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Flexibility Decline Contributes to Similarity of Past and Future Thinking in Alzheimer's Disease

Mohamad El Haj^{1,*}, Pascal Antoine¹, and Dimitrios Kapogiannis²

¹Laboratoire SCALab CNRS UMR 9193, Department of Psychology, Research Unit on Cognitive and Affective Sciences University of Lille, France ²Laboratory of Neurosciences, Department of Neurosciences, National Institute on Aging, Baltimore, Maryland

Abstract

A striking similarity has been suggested between past and future thinking in Alzheimer's Disease (AD), a similarity attributable to abnormalities in common modular cognitive functions and neuroanatomical substrates. This study extends this literature by identifying specific executive function deficits underlying past and future thinking in AD. Twenty-four participants with a clinical diagnosis of probable (mild) AD and 26 older controls generated past and future events and underwent tests of binding and the executive functions of flexibility, inhibition, and updating. AD patients showed similar autobiographical performances in past and future event generation, and so did control participants. In each group, the similarity of past and future thinking was predicted by flexibility. Furthermore, AD patients with low flexibility showed higher similarity of past and future thinking than those with high flexibility. These findings are interpreted in terms of involvement of the hippocampus and frontal lobes in future thinking. Deficits in these brain regions in AD are likely to compromise the ability to recombine episodic information into novel and flexible configurations as scenarios for the future.

Keywords

Alzheimer's disease; binding; flexibility; future thinking; hippocampus

INTRODUCTION

Recent research has established important links between the ability to remember past events and the ability to imagine events that one might plausibly experience in the future. Both abilities emerge approximately at the same time of development (around age three to four; Suddendorf, 2010) and decline in parallel among older adults (Addis et al., 2008), individuals with acquired amnesia (Tulving, 1985; Klein et al., 2002), depression (Williams et al., 1996), or schizophrenia (D'Argembeau et al., 2008). On a cognitive level, both abilities were found to trigger self-projection (Buckner and Carroll, 2007), a capacity referring to mental time travel or the ability to mentally project oneself backward in time to

*Correspondence to: Mohamad El Haj, Université de Lille 3, Département de Psychologie, Domaine du Pont de Bois, B.P 60149, 59653, Villeneuve d'Ascq, France. mohamad.elhaj@univ-lille3.fr.

re-experience past events or forward in time to pre-experience future events (Tulving, 1985). Moreover, both remembering the past and imagining the future involve similar phenomenological characteristics, such as retrieving of contextual details, emotional valence, mental simulation, and imagery (D'Argembeau and Van der Linden, 2004; D'Argembeau et al., 2008, 2012).

The intimate similarity between past and future thinking is also observed in Alzheimer's disease (AD). The pioneer study in this field was done by Addis et al. (2009), who asked AD patients to remember past autobiographical events and imagine future autobiographical events. These researchers observed no significant differences between past and future thinking in regard to temporal distance, personal significance, or emotional intensity. A similar observation was reported in our study (El Haj et al., 2015), where we compared past and future projection in AD in regard to general autobiographical performance, contextual details or pieces of information about "when, where, and who," self-defining memories or events significantly contributing to a sense of identity (Blagov and Singer, 2004), and level of reliving (i.e., mental time travel). Specifically, we found similar autobiographical and contextual performance, similar amount of self-defining memories, and similar reliving during past and future projection in AD.

The similarity between past and future thinking in AD can be interpreted on the basis of neuroimaging studies that implicate the default mode brain network (which includes nodes at medial prefrontal, lateral parietal, medial parietal (precuneus and retrosplenial cortex), and medial temporal areas including the hippocampus (Okuda et al., 2003; Addis et al., 2007; Schacter et al., 2007; Szpunar et al., 2007; Viard et al., 2012) in both functions. Interestingly, the hippocampus (e.g., Pennanen et al., 2004), as well as the posteromedial nodes of the default mode network (Seeley et al., 2009), show early and prominent amyloid deposition in AD and are structurally and functionally compromised by the disease. Further support for hippocampal engagement in future thinking comes from lesion studies in patients with hippocampal damage showing difficulties in constructing imaginary scenarios of everyday scenes (Hassabis et al., 2007; Andelman et al., 2010; Race et al., 2011).

