



A process-model based approach to prospective memory impairment in Parkinson's disease

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ABSTRACT

The present review discusses the current state of research on the clinical neuropsychology of prospective memory in Parkinson's disease. To do so the paper is divided in two sections. In the first section, we briefly outline key features of the (partly implicit) rationale underlying the available literature on the clinical neuropsychology of prospective memory. Here, we present a conceptual model that guides our approach to the clinical neuropsychology of prospective memory in general and to the effects of Parkinson's disease on prospective memory in particular. In the second section, we use this model to guide our review of the available literature and suggest some open issues and future directions motivated by previous findings and the proposed conceptual model. The review suggests that certain phases of the prospective memory process (intention formation and initiation) are particularly impaired by Parkinson's disease. In addition, it is argued that prospective memory may be preserved when tasks involve specific features (e.g., focal cues) that reduce the need for strategic monitoring processes. In terms of suggestions for future directions, it is noted that intervention studies are needed which target the specific phases of the prospective memory process that are impaired in Parkinson's disease, such as planning interventions. Moreover, it is proposed that prospective memory deficits in Parkinson's disease should be explored in the context of a general impairment in the ability to form an intention and plan or coordinate an appropriate series of actions.

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1. Overview and general introduction

Prospective memory (PM) refers to the ability to implement intended actions in the future (e.g., remembering to take medication at appropriate times; see Kliegel, McDaniel, & Einstein, 2008 for a comprehensive overview). While early years of PM research have focused on the communalities and differences between PM and retrospective memory (i.e., the encoding and externally prompted retrieval of episodic information in traditional long-term memory paradigms; e.g., Einstein & McDaniel, 1990, 1996) or have studied the effects of adult aging on PM functioning (Zeintl, Kliegel, & Hofer, 2007; see also Henry, MacLeod, Phillips, & Crawford, 2004; Kliegel, Jäger, & Phillips, 2008, for metaanalytic overviews), recent years have seen a remarkable explosion of research targeting possible impairments in PM functioning across a great range of different neuropsychological populations (cf. Kliegel, Jäger, Altgassen & Shum, 2008, for a first general overview). The present review will serve two aims. The first is to give a comprehensive overview of the available literature on PM functioning in one of those many populations targeted over the last decade, i.e., Parkinson's disease (PD).

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PD is a neurodegenerative disease that afflicts approximately 0.3% of the entire population in industrialised countries and about 1% of people over 60 years of age (de Lau & Breteler, 2006). The primary neuropathological markers of PD are cell death in the substantia nigra and the presence of Lewy bodies (Dickson et al., 2009). The resultant depletion of dopamine causes impaired functioning of the basal ganglia and disruptions to cortico-striatal circuitry (Obeso, Rodríguez-Oroz, & Benitez-Temino, 2008). In fact, even early in the course of PD dopamine depletion occurs not only in the basal ganglia but also in the prefrontal cortex (e.g., Cools, 2006). In addition to the hallmark motor symptoms (e.g., tremor, rigidity, and Parkinsonian gait), a variety of impaired cognitive functions are also associated with PD (Bosboom, Stoffers, & Wolters, 2004; Pillon, Boller, Levy, & Dubois, 2001). Due to fronto-striatal circuitry dysfunction, the greatest cognitive impairments associated with PD tend to be for those tasks which rely on the prefrontal cortex, such as measures of executive functioning (Owen, 2004a,b), working memory (Farina et al., 2000; Lewis, Slabosz, Robbins, Barker, & Owen, 2005; Owen et al., 1992, 1995; Postle, Jonides, Smith, Corkin, & Growdon, 1997), and planning (Culbertson, Moberg, Duda, Stern, & Weintraub, 2004; Hanes, Andrewes, Smith, & Pantelis, 1996; Lewis, Dove, Robbins, Barker, & Owen, 2003; Owen et al., 1995). Although it is generally believed that memory may be relatively preserved in PD, certain types of memory may be more impaired

than others. For example, Drag, Bieliauskas, Kaszniak, Bohnen, and Glisky, (2009) recently showed that individuals with PD have preserved recognition memory for sentences that were heard (item memory), but impaired memory for the person who spoke the sentences (source or context memory; Drag et al., 2009). Regarding PM, as we detail below, a range of different frontally mediated executive processes are required for successful performance, including planning, maintaining multiple goals in working memory, interrupting ongoing activities when the intention is to be performed, shifting attention to performing the intended action, and sequencing the execution of the intended action (McDaniel and Einstein, 2007). Components of all of these functions are known to be impaired in individuals with PD (e.g., Pillon et al., 2001). Therefore, investigating PM performance in PD is an important endeavour.

The second aim of this review is to put the (few) available studies, into a broader, more general perspective of a *conceptual outline for a clinical neuropsychology of PM*. To achieve this goal, we will propose a framework for future research that describes certain factors to consider in order to avoid confounding multiple mechanisms (e.g., if more than one of the variables suggested is manipulated, it becomes more difficult to evaluate which variable has an effect on condition-related PM performance). In addition, from an applied perspective, the framework will also serve as a guideline for exploring novel and theory-based approaches in terms of diagnosis and/or treatment. Finally, we will point to areas of overlap between clinical and experimental neuropsychology of PM and suggest ways of using a population variable (i.e., PD) to inform PM theory.

