13.0$, $SD = 2.0$), and on the MMSE scores (aMCI, $M = 24.8$, $SD = 2.8$; controls, $M = 26.3$, $SD = 1.3$). Elderly with aMCI and controls gave informed written consent prior to the commencement of the study and did not receive financial compensation for participation. The study procedure was approved by the local ethical committee and was performed in accordance with the Declaration of Helsinki.

2.2. Materials and procedure

The experiment was conducted in one single session. Participants mentally re-experienced and pre-experienced four autobiographical episodes (occurred or occurring within the past or next year) in response to eight cue words. More precisely, two sets of eight words, matched for familiarity, frequency, imageability, and concreteness, were selected from Italian norms (Burani, Barca, & Arduino, 2001). Within each set, the words were randomly cycled through temporal direction (remember or imagine). Each participant was then assigned to one of these two lists of words. Half participants performed the past task first, followed by the future task, the other half received the opposite sequence. The experimental procedure was adapted from D'Argembeau and van der Linden (2004) and from Addis et al. (2008). Participants were encouraged to retrieve and imagine temporally and contextually specific events. Future events also had to be plausible, given the participant's plans, and novel, that is, not previously experienced by the participant. Each cue word was displayed on the computer screen together with task instructions concerning the temporal direction (remember or imagine) and the time period (last year or next year). Once an event had been retrieved or imagined (there was no time limit for retrieving or imagining an event), participants were given 60 s to retrieve or imagine as many details as possible. Participants then described their past and future representations (their responses were recorded using a digital audio-recorder for later transcription) and rated each event, using a 7-point scale (Szpunar & McDermott, 2008), on (a) three measures that were summed to form a sensorial details index (visual details, sounds, smell/taste; 1 = none, 7 = a lot), (b) three measures that were summed to form a clarity of context index (clarity of location, clarity of spatial arrangement of objects, clarity of spatial arrangement of people; 1 = vague, 7 = clear), and (c) a measure of the subjective experience associated with the mental image (feeling of experiencing the event, 1 = none, 7 = a lot). Furthermore, participants also indicated the novelty of each imagined event by rating how often they had experienced in the past the same or a very similar event (1 = never; 7 = very often). This question was aimed at ensuring that participants were imagining truly novel scenarios rather than retrieving an event that had already taken place and adjusting it to fit in with the test requirements (see Gamboz, Brandimonte, & De Vito, 2010).

The qualities of the autobiographical recollections and simulations were estimated using the standardized scoring procedure developed by Levine et al. (2002). More precisely, for each past and future-event produced by participants, the central event (the event discussed in most detail that occurred over a brief time-frame) was first identified. The central event was then segmented into details, i.e., unique occurrences, observations, or thoughts (that typically occur as grammatical clauses defined by a subject and predicate, such as "I dropped my sandwich"). Details were classified as internal or external, internal details being those that were specific to time and place, and considered to reflect episodic re- or pre-experiencing, and external details being those that pertained to extraneous information that was not uniquely specific to the main event being described and not anchored to the time and place. Internal details were divided into further subcategories: (a) event (happenings, people involved, actions, nature of the environment), (b) place (information about where the event occurred), (c) time (date, season, or time of day), (d) perceptual (sensory information) and (e) emotion/thought relating to the event. External details were also subcategorized: (a) event (specific details from other incidents, from all of the above categories, external to the main event recalled or imagined), (b) semantic (general knowledge or facts, ongoing events, extended states of being), (c) repetition (unsolicited repetition of details), and (d) other (metacognitive statements, editorializing). The transcriptions were segmented into internal and external details by a single trained rater, who was blind to the hypotheses of the study. It is relevant to note that this rater scored events in a manner that was highly reliable with the ratings provided by the experimenter. The inter-rater reliability (r) was .82 and .88 for internal and external details, respectively.

3. Results

3.1. Design of the analyses

Results concerning group differences in the phenomenal characteristics of past and future events will be reported first. Then, group differences in the qualities of the autobiographical recollections and simulations (i.e., in the number of internal and external details) will be examined. Finally, following Addis et al. (2008), the correlations between internal and external details of past and future events will be reported.

3.2. Ratings of phenomenal characteristics

Separate 2 (Group: aMCI vs. controls) \times 2 (Temporal Direction: past vs. future) mixed analyses of variance (ANOVA) were carried out for each phenomenal characteristic. The mean ratings are presented in Table 1.