According to the constructive episodic simulation hypothesis, as proposed by Schacter and Addis (2007a, 2007b), the hippocampus is important for future simulation as it enables not only the extraction of relevant contextual details, but also their recombination and integration into coherent future events. By this view, the hippocampus binds together distinct multimodal elements to create novel scenes projected to the future. These multimodal elements may include contextual details such as where and when a future event may take place, sensory perceptions such as visual images, sounds, smells, and actions that were encountered during past events (Hassabis and Maguire, 2009). Addis and Schacter (2011, see also, Schacter and Addis, 2009) further suggested that the hippocampus mediates the recombination of features stored in episodic memory, such as places, people, and objects, to form coherent future scenarios. The hippocampal dysfunction in AD may impair binding of these features into coherent future scenes. Consequently, damage to the hippocampus may be responsible for the similarity of past and future thinking in AD.

The similarity between past and future thinking in AD may also be attributed to executive dysfunction attributable to frontal lobe involvement by the disease. First, the phenomenon could be due to impaired flexibility. When foreseeing, AD patients may have difficulties in breaking down stored episodic memories into their modular features and reassemble them in order to try out alternative scenarios. This view is not inconsistent with the constructive episodic simulation hypothesis, which requires flexible recombining of stored elements into coherent simulations of future events (Schacter and Addis, 2009; Addis and Schacter, 2011). Second, the similarity between past and future thinking in AD may be due to decline in inhibitory control. Inhibitory decline may result in failure to inhibit salient motivational drives and the inability to engage in conceptual change, which manifest as perseveration (Hauser, 1999). In a related vein, inhibitory dysfunction may be related to the redundancy or the tendency of older adults to repeat the same discourse. This is suggested by studies showing relationship between age-related inhibitory impairment and off-target verbosity or discourse that may start out on a topic but quickly becomes redundant or irrelevant to the main topic (Arbuckle and Gold, 1993; Trunk and Abrams, 2009). The third executive function potentially implicated is updating. When foreseeing, AD patients may encounter difficulties in updating stored representations by integrating previously unrelated experiences, scripts, or beliefs. In a related vein, a recent study found relationship between updating failures and autobiographical decline for past events in aging (Piolino et al., 2010).

To summarize, past and future thinking in AD were found to trigger similar levels of personal significance, emotional intensity, autobiographical performance, contextual recall, and reliving; a similarity that was attributed to abnormalities in common neuroanatomical pathways (Addis et al., 2009; El Haj et al., 2015). To further advance this field, the present study aimed at assess whether some specific executive dysfunction underlies the striking similarity between past and future thinking in AD. We assessed whether this similarity may be due to AD-related hippocampal decline resulting in impaired binding of disparate elements of past events into coherent future scenarios, but also assessed its association with dysfunction in a range of executive functions, including flexibility, inhibitory control and updating. These executive accounts were tested in an exploratory fashion with correlation and regression analyses, conducted on measures of similarity between past and future thinking, binding, flexibility, inhibition, and updating in AD participants and control older adults.

METHOD

Participants

The study included 24 participants with a clinical diagnosis of probable AD at the mild stage (16 women and 8 men; $M_{age} = 72.08$ years, $SD = 7.20$; $M_{years\ of\ formal\ education} = 8.42$, $SD = 2.46$) and 26 control older adults (17 women and 9 men; $M_{age} = 72.58$ years, $SD = 7.20$; $M_{years\ of\ formal\ education} = 9.58$, $SD = 2.77$). The AD participants were recruited from local retirement homes, and were diagnosed by an experienced neurologist or geriatrician by applying the National Institute on Aging-Alzheimer's association clinical criteria (McKhann et al., 2011). The control participants were often spouses or companions of the AD participants and were living at their homes independently. There were no

significant differences between the two cohorts regarding age [$t(48) = 0.24$, $P > 0.10$], sex [$\chi^2(1, N = 50) = 0.01$, $P > 0.10$], and educational level [$t(48) = 1.56$, $P > 0.10$].

We acquired informed consent and all participants were able to withdraw whenever they wished. Exclusion criteria for all participants were: significant psychiatric or neurological illness, alcohol or drug abuse, major visual or auditory acuity difficulties that would have prevented completion of study tasks.

Neuropsychological Characteristics

We administered tests tapping general cognitive functioning, episodic memory, depression, binding, flexibility, inhibition, and updating. All scores are summarized in Table 1.

