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Reduced Contextual Information During Future Thinking in Alzheimer's Disease

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This study assessed the ability of patients with Alzheimer’s Disease (AD) to produce “when, where, and who” information during future thinking. AD patients and control participants were invited to imagine future scenarios. Future thinking was analyzed with respect to the number of “when, where, and who” details. Analysis showed fewer “when, where, and who” details in AD participants than in control participants. Fewer “when” than “where” details and fewer “where” than “who” details were observed in AD and controls participants. Production of temporal information in participants with AD was found to be associated with general cognitive functioning, as assessed with the Mini Mental State Exam. Future thinking in AD is mainly associated with reduced contextual information. The diminished ability to construct time-related details during future thinking in AD can be mainly associated with the diminished general cognitive ability in AD, and probably with hippocampal compromise in the disease. We also propose a socio-emotional account according to which, confronted with a limited-time perspective during future thinking, AD patients may tend to maximize their emotional well-being by avoiding time-related information and thinking about friends, family and beloved ones.

Keywords: Alzheimer’s Disease; context memory; future thinking; hippocampus; time

Future thinking refers to the ability to imagine possible future scenarios and to mentally construct a range of potential actions before engaging in them [1, 2]. Thanks to future thinking, humans have the extraordinary ability to disengage from the present to contemplate hypothetical future scenarios [3, 4]. Future thinking has a significant adaptive value as it allows humans to evaluate potential consequences before acting [5, 6]. Besides its role in decision-making, future thinking is important for emotion regulation and socio-emotional functioning [7, 8]. Future thinking has been found to be compromised in several disorders including depression [9-11], schizophrenia [12-14], semantic dementia [15, 16] and Parkinson's Disease [17].

Future thinking has been also found to be compromised in Alzheimer's Disease (AD). In a pioneering study, Addis et al. [18] asked AD participants to remember past events and to simulate future ones. AD participants generated fewer specific details in both past and future thinking than controls. A diminished ability to construct specific future events in AD was also observed in several studies [16, 19, 20]. In these studies, specific future thinking was defined as unique events situated in time and space. Although these studies demonstrated a diminished ability to construct specific future scenarios in AD, they did not investigate the ability of AD patients to produce temporal details (e.g., when the event will occur), spatial details (e.g., where it will occur), or "who" details (e.g., who will be present during the event) during future thinking. Evaluating the effect of AD on these contextual dimensions (i.e., the when, where, and who details) is important because it would allow researchers/clinicians to understand which dimension is altered, or preserved, in AD patients during future thinking. The diminished ability of AD patients to construct specific past/future events has been intimately associated with a weakened ability to mentally relive the past/future [21, 22]. Therefore, research assessing the effects of AD on the

specificity of future thinking may contribute to a better understanding of the subjective experience of AD patients when projecting themselves into the future.

To understand the effects of AD on future thinking, we investigated which specific dimension (i.e. when and where an event will occur, or who will be present during the event) is altered, or preserved, in the disease. We evaluated this issue based on a study on past thinking [23], in which AD participants and older controls were invited to remember past events. Participants were invited to remember where and when the events occurred and who was present. Compared to controls, AD participants demonstrated poor memory of “who, where, and when”. Compared to “who” and “where”, both AD participants and older controls had significant difficulties in remembering the “when” details. These findings highlight difficulties in remembering temporal information when retrieving past events. According to the study by El Haj and Antoine[23], the hallmark of decline in the ability to retrieve contextual information during past thinking in AD is the difficulty to retrieve temporal information.

The compromised ability to retrieve temporal information during past thinking in AD can be interpreted in terms of timing failures. These failures have been observed in studies demonstrating deviations from true clock time in the disease [24]. For instance, Nichelli, Venneri[25] asked AD participants to read either 5, 10, 20, or 40 digits appearing one at a time. At the end of each sequence, participants were asked to judge the elapsed time. Results showed inaccurate time estimations in AD. Timing deviations were also observed by Carrasco, Guillem[26], who asked AD participants to produce three empty intervals (5, 10, and 25 s) by pressing a space bar on a keyboard at the beginning and at the end of each estimated interval. Timing deviations were also observed by Rueda and Schmitter-Edgecombe[27], who asked AD participants to provide a verbal estimation of short time intervals. Similar findings were observed

in a study by Caselli, Iaboli[28], who used time bisection tasks, during which AD participants had to decide whether various time intervals (ranging from 100 to 3000 ms) were shorter or longer than a reference interval. Timing distortions were also observed for relatively long intervals (50 s – 120 s) [29]. Interestingly, they have been associated with the diminished ability of AD patients to mentally project themselves in time [30].