Results indicated that there were no group differences, $F(1, 26) = 1.47$, or differences between memories for past events and representations of future events, $F(1, 26) = 0.14$, in terms of sensorial details. Analogously, the interaction between Group and Temporal Direction was not significant, $F(1, 26) = 0.37$. As regards clarity of location, there were no group differences, $F(1, 26) = 0.24$. However, results indicated that memories for past events were more clearly represented than representations of future events, $F(1, 26) = 5.13$, View the MathML source, $p < .05$. A significant Group \times Temporal Direction interaction, $F(1, 26) = 4.59$, View the MathML source, $p < .05$, revealed that the difference between past and future events was evident only in the aMCI group. Concerning the subjective experience associated with the mental image, the control group showed stronger feelings of experiencing the events, $F(1, 26) = 12.91$, View the MathML source, $p < .001$, than aMCI patients. The main effect of Temporal Direction, $F(1, 26) = 2.05$, and the interaction between Group \times Temporal Direction, $F(1, 26) = 0.72$, were not significant.

With respect to the novelty of future representations, Gamboz et al. (2010) hypothesized that, to the extent that participants envisage truly novel scenarios, the novelty of their representations should be rated as high, that is, envisaged future events should be rated as never having happened before. However, an inspection of the frequency distribution of ratings (Table 2) suggests that this was the case only for the control group in this study. In fact, less than 30% of future events produced by aMCI patients were rated as novel. In contrast, the control group rated 66% of future events as novel. Group differences in the mean rating of frequency of occurrence were indeed significant, $t(26) = -5.48$, View the MathML source, $p < .0001$. The implications of this result for the interpretation of group differences in episodic future thinking will be addressed in Section 4.

3.3. Number of internal and external details

A 2 (Group: aMCI vs. controls) \times 2 (Details: internal vs. external) \times 2 (Temporal Direction: past vs. future) mixed analysis of variance (ANOVA), with Group as a between-subjects factor, and Details and Temporal Direction as within-subjects factors, was conducted on the mean number of details produced by aMCI and controls (see Fig. 1). Results showed that, overall, aMCI patients ($M = 5.33$; $SD = 3.06$) and controls ($M = 5.36$; $SD = 3.31$) produced an equivalent number of details, $F(1, 26) = 0.005$, indicating that both groups produced protocols of similar length. Given that group differences in general conversational style may affect the interpretation of the results, we further analyzed whether there were group differences in the mean number of words used to describe past and future events. Results of a 2 (Group: aMCI vs. controls) \times 2 (Temporal Direction: past vs. future) mixed ANOVA showed that there were no differences between groups $F_s(1, 26) < 0.76$. The mean numbers of words used by controls to

describe past and future events were 105.23 (SD = 40.65) and 103.89 (SD = 34.55) respectively; the mean numbers of words used by aMCI patients to describe past and future events were 90.55 (SD = 36.64) and 96.03 (SD = 51.36) respectively.¹

