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On hallucinations and memory: the relationship between hallucinations and autobiographical overgenerality in Alzheimer's Disease

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Abstract

Objectives: Alzheimer's disease (AD) has been associated with autobiographical overgenerality (i.e. a tendency of patients to retrieve general rather than specific personal memories). AD has also been associated with hallucinations. We investigated the relationship between autobiographical overgenerality and hallucinations in AD. *Methods:* We invited 28 patients with mild AD to retrieve autobiographical memories, and we also evaluated the occurrence of hallucinations in these patients. *Results:* Analysis demonstrated significant correlations between hallucinations and autobiographical overgenerality in the patients. *Conclusion:* AD patients who are distressed by hallucinations may demonstrate autobiographical overgenerality as a strategy to avoid retrieving distressing information that may be related with hallucinations. However, hallucinations as observed in our study can be attributed to other factors such as the general cognitive decline in AD.

Significant outcomes

- We assess mental health in a large sample of patients with AD living in retirement homes during the lockdown
- We found increased depression, anxiety, and loneliness during the second compared with the first lockdown
- This decreased mental health can be attributed to restrictive measures during the lockdown

Limitations

- Our study did not include a healthy participants group.

Introduction

With a prevalence ranging from 4 to 76% (median 23%), hallucinations are considered as the most frequent psychotic symptom in Alzheimer's Disease (AD) (Wilson *et al.*, 2000; Bassiony and Lyketsos, 2003; Scarmeas *et al.*, 2005; Ropacki and Jeste, 2005; El Haj *et al.*, 2017b). Hallucinations in AD are mainly visual and auditory (Rubin *et al.*, 1988; Tariot *et al.*, 1995; Jeste and Finkel, 2000) but somatic, olfactory, and tactile hallucinations can sometimes be observed (Burns *et al.*, 1990; Deutsch *et al.*, 1991). At the cognitive level, hallucinations in AD can be associated with memory functioning. More specifically, hallucinations have been attributed to difficulties to suppress irrelevant thoughts and memories (El Haj *et al.*, 2015c; El Haj, 2016). This suppression account has been inspired from the assumption of Hemsley (Hemsley, 2005), according to which inhibitory dysfunction leads to the emergence of redundant or irrelevant information from memory into awareness, generating hallucinations. This assumption is supported by research demonstrating relationship between hallucinations in AD and the ability to suppress irrelevant thoughts and representations (El Haj *et al.*, 2015c). More specifically, a relationship between hallucinations in AD and the ability to suppress irrelevant memories has been reported (El Haj *et al.*, 2018) suggesting that inhibitory dysfunction leads to the emergence of redundant or irrelevant information from long-term memory into awareness, resulting in the generation of hallucinations.

As alluded to above, hallucinations in AD have been associated with the ability to suppress irrelevant memories. To better understand the relationship between hallucinations and memory

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in AD, we assessed the relationship between hallucinations and the ability to retrieve specific autobiographical memories, that is, specific personal memories situated in time and space. Generally speaking, AD has been widely associated with compromise of autobiographical memory (El Haj *et al.*, 2015b), and one of the main characteristics of autobiographical decline in AD is the patients' difficulty in remembering specific memories (Irish *et al.*, 2011; Barnabe *et al.*, 2012; Martinelli *et al.*, 2013; Kirk and Berntsen, 2017; El Haj and Antoine, 2017a; El Haj *et al.*, 2017a). In other words, when asked to retrieve autobiographical memories, AD patients tend to retrieve general memories which refer either to repeated events (e.g. 'I used to spend the holidays on my grandfather's farm') or to extended periods of time (e.g. 'my summer holiday') (El Haj *et al.*, 2017a). The autobiographical overgenerality in AD has been associated with the patients' difficulty to retrieve specific spatiotemporal information (El Haj and Antoine, 2017a; El Haj and Antoine, 2018) as well as with the patients' difficulty to mentally relive past events (Rauchs *et al.*, 2007; El Haj *et al.*, 2016; El Haj and Antoine, 2017b). According to the AMAD (Autobiographical Memory in Alzheimer's Disease) model (El Haj *et al.*, 2015b), the overgenerality of autobiographical memory in AD leads to a shift from the ability to mentally relive past events to a general sense of familiarity that may be expressed by AD patients as a sense of 'having experienced this before'. Taken together, research demonstrates an overgenerality of autobiographical retrieval in AD.