Research suggests a compromised ability to construct specific scenarios during future thinking in AD [16, 18-20]. However, no attempt has yet been made to identify which contextual dimension (i.e., the when, where, and who details) of future thinking is more vulnerable in AD. Our work thus addresses this issue by evaluating the ability of AD patients to construct “when, where, and who” information when imagining future scenarios. To this end, we invited AD participants and older controls to imagine future autobiographical events. We later analyzed the content of future thinking with respect to the number of “when, where, and who” details.

Method

Participants

We recruited 30 participants with a clinical diagnosis of probable mild AD (20 women and 10 men; M age = 71.00 years, SD = 6.94; education level in M years of formal education = 8.83, SD = 2.61) and 32 older controls (22 women and 10 men; M age = 71.63 years, SD = 7.63; M years of formal education = 10.03, SD = 3.09). AD participants were recruited from local retirement homes. Their diagnosis was made by an experienced neurologist or geriatrician according to the AD criteria developed by the National Institute on Aging and the Alzheimer's Association criteria for probable Alzheimer's disease [31]. Control participants were often spouses or companions of AD participants. They were independent and living at home and they were matched with AD

participants according to gender [$\chi^2(1, N = 62) = .03, p > .10$], age [$t(60) = .34, p > .10$], and educational level [$t(60) = 1.64, p > .10$]. Exclusion criteria for all participants were significant neurological or psychiatric illness and alcohol or drug use. All participants freely consented to participating and were able to withdraw whenever they wished. The cognitive characteristics of all participants were evaluated with tests of general cognitive functioning, episodic memory, working memory and depression. Scores are summarized in Table 1. Informed consent was obtained from patients and spouses, in accordance with the principles of the Declaration of Helsinki.

Procedures

General cognitive functioning

General cognitive functioning was evaluated with the Mini Mental State Exam [32] and the maximum score was 30 points.

Episodic memory.

Episodic memory was evaluated with a French version [33] of the episodic task of Grober and Buschke [34]. Participants were invited to retain 16 words, each describing an item belonging to a different semantic category. Immediate cued recall was succeeded by a distraction phase during which participants were invited to count backwards from 374 in 20 s. This distraction phase was succeeded by two minutes of free recall and the score from this phase provided a measure of episodic recall (16 points maximum).

Working memory.

Working memory was evaluated with spans from the WAIS-R [35]. We invited participants to repeat aloud sequences of digits of increasing length read out by the experimenter, either in the

same order (i.e., forward spans) or in the reverse order (i.e., backward spans). Two trials of each sequence length were administered. The forward sequences began with three single digits up to the maximum capacity of participants. The backward sequences also began with three digits up to the maximum capacity of participants. The procedure was stopped if the participants made an error in two consecutive trials of the same length. Performance on the forward and backward spans referred to the number of digits in the correctly repeated last sequence.

Depression.

Depression was evaluated with the Hospital Anxiety and Depression Scale [36], which consists of seven items that were scored by participants on a four-point scale ranging from 0 (not present) to 3 (considerable). The cut-off for definite depression was set at $> 10/21$ points [37].

INSERT TABLE 1 HERE

Future thinking

We assessed two future scenarios by asking each participant to imagine a future event in detail, regardless of whether the event has occurred recently or a long time ago. Participants were invited to imagine any event, lasting no longer than a day. Participants were invited to imagine events that might reasonably occur in the future. They were also instructed not to describe a past event and to imagine something completely new. Importantly, participants were invited to imagine when and where the event would occur, and who would be present. The “when, where, and who” questions were printed on a white A4 sheet that was placed in front of the participants. Participants were allocated two minutes to describe each event and this time limit was stated from the onset so that they could structure the events accordingly. This limit was set to avoid any bias introduced by attention deficits or concomitant distractibility. If the participants ended before the two-minutes

delay, the experimenter encouraged them to add any other information. To avoid any potential contamination (i.e. participants constructing the same event twice), the two scenarios were separated by the cognitive evaluation.

