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Age differences in brain systems supporting transient and sustained processes involved in prospective memory and working memory

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ABSTRACT

In prospective memory (PM), an intention to act in response to an external event is formed, retained, and at a later stage, when the event occurs, the relevant action is performed. PM typically shows a decline in late adulthood, which might affect functions of daily living. The neural correlates of this decline are not well understood. Here, 15 young (6 female; age range = 23–30 years) and 16 older adults (5 female; age range = 64–74 years) were scanned with fMRI to examine age-related differences in brain activation associated with event-based PM using a task that facilitated the separation of transient and sustained components of PM. We show that older adults had reduced performance in conditions with high demands on prospective and working memory, while no age-difference was observed in low-demanding tasks. Across age groups, PM task performance activated separate sets of brain regions for transient and sustained responses. Age-differences in transient activation were found in fronto-striatal and MTL regions, with young adults showing more activation than older adults. Increased activation in young, compared to older adults, was also found for sustained PM activation in the IFG. These results provide new evidence that PM relies on dissociable transient and sustained cognitive processes, and that age-related deficits in PM can be explained by an inability to recruit PM-related brain networks in old age.

Introduction

Implementing intentions is essential for successfully executing actions at some point in the future. The cognitive processes involved in remembering to perform a specific action are usually referred to as prospective memory (PM). In laboratory studies of PM, participants are typically asked to monitor the environment for the presence of a specific target cue or the arrival of a particular time, and interrupt their performance of an ongoing task to complete the intended action (Einstein GO and MA McDaniel, 1996).

The components of PM can be characterized along several hypothetical dimensions including their reliance on long-term memory or executive functions, their involvement of controlled versus automatic processes, or whether they are transient (related to the cue event) or sustained over a delay prior to cue presentation (e.g. monitoring). An ongoing theoretical debate concerns to what extent cognitive operations involved in PM rely primarily on sustained attentional control processes, or automatic and spontaneous transient processes triggered by an environmental cue that is linked to a specific intention. These transient and sustained processes may work in parallel during the execution of a PM task, and investigating them separately has proven difficult solely based on behavioral measures. Although only a handful of studies have investigated the neural underpinnings of component processes in PM using fMRI, results from these studies have revealed separate sets of regions involved in ongoing sustained processes related to intention maintenance and transient processes related to cue detection (Reynolds JR et al., 2009; Kalpouzos G et al., 2010; McDaniel MA et al., 2013). For example, Reynolds et al. (2009) used a mixed event-related/blocked design to investigate transient and sustained processes associated with PM and working memory. They were able to demonstrate that sustained increase in PFC activity was related to PM task demands and not to the need to implement working memory processes. In addition, prospective memory was associated with distinct transient activation in the temporal cortex during the presentation of PM targets. This indicates that distinct regions may subserve sustained (controlled) and transient (automatic) components of PM.

Subjective PM complaints are common in old age (Zeintl M et al., 2006), and failures in performing an intended action might have severe implications in daily life (e.g. remembering to take medicine). Similar to findings on retrospective memory (e.g. episodic memory), older adults show a general impairment in PM, although age differences are more pronounced in some tasks contexts then others (West R and R Bowry,

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2005; McDaniel MA and GO Einstein, 2007; Kliegel M et al., 2008). Age differences may stem from a decreased efficiency of controlled preparatory attentional processes that underlie the detection of PM cues (West R and R Bowry, 2005; Smith RE and UJ Bayen, 2006), a decline in mechanisms related to the retrospective component of PM (Einstein GO et al., 1992; Zimmermann TD and B Meier, 2006; Zöllig J et al., 2007; Gonneaud J et al., 2011) or impairments in underlying working memory and executive control processes associated with PM (Mäntylä T, 2003; Bisiacchi PS et al., 2008; Rose NS et al., 2010; Gonneaud J et al., 2011; Schnitzspahn KM et al., 2013).

Recent neuroimaging and neuropsychological evidence implicate the prefrontal cortex (PFC) as critical for executing delayed intentions in prospective memory tasks. In particular, the medial and lateral part of the anterior PFC has consistently been activated across time-based and event-based PM tasks (see Burgess PW et al., 2011 for a review). Additionally, the dorsolateral and inferior PFC, the inferior parietal cortex, precuneus, and the anterior cingulate cortex (ACC) have commonly shown enhanced activation during PM tasks (Okuda et al., in press; Simons JS et al., 2006; Haynes JD et al., 2007; Reynolds JR et al., 2009; Poppenk J et al., 2010; Bisiacchi PS et al., 2011; Burgess PW et al., 2011; Hashimoto T et al., 2011; Gonneaud J et al., 2014). In line with observations from fMRI and PET, several ERP studies have observed a frontal positivity effect associated with PM cue trials (see West R, 2011 for a review). Activation in the medial temporal lobe (MTL) has also often been observed in individuals during PM tasks performance (Okuda J et al., 1998; Martin T et al., 2007; Poppenk J et al., 2010). Thus, successful PM may rely on frontal control processes that modulate other brain regions responsible for maintaining the intention and/or for processing incoming information to identify event occurrences.