General cognitive functioning, episodic memory, and depression—General cognitive functioning was assessed with the Mini Mental State Exam (MMSE, Folstein et al., 1975), and the maximum score was 30 points. Episodic memory was evaluated with a French adaptation of the task of Grober and Buschke (1987). The participants had to retain 16 words, and after immediate cued recall, they proceeded to a 20-s distraction phase during which they had to count numbers aloud. This phase was followed by two minutes of free recall and the score from this phase (out of a maximum of 16) was retained as episodic score. Depression was assessed with the self-report Hospital Anxiety and Depression Scale (HADS, Zigmond and Snaith, 1983) consisting of seven items scored on a four-point Likert scale from zero (not present) to three (considerable). The maximum score was 21 points, and as recommended by Herrmann (1997), the cut-off was set at $> 10/21$ points.

Binding—As depicted in Figure 1, binding was assessed with a task requiring associating letters with their locations on a grid. The task included 20 trials. On each trial, participants were exposed to four grids and one retention support. Each grid was $16 \times 16 \text{ cm}^2$ printed on a white A4 sheet of paper and was presented for three seconds. In the first three grids, a different letter was presented in a different location on the grid, and participants were asked to remember its location. After a retention support was presented for ~ 3 s, the participants had to decide whether the letter in the fourth grid appeared in the same location as before or not. A recognition score for each participant was calculated as the number of correct “yes” and “no” responses and the maximum score was 20 points.

This binding task provides a reliable assessment of the ability to connect disparate contextual features into coherent events in neurodegenerative diseases (El Haj et al., 2013a, 2013b). Moreover, this binding task may reflect associative processes in the hippocampus (Weniger et al., 2004; Mayes et al., 2007; Langston and Wood, 2010), and was found to be abnormal in AD (Parra et al., 2009, 2010, for a review, see, El Haj and Kessels, 2013).

Flexibility, inhibition, and updating—We chose to measure these three aspects of executive function due to their potential implication in past and future thinking in AD, but also in accordance with the executive model of Miyake et al., (2000) that has been extensively validated in studies of normal aging (e.g., Piolino et al., 2010) and AD (e.g., El Haj et al., 2012a, 2012b).

Flexibility was assessed with the Plus–Minus task that included three lists, each containing 20 numbers. On List 1, participants had to add one to each number, whereas on List 2 they had to subtract one from each number, and, on List 3, to add and subtract one alternately. The score referred to the difference between the time participants needed to complete List 3 and the average time that participants needed to complete Lists 1 and 2.

Inhibition was assessed with the Stroop task that involved three subtests, each displaying 100 stimuli. In the first subtest (word reading), participants had to read 100 words of colors printed in black ink. In the second subtest (color naming), participants had to name the color of 100 colored squares. In the third subtest (color-word interference), they had to name the color of color-words printed in incongruously colored ink (e.g., the word “red” written in green). The inhibition score referred to the completion time for the interference condition minus the average completion time for word reading and color naming.

Updating was evaluated with the two-back task. Thirty letters were sequentially presented and participants were asked to decide whether or not each letter was the same as the letter presented two items before. The updating score referred to the number of erroneous responses and the maximum score was 30 points.

Autobiographical Assessment

The neuropsychological assessment took place in two sessions, counterbalanced and separated by ~1 week. One session included remembering past events and the other imagining future events. In each session, participants were asked to “recount in detail an event in their lives” or “imagine in detail a future event,” regardless of when the event occurred or will occur. When constructing future events, participants were instructed to imagine events that might reasonably happen in the future. Participants were also instructed not to describe a past event or any part of it, but rather to imagine something completely new (for the same instruction, see, D’Argembeau and Van der Linden, 2006; Addis et al., 2007). For future and past events, the investigator explained that participants had to be precise and specific: events had to have lasted/last no more than a day and details had to be provided, such as time and place at which events had/will have occurred. Some examples were provided to illustrate what would be considered as a specific event. Participants were also asked to describe their feelings and emotions during these events. Participants were allowed three minutes, and the duration was stated from the onset so participants could plan accordingly. This time limit was adopted to avoid potential redundancy and/or distractibility (Addis et al., 2009; El Haj et al., 2012a, 2012b, 2013c, 2015) and was kept constant to control for duration of sustained mental effort. All autobiographical constructions were recorded using a smartphone and were transcribed at a later time.