Based on this, it may be hypothesised that there is a relationship between hallucinations and autobiographical overgenerality in AD. For AD patients who experience hallucinations, overgeneral memories may serve, explicitly or implicitly, to support low mood and hopelessness, to maintain a perception of hallucinations as omnipotent and uncontrollable, and/or to limit access to disconfirmatory information about the content/occurrence of hallucinations. The hypothesised role of autobiographical overegenerality in maintenance of hallucinations can be supported with clinical observation, in that patients with schizophrenia who are distressed by hallucinations often struggle to remember disconfirmatory evidence that might be helpful in both changing their beliefs about the power of their hallucinations and increasing a sense of personal control and autonomy (Berna *et al.*, 2016; Jacobsen *et al.*, 2018). According to Jacobsen *et al.* (2018), autobiographical overgenerality bias may contribute to hallucinations in people with psychosis by limiting access to information that might help to disconfirm or counter beliefs about hallucinations. This assumption can be supported by a meta-analysis of 14 studies of memory functioning in schizophrenia reporting a reduced specificity in autobiographical recall (Berna *et al.*, 2016). Also, the assumption of Jacobsen *et al.* (2018) can also be supported by autobiographical generality models suggesting that autobiographical retrieval can be terminated prematurely to avoid emotionally disturbing events (Williams *et al.*, 2007). In a similar vein, and according to the Self Memory System (Conway and Pleydell-Pearce, 2000), memory search may be interrupted earlier in patients with hallucinations because their memories are distressing.

Taken together, at the cognitive level, the hallmark of AD is memory decline (McKhann *et al.*, 2011), and one of the core characteristics of memory decline in AD is the patients' difficulty in remembering specific autobiographical memories (El Haj *et al.*, 2015b; El Haj *et al.*, 2017a). At the psychiatric level, hallucinations are considered as the most frequent psychotic symptom in AD (Bassiony *et al.*, 2000; El Haj *et al.*, 2017b). Our study assessed relationship between autobiographical memory and hallucinations in AD, this in light of previous research suggesting that autobiographical overgenerality serves to limit access to information that might psychotic patients to disconfirm or counter beliefs about hallucinations (Jacobsen *et al.*, 2018). Based on this assumption, we expected significant correlations between performances of AD patients on assessments of autobiographical overgenerality and hallucinations.

Method

Participants

The study included 28 participants with a clinical diagnosis of mild AD (19 women and 9 men; Mean age = 72.64 years, $SD = 6.81$; M years of formal education = 8.79, $SD = 2.88$) who were recruited from local retirement homes. The participants were recruited from a pool of residents of retirement homes based on history of hallucinations. In other words, the study included only patients with a history of hallucinations. Participants were also selected based on diagnosis of probable AD dementia based on the NINCDS-ADRDA clinical criteria (McKhann *et al.*, 2011). Exclusion criteria were neurological disorders, other than AD (e.g. dementia with Lewy bodies or fronto-temporal dementia). Participants freely consented to participate in the study and were given the opportunity to withdraw whenever they wished.

General cognitive functioning of the patients was evaluated with the Mini-Mental State Exam (Folstein *et al.*, 1975), and the mean performance was 23.25 ($SD = 1.45$) out of a maximum of 30 points. Working memory was evaluated with digit span tasks, participants were asked to repeat a string of single digits in the same order (i.e. forward span) or in the inverse order (i.e. backward span). The number of correctly repeated digits was scored, mean performance on the forward and backward spans was, respectively 4.79 ($SD = 1.25$) and 3.64 ($SD = 0.96$). Verbal episodic memory was evaluated with the Grober and Buschke task (Grober and Buschke, 1987). Participants were required to retain 16 words, each of which describes an item that belongs to a different semantic category. After immediate cued recall, participants proceeded to a distraction phase, during which they had to count backwards from 374 for 20s. This phase was followed by two minutes of free recall; the score from this phase (out of a maximum of 16) was retained as the episodic score, and the mean performance was 5.89 ($SD = 2.88$).

