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## Functional correlates of prospective memory in stroke

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## ABSTRACT

**Introduction:** Prospective memory is the ability to remember actions to be performed later in time or when a certain event occurs. Multiple cognitive processes are involved in prospective memory, and the degree to which automatic or effortful processes are involved may differ for different types of prospective memory tasks. This study aimed to investigate prospective memory (dys)functioning in stroke patients, and to get more insight in which cognitive processes are involved in time- versus event-based prospective memory.

**Methods:** We investigated 39 community-dwelling stroke survivors and 53 matched control participants. Assessment included naturalistic and experimental event- and time-based prospective memory tasks, as well as standard neuropsychological measures of (retrospective) memory, processing speed and attention/executive functioning.

**Results:** 41% of the stroke patients performed significantly worse than control participants on prospective memory tasks. Deficits in prospective memory occurred as frequently as impairments in retrospective memory (33%,  $\chi^2(1, N=39)=3.4, p=.066$ ), and more often than impairments in attention/executive functioning (15%,  $\chi^2(1, N=39)=5.2, p=.022$ ) and speed of processing (23%,  $\chi^2(1, N=39)=6.5, p=.011$ ).

Regression analyses showed that event-based ('focal') prospective memory is supported by retrospective memory, indicating that it is a relatively simple and automatic process. Time-based (non-'focal') prospective memory proved to be a more complex process, requiring active monitoring of the environment. Performance was predicted by speed of processing, attention/executive functioning and retrospective memory. Thirteen percent of the patients suffered from selective prospective memory impairment, which was associated with damage to the superior temporal gyrus.

**Conclusions:** Impairment of prospective memory occurs frequently after stroke. Different cognitive operations are involved in distinct types of prospective memory. Results fit within the multi-process framework of prospective memory and help further specify its contents.

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## 1. Introduction

Prospective memory (PM) is the ability to remember intended actions (Einstein & McDaniel, 1990), for example posting a card for your grandmother's birthday. A distinction is often made between event-based and time-based PM (Kliegel, Altgassen, Hering, & Rose, 2011). In event-based PM the intended action is coupled with a specific cue event, as in remembering to tell the latest gossip upon meeting a friend. Time-based PM involves actions to

be performed at a certain moment in time, like making an important phone call Monday morning.

Several authors have described the cognitive complexity of PM (e.g. Carlesimo & Costa, 2011). Einstein and McDaniel proposed a multi-process framework in which separate processes of intention-formation, retention, initiation and execution are distinguished (Einstein & McDaniel, 1990; Rose, Rendell, McDaniel, Aberle, & Kliegel, 2010). Research in healthy participants regarding the cognitive functions involved in PM indicates that attention, memory and executive functioning are important for adequate PM performance (Burgess & Shallice, 1997; Marsh & Hicks, 1998; Mioni, Rendell, Henry, Cantagallo, & Stablum, 2013; Otani et al. 1997). There is evidence that (pre)frontal, parietal and medial temporal brain regions are involved (Burgess, Gonen-Yacovi, & Volle, 2011;

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Gordon, Shelton, Bugg, McDaniel, & Head, 2011; Martin et al., 2007; West & Krompinger, 2005).

PM deficits have been reported in patients with different neurological problems, such as Parkinson's disease, closed head injury, mild cognitive impairment and dementia (Costa, Peppe, Caltagirone, & Carlesimo, 2008; Kliegel et al., 2011; Shum, Levin, & Chan, 2011; van den Berg, Kant, & Postma, 2012). PM failure has significant impact on daily life functioning (Mioni et al., 2013). Not surprisingly, patients more often complain about prospective than about retrospective memory (Baddeley, 1990).

As stroke often leads to chronic cognitive deficits and dependency on support (Appelros, Nydevik, & Viitanen, 2003; de Haan, Nys, & van Zandvoort, 2006), deficits in PM potentially play a pivotal role in many of the problems that stroke patients are faced with. As such, one might expect PM to be a main (sub)field of investigation in stroke patients, but until now there is limited knowledge about PM deficits in stroke. Brooks, Rose, Potter, Jayawardena, and Morling (2004) used a virtual reality paradigm and found that event-based PM was affected after stroke, but time-based PM was not. In contrast, Cheng, Tian, Hu, Wang, and Wang (2010) found that time-based, but not event-based PM, was impaired after thalamic stroke. Kim, Craik, Luo, and Ween (2009) performed a group study investigating PM performance in relation to different cognitive functions in 12 stroke patients. They observed that stroke patients have difficulties in PM operations and speculate that these could be related to problems in self-initiated processing. The results from these studies do not fully clarify yet what cognitive mechanisms underlie PM deficits in stroke, and whether event- or time-based PM is mostly affected. The study by Kim et al. indicates that the type of processing needed to perform the task might be cardinal. There could be differences in task characteristics for both types of PM that determine performance.

In this regard, recent theories (e.g. Einstein et al., 2005) state that 'focality' seems crucial. Tasks where cue features are processed 'focally' (in that they overlap with information relevant to the ongoing task) should require few cognitive operations and resources. In contrast, non-'focal' PM tasks involve effortful self-initiated retrieval processing and strategic monitoring, as in time-based tasks where clock checking is a form of actively monitoring the appropriate moment of execution of an intended action. The extent to which different cognitive functions are addressed in PM task situations might depend on this distinction.