Answers were audio-recorded for transcription and analysis of the “when, where, and who” details. During transcription, details were categorized as “when” information when concerning the year, season, month and/or day. General information such as “once” was not taken into account. The “where” details were names of places where the event occurred, general elements such as “somewhere” not being taken into account. The “who” details were people who were present during the event (e.g. my friend, my spouse, my kid). Again, general information such as “someone” was not taken into account. To avoid bias in scoring, events were rated and categorized by both the experimenter and an independent rater who was blind to the study objective and the participant group. Using Cohen’s Kappa coefficient (κ) [38], a high inter-rater agreement coefficient was obtained ($\kappa = .87$) and cases of disagreement were discussed until a consensus was reached.

Statistical analysis

One point was attributed for each piece of information about the time when and the place where the events occurred and the persons who were present during the events. The sum of the number of “when”, “where” and “who” details in AD participants and older controls are displayed in Figure 1. Owing to abnormal distribution of the data, non-parametric tests were conducted. Between-group comparisons were performed using the Mann-Whitney U test and within-group comparisons were performed using the Wilcoxon signed rank test. Results were provided with effect size: $d = .2$ can be considered a small effect size, $d = .5$ represents a medium effect size and $d = .8$ refers to a large effect size [39]. Importantly, effect size was calculated for non-parametric

tests following recommendations by Rosenthal and DiMatteo[40], and Ellis[41]. For all tests, significance level was set at $p \leq 0.05$, p values between 0.051 and 0.10 were considered as trends, if any.

Results

Poor construction of temporal information during future thinking

Compared to older adults, AD participants constructed fewer “when” ($Z = 4.16, p < .001$, Cohen’s $d = 1.20$), “where” ($Z = -3.62, p < .001$, Cohen’s $d = 1.01$), and “who” ($Z = -3.36, p < .001$, Cohen’s $d = .82$) details during future thinking. AD patients constructed fewer “when” than “where” ($Z = -3.35, p = .003$, Cohen’s $d = .94$) or “who” ($Z = -3.97, p < .001$, Cohen’s $d = 1.17$) details, and fewer “where” than “who” ($Z = -2.28, p = .023$, Cohen’s $d = .60$) details during future thinking. Older controls also constructed fewer “when” than “where” ($Z = 2.48, p = .013$, Cohen’s $d = .60$) or “who” ($Z = -4.16, p < .001$, Cohen’s $d = 1.24$) details, and fewer “where” than “who” ($Z = -2.51, p = .001$, Cohen’s $d = .67$) details during future thinking.

INSERT FIGURE 1 HERE

Correlation analysis

We assessed Spearman correlations between the number of “when, where and who” details and cognitive functioning in AD participants.

Significant correlations

In AD patients, significant correlations were observed between performance on the Mini Mental State Exam and the “when” details ($r = .41, p = .024$),

No significant correlations

In AD patients, analysis demonstrated no significant correlations between the “when” details and performance on the forward span ($r = .12, p = .53$), backward span ($r = .11, p = .56$), or the episodic task of Grober and Buschke ($r = .17, p = .37$). No significant correlations were observed between the “where” details and performance on the forward span ($r = .14, p = .46$), backward span ($r = .12, p = .53$), or the episodic task of Grober and Buschke ($r = .16, p = .40$). No significant correlations were observed between the “who” details and performance on the forward span ($r = .11, p = .56$), backward span ($r = .16, p = .40$), or the episodic task of Grober and Buschke ($r = .17, p = .36$). No significant correlations were observed between performance on the Mini Mental State Exam and the “where” ($r = .30, p = .11$), or “who” details ($r = .29, p = .02$).

Regarding control participants, no significant correlations were observed between the “when” details and performance on the forward span ($r = .18, p = .32$), backward span ($r = .12, p = .51$), the episodic task of Grober and Buschke ($r = .16, p = .40$), or the Mini Mental State Exam ($r = .16, p = .41$). No significant correlations were observed between the “where” details and performance on the forward span ($r = .19, p = .30$), backward span ($r = .18, p = .32$), the episodic task of Grober and Buschke ($r = .12, p = .51$), or the Mini Mental State Exam ($r = .16, p = .40$). No significant correlations were observed between the “who” details and performance on the forward span ($r = .14, p = .44$), backward span ($r = .19, p = .30$), the episodic task of Grober and Buschke ($r = .17, p = .31$), or the Mini Mental State Exam ($r = .20, p = .27$).

Discussion

We evaluated which contextual dimension of future thinking is compromised in AD. To this end, we analyzed the content of future thinking with respect to the number of “when, where

and who” details. Analysis showed fewer “when, where and who” details in AD participants than in older controls during future thinking. Fewer “when” than “where” details and fewer “where” than “who” details were observed in AD and controls participants. Thus, future thinking seems to be associated with reduced temporal information in AD. Interestingly, production of temporal information in participants with AD was found to be associated with general cognitive functioning, as assessed with the Mini Mental State Exam.