The main effect of Details, $F(1, 26) = 5.11$, $\hat{\eta}_p^2 = .20$, $p < .05$, was significant, indicating that, overall, participants produced more internal ($M = 5.89$; SD = 3.15) than external details ($M = 4.75$; SD = 3.12). The interaction between Group and Details, $F(1, 26) = 35.72$, $\hat{\eta}_p^2 = .60$, $p < .0001$, and between Group and Direction, $F(1, 26) = 7.10$, $\hat{\eta}_p^2 = .20$, $p < .01$ were significant. These interactions showed, respectively, that controls produced more internal details ($M = 7.42$; SD = 1.98) than aMCI patients ($M = 4.42$; SD = 1.87), $t(27) = 4.11$, $\hat{\eta}^2 = .38$, $p < .0001$, whereas aMCI patients produced more external details ($M = 6.31$; SD = 2.26) than controls ($M = 3.23$; SD = 1.36), $t(27) = -4.37$, $\hat{\eta}^2 = .41$, $p < .0001$, and that controls produced more details for past ($M = 6.14$; SD = 1.80) than for future events ($M = 4.53$; SD = 1.38), $t(13) = 3.38$, $\hat{\eta}^2 = .47$, $p < .005$, whereas aMCI patients produced an equivalent number of details for past ($M = 5.50$; SD = 1.85) and for future events ($M = 5.58$; SD = 1.60), $t(13) = -0.67$. The interaction between Details and Temporal Direction was also significant, $F(1, 26) = 72.71$, $\hat{\eta}_p^2 = .74$, $p < .0001$, indicating that more internal details were produced for past ($M = 7.48$; SD = 3.0) than for future events ($M = 4.35$; SD = 2.5), $t(27) = 6.50$, $\hat{\eta}^2 = .61$, $p < .0001$, whereas more external details were produced for future ($M = 5.71$; SD = 3.7) than for past events ($M = 3.88$; SD = 2.0), $t(27) = -2.77$, $\hat{\eta}^2 = .22$, $p < .01$. Finally, the Group \times Details \times Temporal Direction interaction was also significant, $F(1, 26) = 28.13$, $\hat{\eta}_p^2 = .52$, $p < .0001$. In order to better describe this three-way interaction, we conducted two separate follow-up Group \times Temporal Direction ANOVAs for internal and external details. The results of the ANOVA on internal details showed main effects of both Group and of Temporal Direction, $F_s(1, 26) > 16.83$, $\hat{\eta}_{ps}^2 > .40$, $p_s < .0001$, indicating that aMCI patients produced less internal details as compared to controls and that, overall, more internal details were produced for past than for future events. The difference between the number of internal details for past and future events was equivalent in the two groups of participants, as indicated by a non-significant Group \times Temporal Direction Interaction (see Fig. 1). The results of the ANOVA on external details showed a main effect of Group and of Temporal Direction, $F_s(1, 26) > 15.57$, $\hat{\eta}_p^2 > .37$, $p_s < .0001$, indicating that aMCI patients produced more external details as compared to controls, and that, overall, more external details were produced for future than for past events. However, a significant Group \times Temporal Direction interaction, $F(1, 26) = 28.82$, $\hat{\eta}_p^2 = .53$, $p < .0001$, revealed that the difference between the number of external details for past and future events was significant only for the aMCI patients, $t(13) = -5.46$, $\hat{\eta}^2 = .69$, $p < .0001$ (see Fig. 1).

3.4. Correlations

We computed correlations between internal and external details for past and future events across all participants. In line with results reported by Addis et al. (2008), we found a significant correlation between past and future internal details ($r = .58$, $p < .001$) and a marginally significant correlation between past and future external details ($r = .35$, $p = .06$). These positive correlations have been accounted for as evidence of the striking overlap between the specificity of past and future events (Addis et al., 2008).

However, we also found a significant negative correlation between future internal and external

details ($r = -.55$, $p < .01$). It is important to note that recently Addis, Sacchetti, et al. (2009) found a negative correlation between future internal and external details, computed using data from healthy old adults and AD patients, that approached significance when few covariates (MMSE, phonemic and semantic fluency) were controlled for. The authors suggested that their finding might indicate that, when controlling for cognitive decline and fluency abilities, those subjects who generate more external details also generate fewer internal details. In the present study, there were no significant differences between aMCI and controls on the MMSE scores. In addition, performance of all aMCI patients in the phonemic fluency task (Carlesimo et al., 1995) was within the normal range for age and education (range = 17–45; $M = 28.1$; $SD = 6.8$; data on controls were not available). It seems therefore plausible to conclude that, in general, the pattern of decreased internal and increased external details for past and future events, commonly observed across the aging process, likely reflects an increased reliance on external semantic details when unable to generate internal-episodic details, as originally suggested by Addis et al. (2008).

4. Discussion

This study is the first to assess episodic future thinking in aMCI patients. Results revealed that aMCI patients produced fewer episodic, event-specific details, and an increased number of semantic details in their recollections and simulation of past and future as compared to controls. Furthermore, both groups produced more internal details for past than for future events, whereas the number of external details was higher for future than past events only for aMCI patients. Differences between controls and aMCI patients in general conversational style were not a factor of concern in the interpretation of these results. In fact, when describing past and future events, aMCI patients and controls produced, overall, an equivalent number of details and used an equivalent mean number of words.