Autobiographical performance was scored with the TEMPau scale (Test épisodique de mémoire du passé, Piolino et al., 2003, 2006, 2007), an autobiographical evaluation instrument inspired by classic autobiographical evaluations (Kopelman et al., 1989) and adapted in French. For each event, we attributed zero if there was no memory or only general information about a theme (e.g., my childhood). We attributed one point for a repeated or an extended event (e.g., I went to school everyday); two points for an event situated in time or/and space (e.g., I went to school everyday in town X); three points for a

specific event lasting < 24 h and situated in time and space (e.g., there were clowns at a particular celebration of Christmas at my school); and four points for a specific event situated in time and space enriched with phenomenological details (e.g., feelings, perceptions, thoughts, or visual imagery) (e.g., I was happy to receive a gift from a clown during a particular celebration of Christmas at my school). Thus, the maximum autobiographical score for each participant was four points.

To avoid bias in scoring, events were rated by the first author and an independent rater who was blinded to the study objectives and to individual participants' group membership (AD patients vs. controls). Using Cohen's Kappa coefficient (κ) (Brennan and Prediger, 1981), high inter-rater agreement coefficients were obtained ($\kappa = 0.91$). Cases of disagreement were discussed until a consensus was reached.

Statistical Methods

We first assessed (1) differences between past and future thinking for each group, and (2) differences between AD patients and older adults for past thinking and future thinking. We then calculated differences between past and future thinking in absolute values (i.e., |past-future|), with smaller values indicating important similarity between the two forms of thinking. This measure served to assess correlations between similarity of past and future thinking and executive performances. Next, we performed stepwise regression analysis in order to determine which cognitive performance measures best predicted the similarity between past and future thinking. Regression analyses were followed by median split of flexibility, this to investigate similarity of past and future thinking in participants with low flexibility versus those with high flexibility. Finally, since it would be of interest to highlight potential relationship between future thinking and executive function, we carried out correlations analysis between both components in AD patients and older adults.

Because of fact that autobiographical scores were scalar, nonparametric tests were used. For all tests, level of significance was set as $P = 0.05$, P values between 0.051 and 0.10 was considered as trends, if any.

RESULTS

Similar Autobiographical Performance During Past and Future Thinking

Wilcoxon signed rank tests showed no significant differences in autobiographical performance during past and future thinking, in AD participants ($Z = -1.48$, $P > 0.10$), and controls ($Z = -1.26$, $P > 0.10$). However, Mann-Whitney's U tests showed worse autobiographical performance in AD participants compared to controls during past thinking ($Z = -3.32$, $P = 0.01$), as well as during future thinking ($Z = -3.46$, $P = 0.01$) (see Figure 2).

Significant Correlations Between Similarity of Past and Future Thinking and Flexibility

Spearman's correlational analysis computed separately for AD patients and controls are depicted in Table 2. Bonferroni correction was not applied due to the exploratory nature of our study. There were significant correlations between similarity of past and future thinking, flexibility, and binding in both groups. To detect whether similarity of past and future

thinking was better correlated with flexibility or binding, we converted correlation coefficients into z scores using Fisher's r - to z -transformation (Zr), using the interactive calculator of Lee and Preacher (2013). The latter transformation showed that similarity of past and future thinking was better correlated with flexibility than with binding, and this pattern was observed in both AD patients ($Zr = 3.62$, $P < 0.001$) and controls ($Zr = 4.21$, $P < 0.001$).

Flexibility Contributes to Similarity of Past and Future Thinking

To investigate which of the four cognitive functions explained a significant amount of variance in similarity of past and future thinking, we carried out a forward stepwise regression analysis. Similarity of past and future thinking was used as the dependent variable, whereas the predictor variables were the four cognitive measures. Regression analysis showed that performance on the Plus-Minus task was the major variable contributing to the similarity of past and future thinking, accounting for 33.1% ($P < 0.01$) of its variance in AD patients and 24.2% ($P = 0.01$) in controls.