Materials

Hallucinations

We used the Launay–Slade Hallucination Scale (Launay and Slade, 1981) which has been validated in a large sample (193 participants) of French-speaking healthy older adults (Larøi *et al.*, 2005). We included items used by previous research on hallucinations in AD (El Haj *et al.*, 2018): '*Sometimes, I have seen objects or animals even though there was nothing there*', '*I have been troubled by hearing voices in my head*', '*I often hear a voice speaking aloud*', '*In the past I have had the experience of hearing a person's voice and then found that no-one was there*', '*On certain occasions I have felt the presence of someone close who had passed away*', and '*On occasions I have seen a person's face in front of me when no-one was in fact there*'. The six items were scored on a five-point Likert scale ranging from zero ('certainly does not apply to me') to four ('certainly applies to me'). The items were filled out by both AD patients than by informants (e.g. caregivers, spouses . . .) who were solicited to

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control for any potential effects of anosognosia, limiting awareness of hallucinations in the patients. In case of discrepancy between scores provided by patients and those provided by informants, we retained the informants' scores. The patients obtained a mean score of 13.68 ($SD = 4.25$) (out of a maximum of 24 points).

Autobiographical overgenerality

Participants were invited to retrieve three autobiographical events. More specifically, the experimenter invited each participant to 'recount in detail a familial event', 'recount in detail a professional event', and 'recount in detail a holiday event'. These three cues (i.e. family, profession, and holiday) were chosen as they tend to elicit autobiographical memories in these subjects (Martinelli *et al.*, 2013; El Haj *et al.*, 2015a; El Haj and Antoine, 2018). In the case that a patient did not retrieve a memory, she/he was invited to retrieve a memory related to the professional life of parents, spouse, or a sibling ((for a similar procedure, see (El Haj and Antoine, 2018). For each event, participants were instructed to be as precise and specific as possible, such that events had to have lasted no more than a day and spatiotemporal details had to be provided (such as when and where the events had occurred). Some examples were provided to illustrate what would be considered as a specific event. Participants were also instructed to describe their feelings and emotions during these events. Recall was limited to two minutes for each event and the duration was stated from the outset so participants could plan their time accordingly. This time limit was adopted to avoid potential redundancy and/or distractibility (Addis *et al.*, 2009; El Haj *et al.*, 2012a; El Haj *et al.*, 2012b; El Haj *et al.*, 2013).

Autobiographical overgenerality was scored using the Test Episodique de Mémoire du Passé (Piolino *et al.*, 2006), an autobiographical instrument based on standard autobiographical evaluations (Kopelman *et al.*, 1989) and adapted for clinical French populations. For each memory, we attributed zero if there was no memory or only general information about a theme; one point for a repeated or an extended event (e.g. my holidays); two points for an event situated in time or/and space (e.g. my holidays on my grandfather's farm); three points for a specific event lasting less than 24 hours and situated in time and space (e.g. one day my grandfather showed me how to collect eggs); and four points for a specific event situated in time and space and enriched with phenomenological details (e.g. thoughts, feelings, perceptions, or visual imagery) (e.g. I had to hold the chicken by its feet and I was very scared). High inter-rater agreement coefficients were obtained (Cohen's Kappa coefficient $\kappa = .91$) (Brennan and Prediger, 1981). The maximum specificity score for each participant was 12 points (four points for each of the three memories), and the patients obtained a mean score of 6.79 ($SD = 1.59$).