These novel results fill the gap in the current literature concerning the ability to simulate future events in patients with episodic memory impairments. On the one hand, it is well known that healthy older adults produce fewer episodic and more semantic details, as compared to younger adults, for both past (Addis et al., 2008, Levine et al., 2002 and Piolino et al., 2002) and future (Addis et al., 2008) events. On the other hand, it has been recently shown that AD patients produce fewer internal and external details as compared to healthy older adults for both past (Addis et al., 2009b, Ivanoiu et al., 2006 and Leyhe et al., 2009) and future (Addis, Sacchetti, et al., 2009) events. Furthermore, there is evidence of reduced episodic specificity in autobiographical memory in aMCI patients (Murphy et al., 2008). Recently, Addis, Sacchetti, et al. (2009) acknowledged that “while amnesic MCI patients exhibit significant declines in memory for internal-episodic details, as do AD patients, it appears they can still rely on strategies also used by older adults when describing past and future events” (p. 2668). The results of the present study extend the impaired episodic-spared semantic trend to simulating future events in aMCI, placing the performance of aMCI patients at an intermediate position between that of healthy elderly and AD patients. We suggest, in line with Addis, Sacchetti, et al. (2009), that the three stages – from healthy aging, through aMCI, to AD – of the impairments affecting past and future thinking may reasonably reflect the progress of the neuropathological changes associated with these conditions, i.e., from initial functional and structural changes that affect the medial temporal area in normal aging (Driscoll et al., 2003), encompassing the hippocampus and surrounding cortical regions, to a more severe, though selective, impairment of the hippocampus and other medial temporal lobe regions in aMCI (e.g., Jack et al., 2000 and Killiany et al., 2002), to a more extensive atrophy beyond the medial temporal regions to larger portions of the neocortex (supporting semantic memory) in AD (Leyhe et al., 2009).

Therefore, the results of the present study, in conjunction with the findings of Addis et al. (2008), Addis, Sacchetti, et al. (2009) and of Murphy et al. (2008), provide evidence for the close linkage between remembering the past and imagining future.

There are, however, some relevant issues that need to be considered. One issue pertains to the status of the semantic component of autobiographical memory in aMCI. In line with results of Murphy et

al. (2008), we found a pattern of reduced episodic but elevated semantic autobiographical memory in aMCI, as compared to controls. However, it is important to note that, in a recent study, Leyhe et al. (2009) detected an impairment in both the semantic and the episodic components of autobiographical memory in aMCI patients. These different results may be due to differences in the experimental task used to assess autobiographical memory. Like Murphy et al. (2008), we used the Autobiographical Interview by Levine et al. (2002), which extracts indices of semantic and episodic autobiographical information from within a single narrative. In contrast, Leyhe et al. (2009) used the Autobiographical Memory Interview by Kopelman, Wilson, and Baddeley (1990), which probes episodic and semantic memory separately, through the recall of specific past events and names, and addresses, respectively, across the lifespan. It has been argued that these separate measures artificially divide these two forms of autobiographical memory, which co-occur and interact in naturalistic autobiographical discourse, assessing them with tasks unmatched in sensitivity, content, and psychometric characteristics (Murphy et al., 2008).

A further relevant issue pertains to our findings concerning the novelty of imagined future events. In the present study, almost all aMCI participants rated their imagined future events as already occurred, more or less frequently, in the past. In contrast, only a small percentage of events produced by controls were rated as already occurred in the past. It is relevant to note that, in a recent study, Gamboz et al. (2010) acknowledged that self-projection into the future may appear much more difficult than remembering the past and may consequently lead the participant to rely, more or less deliberately, on some alternative strategies. In line with their hypothesis, the authors showed that, occasionally, people do indeed reproduce events that have already occurred in the past or that are very similar to past events, rather than envisioning truly novel events. Given that, in the present study, aMCI patients tended, more than controls, to produce future events that were rather similar to past events, it could be posited that they had difficulty constructing scenarios that had never happened and therefore fell back (partially) on old episodic memories. If this were the case, this finding would cast some doubt on the accrued wisdom that future thinking and remembering involve primarily similar processes. One could argue, at least on the basis of this observation, that future thinking involves additional cognitive processes which are impaired in aMCI. This hypothesis is indirectly supported by results of neuroimaging studies. Recently, Addis, Pan, et al. (2009) identified, in healthy young adults, two subsystems within the network involved in remembering and imagining events, the imagining subsystem and the remembering subsystem, consisting, respectively, of neural regions that responded more strongly to imagining than remembering, and of regions showing the reverse pattern. The authors suggested that the imagining subsystem may reflect the increased cognitive demands related to recombining episodic details into an imaginary scenario, as opposed to the recasting of an entire past event. Future research should therefore focus on identifying the neural correlates of remembering and imagining in aMCI patients, as well as in other pathological conditions. This approach, associated with the analyses of subjective and objective detail ratings (i.e., according to Levine et al.'s procedure) may significantly improve our understanding of patients' ability to simulate future events.