Given that pronounced age-related alterations in prefrontal systems
Q5 is a hallmark of normal aging (Rajah MN and M D'Esposito, 2005; Raz et al., in press; Persson J and L Nyberg, 2006), they have been assumed to underlie impairments in PM functioning with increasing age (McFarland CP and EL Glisky, 2011; West R, 2011). While this idea seems reasonable, very few studies have attempted to specifically investigate the brain correlates of age-related changes in PM. Moreover, previous studies that have examined the link between PM-related brain activation and aging have used electrophysiological methods, and, while providing excellent temporal resolution, lack the ability to test predictions about brain regional specificity. Indeed, it is noteworthy that no study to date has examined transient and sustained components of PM in relation to aging using fMRI.

The current study was therefore intended to investigate age-related differences in brain activation patterns associated with transient and sustained components of PM in relation to aging using fMRI. The task was designed to facilitate the separation of transient (event-related) and sustained (blocked) components of PM. The major objectives of this study were to further investigate the previous observation of age-related deficit in PM, to examine the neural underpinnings of ongoing and cue-related components across participants in young and older adults, and investigate age-differences in brain networks underlying these components.

Q4

Methods

Participants

Fifteen young (6 female; age range = 23–30 years) and 16 older individuals (5 female; age range = 64–74 years) participated in the study. One older participants' behavioral and neural data were removed from analysis due to technical problems during fMRI scanning. All participants were right-handed, Swedish speakers, and had no history of neurological or psychiatric problems. All participants were screened for claustrophobia, neurological and psychiatric medications, MRI contraindication, and all had normal or corrected to normal vision using scanner compatible glasses or contact lenses. All participants took part in two separate test sessions; one for behavioral assessment, and one for the fMRI scanning session. Informed consent was obtained from all participants. The investigation was approved by the Ethics Committee in Stockholm. Participants were paid 800 SEK for their participation.

Behavioral and neuropsychological results, and group characteristics are reported in Table 1. As noted, older participants scored high on the MMSE, indicating that they were a high performing group of participants and free of dementia. There were no differences between the groups with regards to education or proportion of males/females. The cognitive data further indicates that the two age groups were representative of their respective cohorts, with an advantage for the young in operation span and Stroop task response latencies. Error rates in the Stroop task were low and did not differ significantly between age groups.

Procedure

The study consisted of two separate sessions that occurred on two separate days: first a behavioral test session on day 1, and a second fMRI scanning session on day 2. The time in between each test session was approximately one week. During the behavioral test session, participants completed the color-word Stroop test, a test if visual attention (Bundesen C, 1990; Vangkilde S et al., 2011), and the operation span working memory task (Unsworth N et al., 2005). Older individuals also completed the mini-mental state examination (MMSE). All participants also received instructions and performed practice runs of the scanner tasks in preparation for the scanning session. During the scanning session on day 2, participants again performed practice runs of the scanner task immediately prior to the scanning session.

fMRI task

A slightly modified version of a previously used PM task (Reynolds JR et al., 2009) was used as the scanner task. In the scanner, participants performed four different tasks, with each task consisting of a sequence of colored words (see Fig. 1). Oddball and PM target colors varied randomly within and between individuals, and each participant was never presented with the same target color twice within each condition (Fig. 2). Q6

In the oddball task, participants were informed of a target color, and asked to respond with their right index finger each time the target color was presented, and with their right middle finger if the word was presented in any other color. The oddball targets occurred with low frequency (~10%) and served as a control task for the low-frequency PM cues used in the PM task.

Table 1
Demographics and cognitive performance for young and older adults.

	Young adults	Older adults	*P*
Demographics			
N	15	15	
Age, years (range, SD)	22.4 (20–26, 1.8)	68.1 (64–74, 3.6)	
Gender (f/m)	6/9	5/10	n.s.
Education, years (range, SD)	2.7 (1–3, 0.5)	2.5 (1–3, 0.8)	n.s.
Cognitive scores			
Operation span	46.9 (20.9)	21.0 (12.6)	.001
MMSE (range, SD)		27.9 (26–30, 1.3)	
Stroop task (RT)			
Neutral	816.7	1311.8	.001
Congruent	851.2	1410.1	.001
Incongruent	1029.3	1654.9	.001
Stroop task (error rate)*	1.81	2.16	n.s.

Note: Values are means (range, SD) except for Gender that represent number of participants. MMSE = mini-mental state examination. Education equals the number of years after high school. *P* = p-value for the comparison of young and older adults. RT = Reaction time. n.s. = non-significant. *Error rates were only available for all conditions combined.

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