Results

We investigated correlations between autobiographical overgenerality and hallucinations in AD patients. We used non-parametric correlations (Spearman's rank correlation coefficient) due to the fact that Shapiro-Wilk test showed a non-normal distribution for the variables. As depicted in Fig. 1, significant negative correlations were observed between scores on the autobiographical specificity assessment and scores on the hallucinations assessment. In other words, low specificity scores (i.e. overgeneral autobiographical retrieval) were correlated with a higher occurrence of hallucinations.

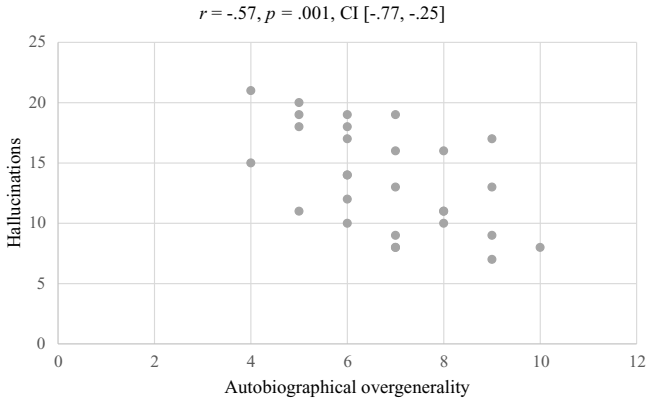


Figure 1. Correlations between autobiographical overgenerality and hallucinations. *Note.* The maximum autobiographical score was 12 points (low scores = less specific memories), and the maximum hallucination score was 24 points (low scores = low occurrence of hallucinations).

Complementary analysis

For consistency, we calculated correlations between autobiographical memory/hallucinations and scores on the Mini-Mental State Exam. Analysis demonstrated significant correlations between autobiographical memory and scores on the Mini-Mental State Exam ($r = .53$, $p = .003$) as well as between hallucinations and scores on the Mini-Mental State Exam ($r = -.50$, $p = .007$).

Discussion

We investigated relationship between autobiographical overgenerality and hallucinations in AD. Results demonstrated significant negative correlations between scores on the assessments of autobiographical specificity and hallucinations, in other words, the low specificity scores (i.e. autobiographical overgenerality) were correlated with high occurrence of hallucinations.

Generally speaking, our study mirrors research demonstrating autobiographical overgenerality (Irish *et al.*, 2011; Barnabe *et al.*, 2012; Martinelli *et al.*, 2013; Kirk and Berntsen, 2017; El Haj and Antoine, 2017a; El Haj *et al.*, 2017a) in AD as well as research on the occurrence of hallucinations in AD (Wilson *et al.*, 2000; Bassiony and Lyketsos, 2003; Scarmeas *et al.*, 2005; Ropacki and Jeste, 2005; El Haj *et al.*, 2017b). Critically, our study demonstrates a relationship between autobiographical overgenerality and hallucinations in AD. This relationship can be attributed to several factors. AD patients who are distressed by hallucinations may demonstrate autobiographical overgenerality as an explicit/implicit strategy to avoid retrieving distressing information that may be related with the content of hallucinations (e.g. remembering that a spouse, as encountered during hallucinations, is actually deceased). This assumption can be supported by autobiographical generality models suggesting that autobiographical retrieval can be terminated prematurely to avoid emotionally disturbing information (Williams *et al.*, 2007). Our assumption can also be supported by the Self Memory System (Conway and Pleydell-Pearce, 2000), according to which memory search may be interrupted earlier in patients with hallucinations because their memories are distressing.

Till now, we suggest that AD patients may demonstrate autobiographical overgenerality as an explicit/implicit strategy to avoid retrieving hallucinations-related distressing information. Conversely, AD patients may develop hallucinations due to

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autobiographical overgenerality. More specifically, owing to difficulty to retrieve specific contextual information (e.g. where, when, and/or how an information was acquired), AD patients may misattribute some autobiographical information to inappropriate source. For instance, patients may attribute an internally generated autobiographical thought, such as thinking about a previous interaction with a given person, to external sources, such as the patients believe that they really interact with this person. This assumption can be supported by a study demonstrating relationship between hallucinations and the ability to retrieve contextual information in patients with AD (El Haj *et al*., 2020), although this study was concerned with item memory (e.g. participants had to remember whether objects were previously manipulated by themselves or by the experimenter) rather than with autobiographical memory.