Finally, another result that is worthy of notice in the present study is the number of internal and external details produced by controls and aMCI patients. Healthy older adults and aMCI patients who participated in earlier studies produced a mean number of internal and external details larger than controls and aMCI patients in the present study.² The differences in the number of details seem not to be related to differences in the participants' selection criteria, as the groups of aMCI patients and controls were almost equivalent across the studies with respect to mean age and education. Therefore, it appears more reasonable that these divergent findings are associated with factors inherent to the specific task used in the different studies. For instance, in Levine et al. (2002) and in Murphy et al. (2008) participants were asked to choose, in the context of the Autobiographical Interview (Levine et al., 2002), a personal past memory event that happened at a specific time and place for specific life periods. These events were presumably the most accessible and, therefore, the most likely to yield detailed recollections. On the other hand, in the studies by Addis et al. (2008), Addis, Pan, et al. (2009) and Addis, Sacchetti, et al. (2009)

participants were cued to recollect past events (and to simulate future events) by means of single words. This procedure is unquestionably more demanding than freely recollecting past experiences. However, these authors also used general probes to clarify instructions and encouraged further description of details. In the study by Murphy et al. (2008) general probes were also given to encourage recall of detailed information, particularly if the participant had trouble coming up with a specific detailed memory or provided a very brief recollection.

In the present study, a relevant aspect of the procedure was that participants were cued to recollect and simulate past and future events by means of single words and no general probe was provided. Apparently, the procedure of the present study provides the participants with the lowest support for recollection and simulation of events, and may thus be responsible for the overall lower number of details produced by controls and aMCI.

Overall, the analysis of extant results in the literature reveals that research in this area is still in its infancy and needs to be further informed in the future by advances in understanding of both the quantitative and qualitative differences in the ability of normal and pathological populations to engage in episodic future thinking.

Acknowledgments

The present research was supported by a grant from the Italian Ministry of Education, University, and Research (PRIN 2008) awarded to Maria A. Brandimonte. We are grateful to two anonymous reviewers for their precious comments and suggestions on an earlier version of the manuscript. We wish to thank Laura Valkonen for editing the manuscript.

References

- Addis, D. R., Pan, L., Vu, M. A., Laiser, N., & Schacter, D. L. (2009). Constructive episodic simulation of the future and the past: Distinct subsystems of a core brain network mediate imagining and remembering. *Neuropsychologia*, *47*, 2222–2238.
- Addis, D. R., Sacchetti, D. C., Allyn, B. A., Budson, A. E., & Schacter, D. L. (2009). Episodic simulation of future events is impaired in mild Alzheimer's disease. *Neuropsychologia*, *47*, 2660–2671.
- Addis, D. R., Wong, A. T., & Schacter, D. L. (2007). Remembering the past and imagining the future: Common and distinct neural substrates during event construction and elaboration. *Neuropsychologia*, *45*, 1363–1377.
- Addis, D. R., Wong, A. T., & Schacter, D. L. (2008). Age-related changes in the episodic simulation of future events. *Psychological Science*, *19*, 33–41.
- American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders DSM-IV* (4th ed.). Washington, DC: American Psychiatric Association.
- Atance, C. M., & O'Neill, D. K. (2001). Episodic future thinking. *Trends in Cognitive Science*, *5*, 533–539.
- Buckner, R. L., & Carroll, D. C. (2007). Self-projection and the brain. *Trends in Cognitive Sciences*, *11*(2), 49–57.
- Buckner, R. L., Andrews-Hanna, J. R., & Schacter, D. L. (2008). The brain's default network: Anatomy, function and relevance to disease. *Annals of the New York Academy of Sciences*, *1124*, 1–38.
- Burani, C., Barca, L., & Arduino, L. S. (2001). Una base di dati sui valori di età di acquisizione, frequenza, familiarità, immaginabilità, concretezza, e altre variabili lessicali e sublessicali per 626 nomi dell'Italiano. *Giornale Italiano di Psicologia*, *4*, 839–856.
- Cabeza, R., & St Jacques, P. (2007). Functional neuroimaging of autobiographical memory. *Trends in Cognitive Sciences*, *11*, 219–227.
- Carlesimo, G. A., Caltagirone, C., Fadda, L., Marfia, G., Gainotti, G., et al., & Gruppo