2. Basic remarks on a clinical neuropsychology of prospective memory

The *common rationale* for clinical neuropsychological research in PM rests on the observation that PM represents a pervasive real-world memory task that is associated with most *everyday memory problems* (e.g., Kliegel & Martin, 2003). Moreover, PM failures are particularly problematic for maintaining patients' health, social relations and careers (e.g., Smith, Della Sala, Logie, & Maylor, 2000). Specifically, in an earlier review we have argued that because of the high prevalence of day-to-day demands on PM, individuals with PM deficits may be unable to sustain independent living (Kliegel, Mackinlay, & Jäger, 2008). Resting on this general motivation, there are four key questions that have been asked in clinical neuropsychology of PM in general, and in the literature on effects of PD on PM functioning in particular. The first question that has largely dominated the clinical literature on PM across most populations studied is a direct consequence of everyday relevance and disease burden and refers to the descriptive issue of determining whether and how severely a clinical condition is in fact impaired in its PM efficiency.

Question #1 (Description): Is there a PM impairment in population X? As we will delineate in more detail in the next section, this has also been the key motivating force for the first studies on PM in PD and it represents the natural first step in a research programme on any clinical population. In order to *structure the descriptive pattern* of PM performance, three dimensions of classifying PM tasks have been used in the literature.

The most prominent classification distinguishes between time-based PM and event-based PM (Einstein & McDaniel, 1996). *Event-based* tasks refer to paradigms in which the cue for the appropriate execution of the PM action is a specific, externally presented event (e.g., the appearance of a specific colleague or a target word on the computer screen), and *time-based* tasks are tasks in which the intended action has to be executed at a specific point in time (e.g., at noon or every 10 min). Often, the first studies in any clinical population examined the degree of impairment in those two task types (Katai, Maruyama, Hashimoto, & Ikeda, 2003, for the

first study on PD or Altgassen, Schmitz-Hübsch, & Kliegel, 2010; Altgassen, Williams, Bölte, & Kliegel, 2009, for Autism Spectrum Disorder). Mostly, those studies have revealed a differential picture with one task type being impaired and the other being spared. For example, Katai et al. (2003) demonstrated event-based tasks to be impaired in PD patients and time-based tasks to be spared; however, the pattern was reversed in two more recent studies by Costa, Peppe, Caltagirone, and Carlesimo (2008) and Raskin et al. (2011) (see similar results for Autism Spectrum Disorder as revealed by Altgassen et al., 2009, 2010).

A second way of structuring the descriptive impairment – that motivated the second study on PM in PD patients (Kliegel, Phillips, Lemke, & Kopp, 2005) – refers to the distinction between *simple, single intention* tasks [such as remembering to ask the experimenter to return a personal item at the end of a session; Rivermead Behavioural Memory Test (RBMT); Wilson, Cockburn, & Baddeley, 1985] and *complex, multi-intention* tasks that require one to plan and carry out several delayed intentions [such as the Six Elements Test from the Behavioural Assessment of the Dysexecutive Syndrome (BADS); Wilson, Alderman, Burgess, Emslie, & Evans, 1996]. While few studies have directly contrasted these task types in clinical populations (see Kliegel, McDaniel, & Einstein, 2000 for an exception in healthy aging), both task types have been widely used in the investigation of clinical neuropsychology of PM. For PD, for example, Kliegel, Zimprich and Eschen (2005) revealed marked impairments only in specific aspects of multi-intention PM: in the planning and encoding of multiple task intentions (see, e.g., Wandschneider et al., 2010, for similar descriptive patterns in Juvenile Myoclonic Epilepsy or Kliegel, Eschen, & Thöne-Otto, 2004, for Traumatic Brain Injury or Shallice & Burgess, 1991, for frontal lobe patients).

Another multi intention paradigm that has recently received increasing attention in the clinical literature is the Virtual Week task (initially developed by Rendell & Craik, 2000). Besides requiring the execution of multiple intentions in a realistic contextual game setting simulating the course of everyday life, Virtual Week adds another level of descriptive differentiation: extending the traditional time- versus event-based task distinction, Virtual Week separates *regular* from *irregular* PM tasks. Regular tasks represent routine medical tasks (e.g., taking medication at breakfast and 9 p.m.) that are repeated on each day. Irregular tasks represent errand-type tasks that occur while doing normal daily activity (e.g., returning a library book for a friend when you visit the library). The critical features of irregular tasks are that the participants are informed periodically during the game about new PM tasks and the tasks are one-at-a-time tasks that are not repeated. Importantly, similar to time- versus event-based tasks, those task dimensions have often (but not always) resulted in differential patterns of impairment in several clinical populations (see Henry and Rendell, 2009 for a comprehensive review on clinical studies and Rose, Foster, McDaniel, & Rendell, 2010, for application of Virtual Week in PD).

A third descriptive task distinction that has so far only received limited attention in the clinical literature stems from research on adult aging effects. Here, a remarkable pattern has emerged that has been called the *age-PM paradox* (e.g., Rendell & Craik, 2000) and that refers to differential age effects for experimental *laboratory* PM tasks in comparison to *naturalistic* tasks to be performed in participants' *everyday life*. Specifically, research on normal adult aging has revealed age-related *deficits* in standard laboratory-based PM tasks but age-related *benefits* in naturalistic tasks, which are tasks that are carried out in the everyday life of participants (Henry et al., 2004; Phillips, Henry, & Martin, 2008). While no study has so far revealed such a reversed pattern in clinical populations, an increasing number of clinical studies (and recently also on PD; e.g., Foster, McDaniel, Repovs, & Hershey, 2009) have started to

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