The relationship between hallucinations and autobiographical overgenerality in AD can be mediated by depression. Depression is frequently observed in individuals suffering from hallucinations (Birchwood and Chadwick, 1997). Patients with severe depression commonly report auditory hallucinations, which are generally transient and limited to single words or short phrases and, usually, communicating thoughts consistent with the patients' negative mood (Chaudhury, 2010). Depression has been also widely associated with autobiographical overgenerality. According to Williams *et al.* (2007), autobiographical overgenerality can be considered as a strategy to avoid distressing memories in depression, in other words, this functional avoidance occurs as the recollection of general information reduces the affective impact of emotional material in depression. Although the depression account is of interest, it should be noted that our study did not include an assessment of depression.

While, in this paper, we mainly consider relationship between hallucinations and autobiographical memory, it would be of interest to shed light on other factors that can be related to hallucinations. Visual hallucinations can be attributed to disorders of attentional network activity (Collerton *et al*., 2005). According to Shine *et al.* (2014), simple visual hallucinations can be attributed to disturbances within regions responsible for the primary processing of visual information, whereas complex visual hallucinations can be attributed to dysfunction within and between the regions involved in attentional processing. Similar assumption was made by Diederich *et al.* (2005) who attributed hallucinations in Parkinson's disease to difficulties to activate the dorsal attention network in the presence of an ambiguous percept, leading to overreliance on regions in the default mode network and the ventral attention network. The neural architecture of hallucinations can also be emphasised in light of a model by Ffytche (2008) who proposed that visual hallucination occurs within the context of persistent hypo-connection between the occipital lobe and other brain regions and, in some circumstances, hyper-connection within the occipital lobe, whereas auditory hallucinations occur within the context of hyper-connectivity between the temporal and frontal lobes. Although these models offer a comprehensive neural approach to explain hallucinations, it should be noted that these models address hallucination in populations other than patients with AD. It thus would be of interest to test these models in patients with AD. The same thing can be said regarding a model proposed by Benrimoh *et al.* (2019) to explain hallucinations in psychotic conditions such as schizophrenia. According to Benrimoh *et al.* (2019), hallucinations can occur either in context (i.e. they can be consistent with the environment) or out of context (i.e. they can be inconsistent with the environment).

Throughout this manuscript, we suggest that AD patients who are distressed by hallucinations may demonstrate autobiographical overgenerality as a strategy to avoid retrieving distressing information that are related with the content of hallucinations. We also attribute the relationship between hallucinations to several factors such as source monitoring and depression. Besides this account, it should be noted that, as demonstrated by our correlation analysis, hallucinations in AD can be associated with general cognitive decline. Not surprisingly, general cognitive decline in AD can be associated with the occurrence of psychiatric symptomatology.

Considering our procedures, one could argue that a limitation of our study is the lack of a healthy participants group. While healthy elderly may demonstrate a diminished specificity of autobiographical retrieval (Piolino *et al*., 2006; Piolino *et al*., 2010), they demonstrate little, if any, hallucinations; not surprisingly as they, by definition, present no major psychiatric disorders. This is why we did not include a control group.

To summarise, beyond demonstrating significant correlations between hallucinations and autobiographical overgenerality in AD, this paper demonstrates how the cardinal cognitive hallmark of AD (i.e. memory decline) can be associated with psychiatric symptoms of the disease. By doing this, our findings bridge a gap between research on memory dysfunction in AD and research on psychiatric symptomatology of the disease. In our view, memory dysfunction in AD cannot be solely associated with cognitive and neurological factors, psychiatric factors such as hallucinations can also be associated with memory dysfunction in the disease.

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Ethical standards. This study complied with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Description of authors' roles. MEH collected data. All authors contributed to the study design, data interpretation & analysis and writing of paper.

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