- per la standardizzazione della batteria per il Deterioramento Mentale. (1995). Batteria per la valutazione del Deterioramento Mentale (parte III): analisi dei profili qualitativi di compromissione cognitiva. *Archivio di Psicologia, Neurologia e Psichiatria*, 4, 489–502.
- Carlesimo, G. A., Caltagirone, C., & Gainotti, G. (1996). The Mental Deterioration Battery: normative data, diagnostic reliability and qualitative analyses of cognitive impairment. The Group for the Standardization of the Mental Deterioration Battery. *European Neurology*, 36, 378–384.
- Chertkow, H., & Bub, D. (1990). Semantic memory loss in dementia of Alzheimer's type: What do various measures measure? *Brain*, 113, 397–417.
- Conway, M. A. (2001). Sensory-perceptual episodic memory and its context: Autobiographical memory. *Philosophical Transactions of the Royal Society of London, Series B: Biological Sciences*, 356, 1375–1384.
- Conway, M. A., & Pleydell-Pearce, C. W. (2000). The construction of autobiographical memories in the self-memory system. *Psychological Review*, 107, 261–288.
- D'Argembeau, A., & van der Linden, M. (2004). Phenomenal characteristics associated with projecting oneself back into the past and forward into the future: Influence of valence and temporal distance. *Consciousness and Cognition*, 13, 844–858.
- D'Argembeau, A., & van der Linden, M. (2006). Individual differences in the phenomenology of mental time travel: the effects of vivid visual imagery and emotion regulation strategies. *Consciousness and Cognition*, 15, 342–350.
- Driscoll, I., Hamilton, D. A., Petropoulos, H., Yeo, R. A., Brooks, W. M., Baumgartner, R. N., et al. (2003). The aging hippocampus: cognitive, biochemical and structural findings. *Cerebral Cortex*, 13, 1344–1351.
- Dubois, B., Slachevsky, A., Litvan, I., & Pillon, B. (2000). The FAB: A frontal assessment battery at bedside. *Neurology*, 55, 1621–1626.
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12, 189–198.
- Gamboz, N., Brandimonte, M. A., & De Vito, S. (2010). The role of past in the simulation of autobiographical future episodes. *Experimental Psychology*.
- Gauthier, S., Reisberg, B., Zudig, M., Petersen, R. C., Ritchie, K., Broich, K., et al. (2006). Mild cognitive impairment. *Lancet*, 367, 1262–1270.
- Giovanello, K. S., Schnyer, D. M., & Verfaellie, M. (2004). A critical role for the anterior hippocampus in relational memory: evidence from an fMRI study comparing associative and item recognition. *Hippocampus*, 14, 5–8.
- Hassabis, D., & Maguire, E. A. (2007). Deconstructing episodic memory with construction. *Trends in Cognitive Sciences*, 11, 299–306.
- Hassabis, D., Kumaran, D., Vann, S. D., & Maguire, E. A. (2007). Patients with hippocampal amnesia cannot imagine new experiences. *Proceedings of the National Academy of Sciences of the United States of America*, 104, 1726–1731.
- Hodges, J. R., & Patterson, K. (1995). Is semantic memory consistently impaired early in the course of Alzheimer's disease? Neuroanatomical and diagnostic implications. *Neuropsychologia*, 33, 441–459.
- Hou, C. E., Bruce, L., Kramer, M., & Kramer, H. (2005). Patterns of autobiographical memory loss in dementia. *International Journal of Geriatric Psychiatry*, 20, 809–815.
- Iavarone, A., Ronga, B., Pellegrino, L., Loré, E., Vitaliano, S., Galeone, F., et al. (2004). The Frontal Assessment Battery (FAB). Normative data from an Italian sample and performances of patients with Alzheimer's disease and frontotemporal dementia. *Functional Neurology*, 19, 191–195.
- Ivanoiu, A., Cooper, J. M., Shanks, M. F., & Venneri, A. (2006). Patterns of impairment in autobiographical memory in the degenerative dementias constrain models of memory. *Neuropsychologia*, 44, 1936–1955.
- Jack, C. R., Jr., Petersen, M. O., O'Brien, P. C., Smith, G. E., Ivnik, R. J., Boeve, B. F., et al.

