



Future thinking in Parkinson's disease: An executive function?

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ABSTRACT

Contrary to what was originally thought (Hassabis, Kumaran, Vann, & Maguire, 2007) recent data have shown that imagining the future is not entirely dependent on the hippocampus (Squire et al., 2010) and neuroimaging studies have demonstrated a frontopolar activation during future thinking tasks (Okuda et al., 2003). The present study investigated whether the performance of people with Parkinson's disease (PD) on future simulation tasks was dependent on memory or executive control. Thirty-one PD patients, asked to imagine possible future scenarios, generated fewer future episodic details than matched controls. The seven patients who clearly performed below the range of controls in future thinking, were also significantly poorer on the Frontal Assessment Battery (FAB), a battery assessing executive control, but showed no deficits in immediate or delayed memory tests. These results suggest that poor performance in the future thinking task is associated with poor executive control and less so with memory impairment. Flexible searching activities of past details might be crucial capacities for envisaging one's own future.

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1. Introduction

The human brain is continuously engaged in devising simulations that approximate real future events (de Vito & Della Sala, 2011; Ingvar, 1979). Most people can shift their perspective from the immediate environment to richly imagined hypothetical future situations. This skill, labelled "episodic future thinking" (Atance & O'Neill, 2001), allows humans to place themselves in potential scenarios by using imagination.

It has long been posited that an intimate relation underpins episodic past and future thoughts: "It may be said that we have no grasp of the future without an equal and corresponding outlook over the past" (Bergson, 1913, pp. 69–70). Bartlett (1932) noticed that remembering is not entirely distinct from imagining or from constructive thinking, but it has a close linkage with them. In 1973 it was already "abundantly clear that human behaviour is active in character, that it is determined not only by past experiences, but also by plans and designs formulating the future" (Luria, 1973, p. 13). Therefore, when people with memory disorders cannot completely rely on their past, their future remains "hazier, more vague and more confused" (Lidz, 1942, p. 596).

Consistent with these early intuitions, the presence of a common core network, which underlies autobiographical episodic remembering and future thinking, has been recently experimentally supported (for a review see Schacter, Addis, & Buckner, 2008; Szpunar, 2010). Certain cortical areas (specifically the medial prefrontal cortex, posterior regions in the medial and lateral parietal cortex, the lateral temporal cortex, and the medial temporal lobe including the hippocampus) have been shown to be associated with episodic memory and imagination of the future (e.g., Hassabis, Kumaran, Vann, & Maguire, 2007; Schacter, Addis, & Buckner, 2007; Schacter & Addis, 2009). This evidence has led to the claim that we need to access past experiences in order to anticipate future events (Schacter et al., 2008; Schacter & Addis, 2007; Szpunar, 2010).

Patient studies have corroborated this hypothesis. It has been noted, for example, that amnesic patients (O.S., Lidz, 1942; K.C., Tulving, 1985; D.B., Klein, Loftus, & Kihlstrom, 2002), seemed almost mentally locked in a permanent present, since the preceding events were "not available to meet the new" ones (Lidz, 1942, p. 595). The famous patient H.M., who became amnesic in 1953 after the bilateral resection of medial temporal lobe structures, was interviewed in 1992 by Suzanne Corkin. When asked "What do you think you'll do tomorrow?", he answered "Whatever is beneficial", since he "had no database to consult" to respond about his personal future (S. Corkin, personal communication, 01/26/11).

Similarly, Hassabis et al. (2007) reported on five memory-impaired patients with a bilateral hippocampus damage, four of

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whom had difficulty constructing detailed and spatially coherent fictitious scenarios. Lastly, patients with Alzheimer's disease (AD; Addis, Sacchetti, Ally, Budson, & Schacter, 2009) presented impairments in envisaging new experiences.

However, it is still unclear which cognitive functions, other than episodic memory, are necessary prerequisites for imagining one's own future and whether the hippocampus plays the crucial role in the construction of future scenes (Squire et al., 2010). The findings gleaned from the literature are controversial. Hassabis et al. (2007) reported that focal amnesics had trouble constructing novel events. Likewise, patients suffering from amnesic MCI generated fewer details in a future thinking task than their matched controls (Gamboz et al., 2010). On the other hand, Squire et al. (2010) reported that patients suffering from hippocampal lesions, despite their impairment in recollecting recent personal memories, performed similarly to controls when simulating future episodes. The authors concluded that difficulty in imagining the future is unlikely to be due only to pure amnesia if the past-future network of brain areas postulated by Schacter et al. (2007) is largely spared.

Moreover, neuroimaging studies have indicated a frontopolar activation during future thoughts. Compared to the construction of past episodes, future thinking tasks recruit several additional regions, such as the frontopolar cortex and left ventrolateral prefrontal cortex (Addis, Wong, & Schacter, 2007). Okuda et al. (2003) demonstrated that specific frontal polar areas, including Brodmann's area 10 (BA 10), were more activated when imagining the future than when remembering the past. In particular, the activity of the right frontopolar cortex (BA 10) positively correlates with the amount of detail comprising the future events (Addis & Schacter, 2008). Furthermore, damage to the prefrontal cortex can impair the conscious awareness of one's continued experience in a subjective time. This ability, also known as chronesthesia, might be closely related to the capacity of projecting one's self toward the future (for a review see Wheeler, Stuss, & Tulving, 1997; Szpunar, 2011).