Compared to older controls, AD participants produced fewer contextual (i.e., “when, where and who”) details during future thinking. These findings replicate previous research demonstrating a compromised specificity of future thinking in AD [16, 18-20]. However, our findings extend the previous research by revealing difficulties in constructing temporal information during future thinking. These findings are important because they are the first to show that overgenerality of future thinking in AD is characterized by poor temporal information. This poor ability to produce temporal information can be associated with a diminished ability of AD patients to project themselves in time, i.e., a diminished subjective experience of the future. Our claim is supported by the AMAD (Autobiographical Memory in Alzheimer’s Disease) model [21], according to which the compromised ability to retrieve contextual information leads to a diminished subjective experience of the past/future. This theoretical account is supported by experimental evidence demonstrating the poor ability of AD patients to retrieve specific past autobiographical events, a distortion associated with a weakened ability to mentally relive those events [42-44]. In our view, the loss of contextual autobiographical details during future thinking in AD may lead to the de-contextualization of future thinking and to a shift from the ability to mentally relive future events to a general sense of familiarity or to the feeling that one may encounter a future event without the detailed construction of that event.

As demonstrated in our correlation analysis, the difficulty of AD patients to construct temporal information during future thinking can be mainly associated with the decline in general cognitive ability, as assessed with the Mini Mental State Exam. Because AD is mainly characterized by decline in cognitive functioning [31], this decline can explain the diminished ability of AD patients to produce temporal information during future thinking, as observed in our study. From a neurological standpoint, the decreased ability of AD patients to construct temporal information during future thinking can be attributed to a compromised hippocampus. Time distortions have generally been observed in patients with hippocampal lesions [45]. Evidence from studies in both human and animal research has shown the hippocampus to be a key brain region mediating the temporal organization of memories [46]. Besides its involvement in timing, the hippocampus has been attributed a key role in future thinking (for a recent review, see [47]). Several neuroimaging studies have shown that when healthy individuals are invited to retrieve past experiences and imagine future scenarios, a common core network of brain areas is activated that includes the hippocampus and the medial temporal lobes [48-50]. There is therefore a body of evidence suggesting the involvement of the hippocampus in future thinking as well as in timing, which is worth considering since this brain region is preferentially targeted by AD neuropathology [51]. This degeneration may explain general difficulty in future thinking and the difficulty to construct time-related information in AD. This degeneration may also explain the difficulty to construct space-related information in AD as the hippocampus is involved in retrieval of spatial information [52, 53]. According to Burgess[54], the hippocampal role in episodic memory relates to its ability to retrieve spatial information.

A complementary, but not alternative, hypothesis to explain the diminished ability of AD patients to produce temporal information during future thinking is that these patients have to cope

with the realization of their own premature demise. When projecting themselves into the future, AD patients should accept the idea that they have limited time before undergoing substantial physical and cognitive decline. Diagnosis and the gradual loss of cognition and physiological functions in AD may result in the impression of having relatively little time left before death. This assumption is supported by a study demonstrating a major preoccupation with death in AD patients [55]. This may be at the heart of future projections in AD, as patients know that their future time is limited. To cope with this, AD patients may avoid devoting their cognitive resources to time-related information in favor of space-related information or people (e.g., beloved ones) present in these future scenarios. From this point of view, future thinking can be regarded as a mechanism of continued existence in AD; while patients are conscious of their limited future perspective, they continue to imagine space-related elements and people who will be present in these future scenarios. The latter assumption is supported by the fact that AD participants produced fewer “when” than “where” details, and fewer “where” than “who” details.

With a limited time perspective in future thinking, AD patients may thus tend to promote their emotional well-being by avoiding time-related information and thinking about friends, family and their beloved ones. The same can be said for older controls. Young adults generally want to explore the future, have new experiences and new interactions. In contrast, older adults tend to be more aware of the fragility of life and to perceive time as “running out” [56, 57]. With age, people thus tend to focus on savoring life and deepening existing relationships [58, 59]. Since older adults may perceive their time as limited during future thinking, we suggest that they prefer avoiding time-related information and focusing on more positive information, such as who will be present in future scenarios. This hypothesis is supported by the findings of Fung, Carstensen[60], who asked younger adults to reflect on “running out of time” by imagining a hypothetical geographic

move. They found that, just like older adults, these young participants prioritized spending time with friends and family. This shows that, when confronted with a limited time perspective, people tend to put their emotional well-being first by focusing on their beloved ones. This may explain why both older adults and AD patients produced more “who” than “where” or “when” details during future thinking.