- (2000). Rates of hippocampal atrophy correlate with change in clinical status in aging and AD. *Neurology*, 55, 484–489.
- Killiany, R. J., Hyman, B. T., Gomez-Isla, T., Moss, M. B., Kikinis, R., Jolesz, F., et al. (2002). MRI measures of entorhinal cortex vs hippocampus in preclinical AD. *Neurology*, 58, 1188–1196.
- Klein, S. B., & Loftus, J. (2002). Memory and temporal experience: The effects of episodic memory loss on an amnesic patient's ability to remember the past and imagine the future. *Social Cognition*, 20, 353–379.
- Kopelman, M. D., Wilson, B. A., & Baddeley, A. D. (1989). The autobiographical memory interview: A new assessment of autobiographical and personal semantic memory in amnesic patients. *Journal of Clinical and Experimental Neuropsychology*, 11, 724–744.
- Kopelman, M. D., Wilson, B. A., & Baddeley, A. D. (1990). The autobiographical memory interview. Bury St. Edmunds: Thames Valley Test.
- Levine, B., Svoboda, E., Hay, J. F., Winocur, G., & Moscovitch, M. (2002). Aging and autobiographical memory: Dissociating episodic from semantic retrieval. *Psychology and Aging*, 17, 677–689.
- Leyhe, T., Müllera, S., Miliana, M., Eschweiler, G. W., & Saura, R. (2009). Impairment of episodic and semantic autobiographical memory in patients with mild cognitive impairment and early Alzheimer's disease. *Neuropsychologia*, 47, 2464–2469.
- Maguire, E. A. (2001). Neuroimaging studies of autobiographical event memory. *Philosophical Transactions of the Royal Society of London Series B: Biological Sciences*, 356, 1441–1451.
- Measso, G., Cavarzeran, F., Zappalà, G., Lebowitz, B. D., Crook, T. K., Pirozzolo, F. J., et al. (1993). The Mini-Mental State Examination: Normative study of an Italian random sample. *Developmental Neuropsychology*, 9, 77–85.
- Murphy, K. J., Troyer, A. K., Levine, B., & Moscovitch, M. (2008). Episodic, but not semantic, autobiographical memory is reduced in amnesic mild cognitive impairment. *Neuropsychologia*, 46, 3116–3123.
- Nestor, P. J., Graham, K. S., Bozeat, S., Simons, J. S., & Hodges, J. R. (2002). Memory consolidation and the hippocampus: Further evidence from studies of autobiographical memory in semantic dementia and frontal variant frontotemporal dementia. *Neuropsychologia*, 40, 633–654.
- Okuda, J., Fujii, T., Ohtake, H., Tsukiura, T., Tanji, K., Suzuki, K., et al. (2003). Thinking of the future and the past: The roles of the frontal pole and the medial temporal lobes. *Neuroimage*, 19, 1369–1380.
- Petersen, R. C., & Negash, S. (2008). Mild cognitive impairment: An overview. *CNS Spectrums*, 13, 45–53.
- Petersen, R. C., Doody, R., Kurz, A., Mohs, R. C., Morris, J. C., Rabins, P. V., et al. (2001). Current concepts in mild cognitive impairment. *Archives of Neurology*, 58, 1985–1992.
- Petersen, R. C., Smith, G. E., Waring, S. C., Ivnik, R. J., Tangalos, E. G., & Kokmen, E. (1999). Mild cognitive impairment: Clinical characterization and outcome. *Archives of Neurology*, 56, 303–308.
- Piolino, P., Desgranges, B., Benali, K., & Eustache, F. (2002). Episodic and semantic remote autobiographical memory in ageing. *Memory*, 10, 239–257.
- Schacter, D. L., & Addis, D. R. (2007). The cognitive neuroscience of constructive memory: Remembering the past and imagining the future. *Philosophical Transactions of the Royal Society of London, Series B: Biological Sciences*, 362, 773–786.
- Schacter, D. L., Addis, D. R., & Buckner, R. L. (2008). Episodic simulation of future events. Concepts, data, and applications. *Annals of the New York Academy of Sciences*, 1124, 39–60.
- Snowden, J. S., Griffiths, H. L., & Neary, D. (1996). Semantic -episodic memory interactions in semantic dementia: Implications for retrograde memory function. *Cognitive Neuropsychology*, 13, 1101–1137.