According to this idea, some authors noted strong correlations between tasks generating event-related details and tasks engaging executive functions. Addis, Wong, and Schacter (2008) observed that the episodic specificity of past recollections and future constructions correlates with a standardized measure of executive control, the Backward Digit Span task, known to activate the dorsolateral prefrontal cortex (Hoshi et al., 2000). Furthermore, a new task was devised by Summerfield, Hassabis, and Maguire (2010), in order to better investigate the process of constructing coherent and vivid scenarios. The participants of this study were instructed to begin the trial clearing their imagination. Then, they were auditorily presented with single scene elements (from three to six) in a serial manner. They had to imagine the first element in a "clean state" (i.e., with no context) and, successively, they had to combine each single element together with the previous ones to build up naturalistic scenes of increasing complexity. In this study, fMRI showed the activation of the different areas of the core network (Schacter et al., 2007), being engaged and disengaged, as required during each step. The hippocampus and the dorsolateral prefrontal cortex were both significantly activated during the oral presentation of the first element. The addition of the second element required an increasing activity of the dorsolateral prefrontal cortex (maybe to allow the maintenance of the two elements in working memory, as the authors suggested). However, crucially, in this phase, the hippocampus (together with other areas of the core network activated during the first step) down-regulated. With the introduction of the third element, the authors observed a greater activity in additional regions (i.e., the medial parietal cortex) and once more an up-regulation of many areas, like the hippocampus, activated during the first phase, but down-regulated in the second phase. Such observations provide us with clues as to the possible alternative

role played in the scene construction by hippocampus-related memory functions and by frontally based executive functions.

Taken together, these lines of evidence suggest that executive functioning plays an essential part in the production and recombination of event-related details. Should this be the case, an executive dysfunction ought to cause some degree of impairment in the simulation of episodic future events, even when episodic memory is spared.

We sought to further our understanding of this issue by testing people with Parkinson's disease (PD). PD is a neurodegenerative disorder that progresses slowly and is characterized by degeneration of the dopaminergic system. A wide range of cognitive impairments is often associated with PD, the most prominent of which is a dysexecutive syndrome (Bosboom, Stoffers, & Wolters, 2004; Rowe et al., 2002). Our patients were selected for being at the very early stages of the disease (no later than the second stage, according to Hohen and Yahr's classification, 1967). Their magnetic resonance imaging had to be normal.

The present study assesses for the first time episodic future thinking in PD patients. The choice of this particular population, early non amnesic PD, was directly linked to the question posed in our study as to whether people with no overt memory problems, and who might have other mild cognitive deficits, could nonetheless present with future thinking deficits.

More specifically, the main goal of the current study was to assess whether or not patients with no memory deficits may present with impairment in future thinking and whether this impairment might be specific, sparing other tasks requiring event generation. Mental time travel into the past was included because it implies a search for a combination of information and it allowed us to ascertain whether or not participants were still able to retrieve personal memories. The key experimental variable was mental time travel into the future, which might place a considerable demand on executive functions, given that a future event can be constructed from a combination of an infinite assortment of information that is to be monitored and re-combined within precise restrictions (e.g., plausibility, time) (Anderson, Dewhurst, & Nash, 2012). Imagination of fictitious, non-temporal events was included because it implies a more open-ended and generative capacity of scene construction, given that the events, in this case, might also be implausible and unlikely and are not to be restricted to a specific time frame. We predicted that future thinking might be more cognitively demanding than a simple scene construction, since it implies a flexible search within past autobiographical memories by taking into account more restrictions, hence more monitoring, than a scene construction task. Thus, it might involve different and distinctive cognitive sub-processes.

2. Method

2.1. Participants

Thirty-one old adults affected by PD and 31 healthy controls took part in this experiment.

The participants with PD were selected from a larger panel at the Parkinson and Movement Disorder Centre, Department of Neurological Sciences (Federico II University, Naples). The diagnosis of PD fulfilled the UK Parkinson's disease Society Brain Bank clinical diagnostic criteria (Gibb & Lees, 1988). All patients were under anti-parkinsonian treatment at a stable and optimized daily dosage during the 4 weeks prior to study entry. Exclusion criteria were: (1) dementia according to clinical diagnostic criteria for dementia associated with PD (Emre et al., 2007); (2) major depression according DSM-IV criteria for current major depression (American Psychiatric Association, 1994); (3) clinically significant or unstable medical condition including serious cardiovascular or cerebrovascular disease; and (4) anti-cholinergic or neuroleptic treatment.

According to Hohen and Yahr's classification (1967), our PD patients were to be at no later than the second stage of Parkinson's disease. More specifically, 16 of them were at stage 2; 11 of them were at stage 1.5 and 4 of them were at the stage 1. Their magnetic resonances were normal. None of our patients had detectable MTL damage, as evinced by structural MRI scans.

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