While general cognitive performance was significantly correlated with production of the “when” details, this performance was not significantly correlated with the spans task or Grober and Buschke’s task in AD patients. In other words, the diminished ability to produce time-related information during future thinking in AD seems not be associated with working or episodic memory. The diminished ability to produce “where and who” information during future thinking does not seem neither to be associated with cognitive performance in AD patients. Regarding control participants, the production of “when, where, and who” details were not significantly correlated with any cognitive test. Results of our correlation analysis may be, somehow, surprising as one may expect significant correlations between the “when, where, and who” details and episodic memory, as may be assessed with the Grober and Buschke’s task. This lack of significant correlation can be attributed to the fact that the Grober and Buschke’s task simply assesses item memory (i.e., memory for the 16 words) rather than context memory (e.g., where these words were encoded).

Regarding the control participants, they also produced fewer “when” than “where” details, and fewer “where” than “who” details. These findings suggest that future thinking in normal aging is characterized by difficulties on remembering “when” details and, to some extent, difficulties on remembering “where” details. These findings mirror research demonstrating diminished ability on remembering where and when episodic events have been encoded in normal aging [61, 62]. Our

findings add to this literature by showing that, during future thinking, older adults produce fewer “when” than “where” details.

One shortcoming of this paper may be the relatively small sample size, although many effect sizes, as indexed by Cohen’s d , were fair.

To summarize, this study demonstrates the effect of AD on the ability to construct “when, where, and who” information during future thinking. It emphasizes both the neurological and socio-emotional bases for the diminished ability of AD patients to construct time-related information during future thinking. A limited time perspective during future thinking may result in a tendency to process information related to a (positive) social environment rather than to a (negative) limited period of time.

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Table1*Cognitive characteristics of Alzheimer's disease patients and older adults*

| | Task | Alzheimer <i>n</i> = 30 | Older adults <i>n</i> = 32 |
|--|-------------------------------|----------------------------|-------------------------------|
| General cognitive functioning/30 points | Mini-Mental State Examination | 21.48 (1.44)*** | 28.40 (1.25) |
| Episodic memory/16 points | Grober and Buschke | 5.71 (2.13)*** | 11.46 (3.31) |
| Working memory | Forward span | 5.30 (1.37)** | 6.54 (1.72) |
| | Backward span | 3.60 (1.19)*** | 5.44 (1.43) |
| Depression/21 points | HADS | 7.10 (2.00)*** | 4.50 (2.84) |

Note. Standard deviations are given between brackets; the maximum score on the Mini-Mental State Examination was 30 points; the score obtained to the Grober and Buschke (maximum score = 16 points) refers to the first free recall; performance on the forward and backward spans refer to the number of correctly repeated digits; the cut-off on the HADS (Hospital Anxiety and Depression Scale) was > 10/21 points; differences between groups were significant at: ** $p < .01$, *** $p < .001$; after checking for normality of distributions, comparisons were made with Student's t-test.