- Spreng, R. N., & Levine, B. (2006). The temporal distribution of past and future autobiographical events across the lifespan. *Memory and Cognition*, 34, 1644–1651.
- Szpunar, K. K., & McDermott, K. B. (2008). Episodic future thought and its relation to remembering: Evidence from ratings of subjective experience. *Consciousness and Cognition*, 17, 330–334.
- Szpunar, K. K., Watson, J. M., & McDermott, K. B. (2007). Neural substrates of envisioning the future. *Proceedings of the National Academy of Sciences of the United States of America*, 104, 642–647.
- Tulving, E. (1985). Memory and consciousness. *Canadian Psychologist*, 25, 1–12.
- Tulving, E. (2002). Episodic memory: From mind to brain. *Annual Review of Psychology*, 53, 1–25.

Tables and Figures

Table 1. Mean ratings (and standard deviations) as a function of event type (past, future) and group (aMCI, control).

| | Past events | | Future events | |
|-----------------------------------|-------------|-----------|---------------|-----------|
| | C | aMCI | C | aMCI |
| Sensorial details | 4.2 (1.1) | 3.6 (1.3) | 4.0 (1.3) | 3.6 (1.0) |
| Clarity of location | 5.1 (1.0) | 5.7 (0.6) | 5.1 (0.9) | 4.8 (0.9) |
| Feeling of experiencing | 6.2 (0.9) | 5.1 (1.6) | 6.0 (0.9) | 4.4 (1.7) |
| Frequency of occurrence (novelty) | | | 1.6 (0.9) | 4.2 (1.5) |

Note: Novelty decreases proportionately as frequency of occurrence increases, i.e., the lower the rating, the higher the novelty.

Table 2. Frequency distribution of ratings concerning the novelty of future scenarios in aMCI patients and controls.

| Ratings | aMCI | C |
|---------|------|------|
| 1 | 28.6 | 66.1 |
| 2 | 1.8 | 26.8 |
| 3 | 3.6 | 0 |
| 4 | 12.5 | 0 |
| 5 | 17.9 | 5.4 |
| 6 | 12.5 | 0 |
| 7 | 23.2 | 1.8 |

Note: The numbers indicate the percentage of events that received ratings from 1 to 7 (out of 56 near events and 56 distant events).

Fig. 1.

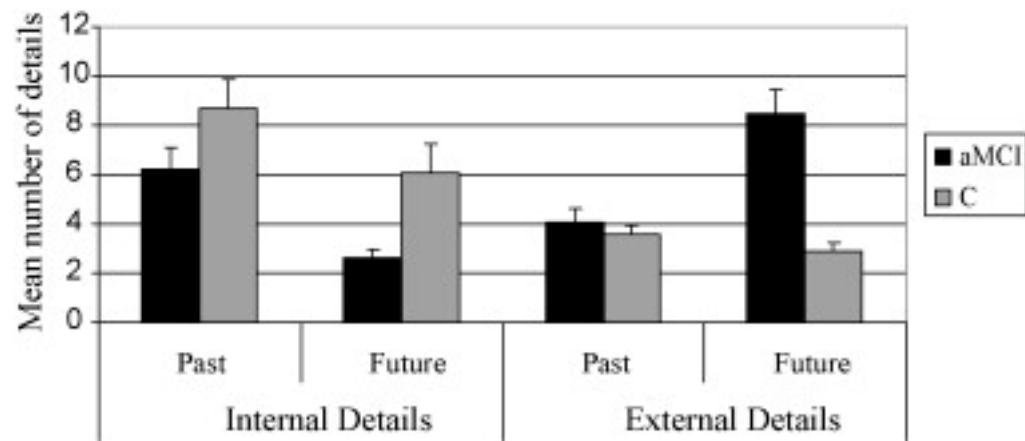


Fig. 1 Mean number of internal and external details per event generated for past and future events by aMCI patients and controls. Error bars are standard errors of the mean.