Higher Similarity of Past and Future Thinking in AD Patients and Controls With Lower Flexibility

To provide further support for the relationship between similarity of past and future thinking and flexibility, we carried out a median split, dividing AD patients into participants with high flexibility (score < 9.76 , $n = 12$) and low flexibility (score > 9.76 , $n = 12$). It is important to note that (1) on the Plus-Minus task, high scores meant longer reaction times, and consequently, poorer performance, and 2) low scores on similarity of past and future thinking referred to higher similarity between the two forms of thinking. There was higher similarity of past and future thinking in AD patients with low flexibility ($M = 0.08$, $SD = 0.27$) than in those with high flexibility ($M = 0.77$, $SD = 0.59$), ($Z = -2.83$, $P = 0.01$). The same conclusion was reached in controls divided into participants with high flexibility (score < 5.77 , $n = 13$) and low flexibility (score > 5.77 , $n = 13$): higher similarity of past and future thinking was observed in those with low flexibility ($M = 0.50$, $SD = 0.64$) than in those with high flexibility ($M = 1.33$, $SD = 0.65$), ($Z = -3.16$, $P < 0.01$).

Because binding was significantly correlated with similarity of past and future thinking, we considered the possibility that higher similarity would be observed in participants with low than in those with high binding. To address this hypothesis, we implemented a median split, dividing AD patients into those with high binding (score > 14.00 , $n = 14$) versus low binding (score < 14.00 , $n = 9$). One participant with score equal to the median value was not included in the analysis. No significant differences were observed between AD patients with high binding ($M = 1.11$, $SD = 0.60$) and those with low binding ($M = 0.79$, $SD = 0.89$) in similarity of past and future thinking ($Z = -1.31$, $P > 0.10$). The same conclusion was reached in controls divided into those with high binding (score > 18.50 , $n = 11$, M similarity $= 0.64$, $SD = 0.67$) versus low binding (score < 18.50 , $n = 15$, M similarity $= 0.27$, $SD = 0.46$) ($Z = -1.52$, $P > 0.10$).

Significant Correlations Between Future Thinking and Binding in AD

Spearman's correlational analysis showed significant correlation between future thinking and binding in AD ($r = -0.43$, $P < 0.05$). Correlations between future thinking and other cognitive functions were not significant. Past thinking was only significantly correlated with updating ($r = 0.44$, $P < 0.05$). In controls, future thinking was only significantly correlated with flexibility ($r = 0.63$, $P < 0.01$), and binding ($r = -0.44$, $P < .05$), whereas past thinking was only significantly correlated with updating ($r = 0.40$, $P < 0.05$). It is noteworthy that, in controls, the correlation between future thinking and flexibility was higher than that with binding ($Zr = 4.12$, $P < 0.001$).

DISCUSSION

In light of empirical research showing striking similarity of past and future thinking in AD (Addis et al., 2009; El Haj et al., 2015), this article aimed at investigating the cognitive underpinnings of this similarity. In particular, we examined the implication of a hippocampal-dependent function and several frontal-lobe-dependent executive functions. When asked to describe past and future events, AD patients showed similar autobiographical performances. This similarity was reliably correlated with and predicted by flexibility. Further supporting the relationship between flexibility and similarity of past and future thinking, AD patients with lower flexibility showed higher similarity whereas those with higher flexibility showed lower similarity. Prior to discussing the relationship between flexibility and similarity of past and future thinking, it is appropriate (1) to discuss autobiographical performance as observed in our study vis-à-vis previous studies, and (2) to emphasize the relationship between future thinking and executive functions.

Autobiographical Recall in AD Participants

There is a substantial body of literature suggesting that memory for past autobiographical events is impaired in AD (Greene et al., 1995; Addis and Tippett, 2004; Ivanoiu et al., 2006; Leyhe et al., 2009; El Haj et al., 2011, 2012c, 2013b). More specifically, this literature demonstrates a substantial shift from specific to general recall, attributed to transition from an experience of remembering to an experience of just knowing (Greene et al., 1995; Addis and Tippett, 2004; Ivanoiu et al., 2006; Martinelli et al., 2013). This body of literature fits with our finding of poorer autobiographical recall in AD patients compared to control participants. Previous studies have also shown reduced specificity of autobiographical recall for past events in older adults, due to impaired updating (Piolino et al., 2010).