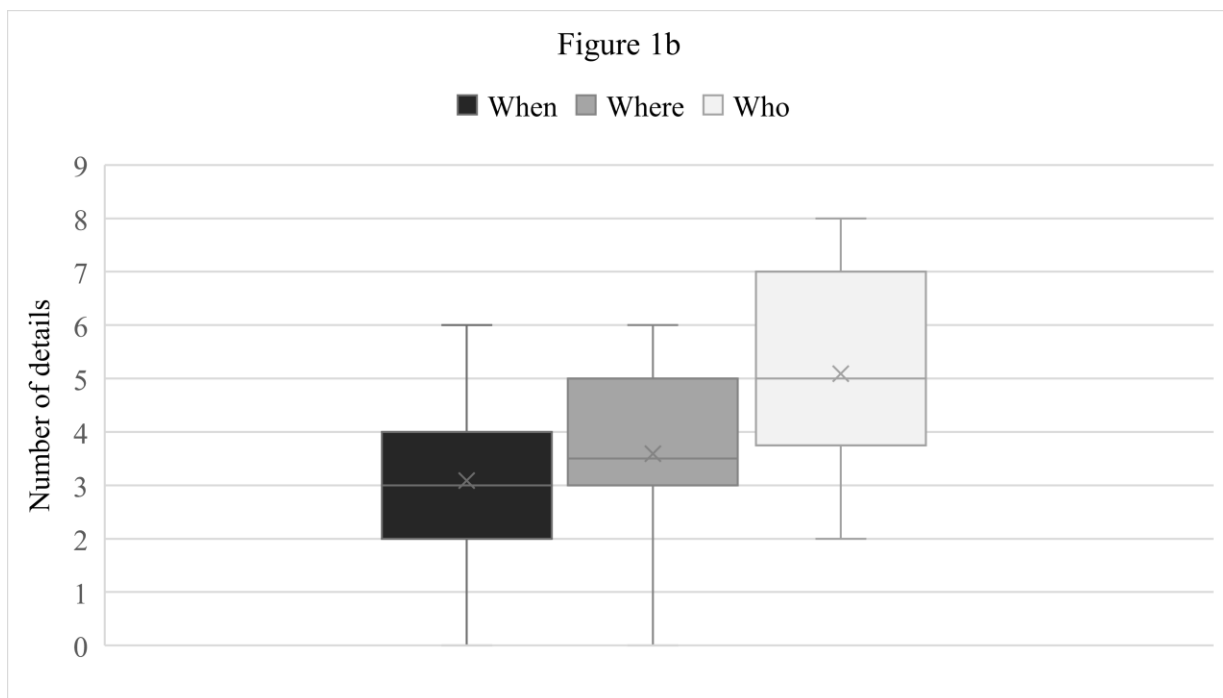
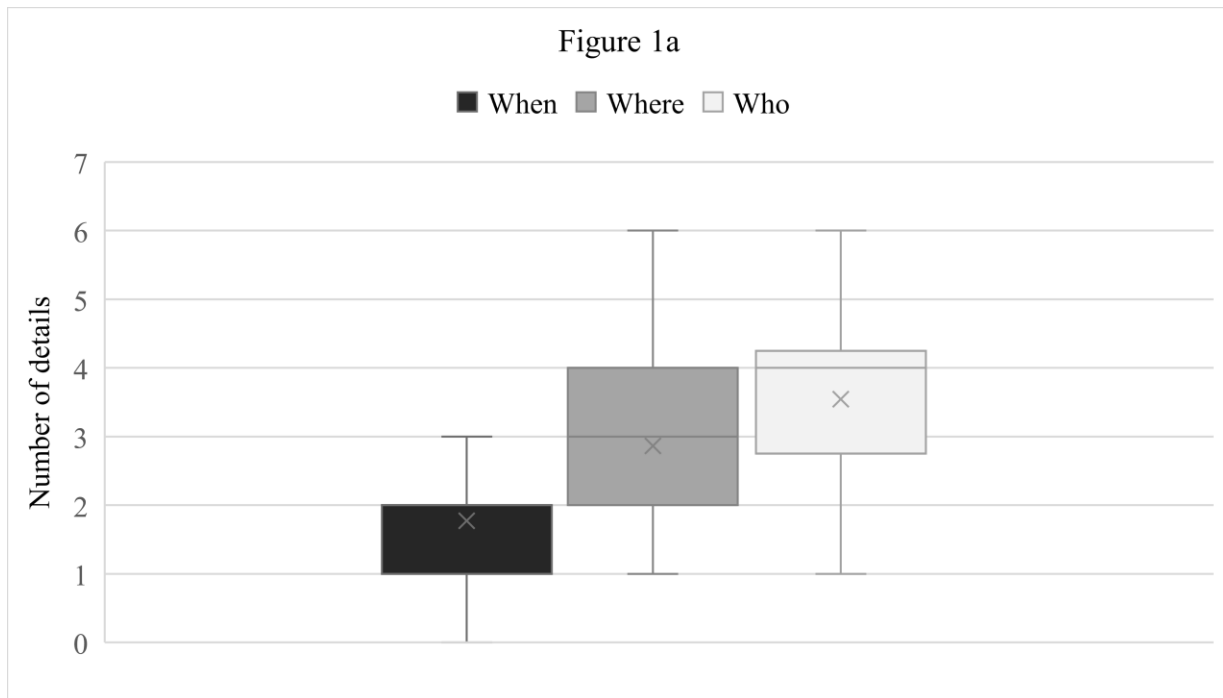


Figure 1.

Number of contextual details (“when and where did the events will occur” and “who will be present during these events”), as evoked by AD participants (Figure 1a) and older adults (Figure 1b).