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Review

Using memories to understand others: The role of episodic memory in theory of mind impairment in Alzheimer disease

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ABSTRACT

Theory of mind (TOM) refers to the ability to infer one's own and other's mental states. Growing evidence highlighted the presence of impairment on the most complex TOM tasks in Alzheimer disease (AD). However, how TOM deficit is related to other cognitive dysfunctions and more specifically to episodic memory impairment – the prominent feature of this disease – is still under debate. Recent neuroanatomical findings have shown that remembering past events and inferring others' states of mind share the same cerebral network suggesting the two abilities share a common process .This paper proposes to review emergent evidence of TOM impairment in AD patients and to discuss the evidence of a relationship between TOM and episodic memory. We will discuss about AD patients' deficit in TOM being possibly related to their difficulties in recollecting memories of past social interactions.

Contents

1. Introduction

Alzheimer disease (AD) is clinically defined by an early and prominent episodic memory impairment, associated with at least one other cognitive dysfunction, and behavioural symptoms affecting autonomy in daily living activities (McKhann et al., 1984, 2011). The amnesic syndrome constitutes its core feature and is thus the most described symptom of this disease, even in prodromal stages, i.e., mild cognitive impairment (MCI) due to AD (Albert et al., 2011; Petersen, 2004). Recently, research on social cognition in neurodegenerative diseases, mainly in frontotemporal dementia, has grown considerably. Impaired social cognition was described as a prominent feature of frontotemporal lobar degeneration (Adenzato et al., 2010; Bertoux et al., 2012; Lough et al., 2006, 2001). This set of studies has led to the formulation of new neuropsychological criteria in the future publication of the DSM-5 manual of American Psychiatric and Association (2013). Social cognition would take part in the DSM-5 classification for "Major Neurocognitive Disorders", including frontotemporal and Alzheimer dementias. Such inclusion suggests that deficit in social cognition would soon be considered as a hallmark of neuropsychological impairment in these diseases and would have to be systematically assessed through cognitive evaluations. However, little is known about social cognition dysfunction in AD patients.

Social cognition is defined as the capacity to interpret and predict others' behaviours according to their beliefs, intentions, emotions, and to decode social stimuli from the environment in order to adapt one's own behaviour in social situations (Adolphs, 2006). Mentalizing or theory of mind (TOM), is the ability whereby "*an individual attributes mental states to himself and others*" (Premack and Woodruff, 1978) and so constitutes a central aspect of social cognition. In other words, TOM refers to the capacity to

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understand that people's behaviours are directed by their mental states, their intentions and beliefs about the world. Some authors suggested that TOM would not be a specific module of human cognition but would rather rely on several different mechanisms (Samson, 2009; Stone and Gerrans, 2006). More precisely, TOM would involve low bottom-up processes, also called "precursors" (i.e., face and emotion processing, eye gaze and body movement detection), in interaction with high top-down mechanisms involved in meta-representational abilities and more cognitively demanding (i.e., executive functions, language, working memory and episodic memory).

The question of an involvement of memory in mentalizing ability is raised, as many studies have not only shown correlations between episodic memory and TOM performances but also evidenced that they would share a common pattern of brain activity. This common cerebral network observed in fMRI for remembering and mentalizing indeed suggests common processes and some authors put forward the hypothesis that these two activities would imply a mechanism referred to as self-projection (Buckner and Carroll, 2007; Spreng and Grady, 2010).

Research on TOM abilities in AD patients is restricted to eight studies (Castelli et al., 2011; Cuerva et al., 2001; Fernandez-Duque et al., 2009; Gregory et al., 2002; Le Bouc et al., 2012; Verdon et al., 2007; Zaitchik et al., 2006, 2004), and only one study was conducted in MCI individuals (Baglio et al., 2012). But, to date, they have not provided enough evidence to clearly characterize TOM deficit and relate it or not to other cognitive disorders, especially episodic memory.

The aim of this paper is to review emergent evidence on TOM impairment in AD patients and to discuss findings concerning the relationship between TOM and episodic memory. After reviewing the results of the studies assessing TOM in AD and amnesic MCI, we will present data suggesting common processes supported by a neural substrate common to remembering and mentalizing. Then, we will discuss the issue of mentalizing deficits in AD patients being possibly related to their difficulties in recollecting memories of past social interactions. This article is based on a MEDLINE survey of the relevant literature published between 2001 and 2012. Keyword searches were conducted using the following terms: (1) "Alzheimer disease" or "mild cognitive impairment" and (2) "social cognition" or "theory of mind" or "mentalizing" or "mind reading" and (3) "autobiographical memory" or "episodic memory" or "remembering".