The current study aimed to systematically investigate the extent and nature of PM deficits in a considerably large group of stroke patients using a variety of event- and time-based PM tasks, and to link these to concurrent impairments in different cognitive domains.

## 2. Material and methods

### 2.1. Participants

In the University Medical Center Utrecht (UMCU) stroke patients are asked to participate in a longitudinal study on cognitive functioning after stroke, in accordance with inclusion regulations described in protocol 05–109 of the UMCU Medical Ethical Committee. For the current study we selected 39 patients. Inclusion criteria were diagnosis of stroke based on clinical assessment and imaging (CT, MRI), ability to travel independently, living at home, and willingness to participate. Exclusion criteria were diagnosed dementia, significant current psychiatric disorders (such as major depressive disorder), insufficient communicative ability (severe aphasia or non-fluent Dutch speakers), and other impairments that would limit participation or completion of the assessment (such as blindness).

Ischaemic strokes predominated (31% haemorrhagic). Average interval between date of stroke and testing was 17 months ( $SD=8.3$ ). No influence of elapsed time between event and test date was found on any variable. Location of lesion was confirmed by an experienced neurologist (CJMF), using Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) scans that were obtained according to

**Table 1**

Patient and control participant demographics.

Variable	Patients N=39	Control participants N=53	<i>p</i>
Gender (% male)	69%	38%	.003*
Dexterity (right/left/ambidextrous)	89/8/3%	89/9/2%	.649
Educational level (median, IQR)	5 (5–6)	6 (5–6)	.156
Age ( $M \pm SD$ )	58.2 $\pm$ 14.2	51.7 $\pm$ 17.4	.062
IQ ( $M \pm SD$ )	107.8 $\pm$ 18.0	107.9 $\pm$ 12.9	.990

Note. Group differences between patients and control participants were tested using chi-square tests (gender, dexterity), Mann–Whitney *U* (educational level) and two-tailed independent *t*-tests (age, IQ).

\*  $p < .05$ .

clinical practice. For 15 patients only CT scans were available. All available scans were used to determine the ultimate structural damage as exactly as possible, using a human brain atlas as reference (Duvernoy, 1999). Time between the index event and most recent scan varied, with a median of 5 days (range 0–741). Lesion locations in patients were widespread throughout the brain; 18 patients had strokes in the right hemisphere, 13 in the left, and 8 showed bilateral damage. Two patients had a history of a previous stroke.

Fifty-three age- and education-matched control participants, without self-reported neurological or psychiatric disorders, were included. The control participants were either spouses or family of patients or volunteers who came to our attention through word of mouth. Written informed consent for patients and control participants was obtained. Participants were compensated for their time and travel expenses and treated in accordance with the Declaration of Helsinki.

Table 1 shows the characteristics of the patients and the control group. Control participants did not differ from the patients with respect to level of education (coded according to Verhage (1983), range 1 through 7 from less than primary school to university degree), (premorbid) intelligence (estimated using the Dutch version of the National Adult Reading Test, scores corrected for age and gender (Schmand, Lindeboom, and van Harskamp (1992))), dexterity, and age, but were more often female than the stroke patients. Stroke is more prevalent in males (Wilson, 2013), and control participants typically included spouses and family members from the opposite sex. Potential influence of gender was therefore examined in all primary analyses.

### 2.2. Tasks

An experimental prospective memory paradigm was developed, in which event-based and time-based assignments were integrated in a continuous performance task, the Bourdon–Wiersma task (Lezak, 1995). See Appendix A for a detailed description of the PM tasks. Briefly, the Bourdon–Wiersma task entails marking arrays of four dots among arrays of 3–5 dots in varying configurations on a sheet of paper (see Fig. A.1). Two PM instructions were added to the standard instructions of the task. Participants were asked to call out the Dutch word for line ("regel") whenever the last configuration in a line contained 3 dots (event-based PM), and to insert a coin in a designated container after each minute passed (time-based PM). Participants were given the assistance of an external aid to monitor time.

As primary measures of event- and time-based PM, the percentages of correct responses on both tasks were calculated. The number of times participants used the timing aid was used as measure of monitoring behaviour. Ongoing task performance was measured by counting the number of lines finished within the task duration of 10 min. An error score was calculated by the number of errors on the continuous performance task (false alarms and misses of crossing the configurations of 4 dots) per line.

In addition to the experimental task, two naturalistic PM tasks were administered that were designed to resemble every-day functioning. Participants were asked to remind the experiment leader to return their watch after finishing the last task (event-based), and to make a phone call after half an hour (time-based).

Scores were based on the accuracy of the performance of the time-based task (within a range of 5 min around the appropriate time a maximum score of 3 was given), and the amount of additional cues that were given before the task was executed (score 3 for correct performance without any (additional) cues, 2 or 1 depending on how many additional cues were needed and 0 for no recollection of the intention when asked). An example of a cue was the experimenter asking after 40 min "how much time do you think has passed since the first task?" (see Appendix A for a description of all cues).

Cognitive functioning was assessed by using standard neuropsychological tasks in the domains of retrospective memory, speed of processing and attention/executive functioning.

To measure retrospective memory, the Dutch version of the Rey Auditory Verbal Learning Test (Saan & Deelman, 1986) was administered. Three variables were used: immediate recall total score, delayed recall and recognition score.

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