The Relationship between Future Thinking and Modular Cognitive Functions

A relationship has been reported between difficulties in autobiographical memory for past events and working memory decline in AD (Greene et al., 1995). In agreement with prior research, we observed a significant correlation between past thinking in AD and updating, a crucial component of working memory (Baddeley, 1986). Regarding future thinking in AD, we observed a significant correlation between this ability and binding. Hence, future thinking decline may be related to poor recombination of contextual and multimodal sensory information, as encountered during past events, into coherent future events. Regarding our cognitively normal older participants, prior research has linked age-related episodic memory

decline to binding difficulties (Mitchell et al., 2000a, 2000b). Our data extend these studies by showing a reliable relationship between future thinking in normal aging and the ability to bind disparate elements of past events into coherent future scenarios.

The Relationship Between Flexibility and Similarity of Past and Future Thinking

Past and future thinking in AD have been shown to trigger representations with similar personal significance, emotional intensity, autobiographical performance, contextual recall, and reliving (Addis et al., 2009; El Haj et al., 2015). Our study replicates these outcomes by showing similar autobiographical performance during past and future thinking in AD. Our study also extends this research by linking the similarity of past and future thinking to flexibility decline. This suggestion is supported by a correlation analysis showing longer reaction times on the Plus-Minus task (i.e., poorer performance) being correlated with higher similarity in past and future thinking, as well as by a regression analysis, where the latter factor was reliably predicted by the former one. Furthermore, AD patients with low flexibility showed higher similarity of past and future thinking than those with high flexibility. Supporting the constructive episodic simulation hypothesis (Schacter and Addis, 2007a, 2007b), our AD participants had difficulties in flexibly recombining past scenarios into coherent simulations of the future. More precisely, when foreseeing, AD patients have difficulties breaking down preexisting links between available pieces of episodic information in order to establish new links and create new scenarios. This difficulty is also present to a degree in normal aging.

The link between impaired flexibility and higher similarity of past and future thinking may be interpreted in terms of impaired hippocampal and frontal lobes functions. Neuroimaging studies implicate the frontopolar region and future thinking (Okuda et al., 2003; Addis and Schacter, 2008). Age-related executive dysfunction is largely attributable to frontal lobe impairments (West, 2000). In a related vein, flexibility decline as may be observed in aging has been linked to decreased activity in dorsolateral and medial prefrontal cortex (DiGirolamo et al., 2001). Beside the involvement of frontal lobes, flexibility also engages the hippocampal formation. Studies have consistently demonstrated flexibility deficits after damage to the hippocampal formation in rats (Kimble and Kimble, 1965; Nonneman et al., 1974; Fagan and Olton, 1986). In a related vein, Eichenbaum (1992) suggested the hippocampus as an underpinning of representational flexibility in memory, or the process that permits inferential use of memories in novel situations. Taken together, impairment in the frontal lobes and hippocampus are likely to underlie the flexibility decline, and consequently, the higher similarity of past and future thinking in ageing-related cognitive decline and AD.

The Relationship Between Binding and Similarity of Past and Future Thinking

Besides flexibility, significant correlations were observed between binding and similarity of past and future thinking in both AD and control participants. Future thinking is argued to require binding of disparate contextual and multimodal sensory elements of past events into coherent new scenes (Hassabis and Maguire, 2009; Schacter and Addis, 2009; Addis and Schacter, 2011). This scene reconstruction requires the hippocampus, particularly the anterior hippocampus (for a review, see, Addis and Schacter, 2011). Because the

hippocampus is structurally and functionally compromised in AD (e.g., Pennanen et al., 2004), including its binding function (Parra et al., 2009, 2010), it is not surprising that significant correlations were observed between binding ability and the similarity between past and future thinking in our AD participants. More insight on the hippocampal involvement in binding and future thinking can be found in research suggesting a functional distinction within the hippocampus between input structures (dentate gyrus/CA2/CA3) and output structures (subiculum/CA1) (Carr et al., 2010). While the former structures seem to be more involved in encoding, the latter structures seem to be more involved in binding (Carr et al., 2010). According to Addis and Schacter (2011), information recombination during future simulation is mainly supported by CA1/subiculum. This distinction is of further interest since the CA1/subiculum is early and preferentially affected by AD (Kerchner et al., 2010; Small et al., 2011).

Limitations and Prospects for Future Research

Although the present article highlights similarity between past and future thinking, some differences may be observed between both abilities. Whereas past thinking is related to updating in our AD participants, future thinking is related to binding. Differences in executive correlates are also observed between past and future thinking in cognitively normal older adults, wherein the former ability is related to updating whereas the latter is related to flexibility and binding. Hence, although past and future thinking both imply executive correlates, they may engage different specific executive processes. A similar conclusion was reached by a study assessing similarity and dissociation between past and future thinking in terms of mental imagery (de Vite et al., 2014). This study suggested that past thinking is dominated by visual imagery, whereas future thinking is dominated by spatial imagery.