2. TOM impairment in AD and amnesic MCI

The above-mentioned studies investigated TOM deficit in AD patients (Castelli et al., 2011; Cuerva et al., 2001; Fernandez-Duque et al., 2009; Gregory et al., 2002; Le Bouc et al., 2012; Verdon et al., 2007; Zaitchik et al., 2006, 2004) and only one in amnesic MCI individuals (Baglio et al., 2012). In AD, all these studies showed a deficit in high levels of TOM, even in the early stages of the disease. They reported a significant decline in the performance on second-order tasks, in which patients had to infer the mental state of a person about another person (Castelli et al., 2011; Cuerva et al., 2001; Fernandez-Duque et al., 2009; Gregory et al., 2002; Zaitchik et al., 2006). Similarly, patients were impaired on Faux-Pas tasks, which require to detect that someone has done or said something that should not have been done or said in a particular situation (Gregory et al., 2002). They also had difficulties with Strange Stories task (Happé, 1994) involving lies, double-bluffing or pretending, in which understanding the story depends on the character's mental state (Castelli et al., 2011; Cuerva et al., 2001).

The results are more contrasted concerning the tasks evaluating first-order TOM, in which patients had to infer someone else's mental state, or in tasks assessing pragmatic abilities. Some studies reported preserved first-order TOM abilities (Castelli et al., 2011; Fernandez-Duque et al., 2009; Gregory et al., 2002; Zaitchik et al., 2006, 2004) while one study showed impairment in AD patients on such tasks (Le Bouc et al., 2012). Moreover, some results demonstrated difficulties in eye gaze detection for AD patients (Castelli et al., 2011), attribution of an intention to a short comic strip character or even in pragmatic abilities such as indirect requests or implicit speech (Castelli et al., 2011; Cuerva et al., 2001). It was also demonstrated that AD patients had difficulties in perspective taking when they have to judge whether adjectives describe or not their personality, adopting theirs relatives' point of view. In other words, they were impaired when they had to infer or imagine what their relatives could think about their personality trait (Ruby et al., 2009).

In the only work investigating TOM in amnesic MCI patients, results are similar to those found for AD patients. Participants achieved worse performances on complex second-order task compared to healthy controls, while performances on Strange Stories task, eye gaze detection and first-order false belief tasks were similar to controls (Baglio et al., 2012). This suggests that TOM impairment is already observed in patients with spared general cognitive functioning and whose deficits are more isolated than in AD. Unfortunately, in Baglio et al. (2012) TOM was assessed only once whereas other functions where investigated at baseline and 12–18 months later. Thus, despite the follow-up in neuropsychological assessment, this study did not provide any data about TOM deficit increasing as cognitive impairment worsens, especially in patients who had converted to AD.

Several authors hypothesized that mentalizing deficit in AD and MCI patients is secondary to other cognitive dysfunctions, especially in executive and memory domains (Castelli et al., 2011; Cuerva et al., 2001; Fernandez-Duque et al., 2009; Zaitchik et al., 2004). However, findings on this issue differ. All the studies cited above conducted neuropsychological evaluation in parallel to TOM assessment, except one in which patients just underwent Mini Mental State Evaluation (MMSE) (Verdon et al., 2007). They all investigated executive functions such as abstraction, mental flexibility or inhibition. Nevertheless, the results did not provide enough evidence of an executive involvement in TOM deficit. Indeed, some studies showed correlations between impaired performances in one or several measures of executive functioning and TOM performances (Baglio et al., 2012; Castelli et al., 2011; Gregory et al., 2002; Le Bouc et al., 2012; Zaitchik et al., 2004), while another did not find any correlation with executive tasks (Zaitchik et al., 2006). Concerning episodic memory, the central deficit in AD and amnesic MCI, only two studies reported positive correlations between memory performances and TOM tasks (Castelli et al., 2011; Cuerva et al., 2001) whereas some did not find any correlation (Baglio et al., 2012; Fernandez-Duque et al., 2009). The remaining studies did not explore memory function (Zaitchik et al., 2004), or did not conduct any correlation analyses between memory and TOM tasks (Gregory et al., 2002; Le Bouc et al., 2012; Zaitchik et al., 2006). More precisely, Cuerva et al. (2001) compared their AD patients with "impaired TOM" to the AD patients with "preserved TOM". They showed that they differed only in their episodic and short-term memory performances, assessed by Buschke Selective Reminding Test and digit span. This difference remained significant even after controlling for general cognitive decline by matching MMSE scores. Castelli et al. (2011) showed various correlations between verbal and visual episodic memory measures and second-order false belief tasks. These results only show correlations but they suggest that performances on TOM and memory tasks may rely on common mechanisms, which should be further explored using other statistical methods.