One limitation of our study may be that we assessed only one past and one future autobiographical event per participant due to the desire to limit the testing burden on AD participants. With regard to the theoretical background of the present study, our findings contribute to the constructive episodic simulation hypothesis by providing solid empirical support for the hypothesized involvement of flexibility (Schacter and Addis, 2007a, 2007b, 2009; Addis and Schacter, 2011). Our study also extends this hypothesis by testing the potential involvement of executive functions other than flexibility in future thinking.

Drawing on our findings, subsequent clinical research should assess whether rehabilitation of flexibility may reduce similarity between past and future thinking. As for empirical research, past and future thinking is worth assessing in a wide range of neurological and psychiatric conditions since compromised future thinking has already been observed in individuals with amnesia (Klein et al., 2002), depression (Williams et al., 1996), or schizophrenia (D'Argembeau et al., 2008).

CONCLUSION

Besides highlighting relationship between binding and construction of future autobiographical scenarios in normal aging and AD, the present work emphasizes the relationship between flexibility and similarity of past and future thinking. The present work

also enriches the hippocampal-centered models of future thinking by shedding light on potential frontal involvement. Engagement of the hippocampus and frontal lobes is likely to support binding of past contextual and sensorial information into novel and flexible configurations to script alternative scenarios to approach upcoming situations. Our findings highlight the constructive and adaptive functions of memory, besides its view as a repository of information about the past.

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FIGURE 1.

In the binding task participants had to remember the location of the letters in the first three grids. After the retention support “+” had been displayed, they had to decide whether the letter in the fourth grid appeared in the same location as before or not.

FIGURE 2.

Autobiographical performance of Alzheimer's disease participants and cognitively normal older adults during past and future thinking. Error bars represent intervals of 95% within subjects confidence.

TABLE 1

Neuropsychological and Clinical Characteristics of Alzheimer's Disease (AD) Patients and Control Participants

	Task	AD; <i>n</i> = 24	Older adults; <i>n</i> = 26
General cognitive functioning	Mini-mental state examination (MMSE)	21.83 (1.52) ***	28.31 (1.28)
Episodic memory	Grober and Buschke	5.92 (2.41) ***	10.92 (3.17)
Depression	Hospital Anxiety and Depression Scale (HADS)	7.25 (2.31) **	4.75 (2.85)
Binding	Binding task	13.63 (3.38) ***	17.31 (3.61)
Flexibility	Plus-Minus	11.71 (6.44) ***	5.95 (3.35)
Inhibition	Stroop	64.54 (7.31) ***	36.31 (10.17)
Updating	Two-back	13.46 (6.62) **	8.62 (4.02)

Note: Standard deviations are given between brackets; the maximum score on the MMSE was 30 points; performance on the Grober and Buschke's task referred to free recall and the maximum score was 16 points; the cut-off on the HADS was > 10/21 points; performance on the binding task referred to hits and the maximum score was 20 points; scores on the Plus-Minus and Stroop tasks referred to completion time; performance on the Two-Back task referred to errors and the maximum score was 30 points; differences between groups were significant at:

**
 $P < 0.01$,

 $P < 0.001$; due to abnormal distribution of data, comparison was established with Mann-Whitney's U test.

Correlation Matrix for Similarity of Past and Future Thinking and Cognitive Functions in Alzheimer’s Disease (AD) Patients and Control Participants

TABLE 2

	1	2	3	4	5
AD	1. Similarity	–			
	2. Binding	0.45*	–		
	3. Flexibility	–0.56**	–0.30	–	
	4. Inhibition	–0.14	–0.47*	0.30	–
	5. Updating	–0.25	–0.29	0.13	0.01
Older adults	1. Similarity	–			
	2. Binding	0.50*	–		
	3. Flexibility	–0.61**	–0.42*	–	
	4. Inhibition	–0.12	–0.18	0.21	–
	5. Updating	–0.16	–0.38	0.22	0.08

Note: Similarity referred to differences between past and future thinking in absolute values.

* $P < 0.05$,

** $P < 0.01$.