



Contents lists available at ScienceDirect

Journal of Experimental Child Psychology

journal homepage: www.elsevier.com/locate/jecp



Relations among prospective memory, cognitive abilities, and brain structure in adolescents who vary in prenatal drug exposure



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ARTICLE INFO

Article history:

Available online 12 March 2014

Keywords:

Prospective memory
Prenatal drug exposure
Adolescence
Executive functioning
Retrospective memory
Brain structure

ABSTRACT

This investigation examined how prospective memory (PM) relates to cognitive abilities (i.e., executive function, attention, working memory, and retrospective memory) and brain structure in adolescents who vary in prenatal drug exposure (PDE). The sample consisted of 105 (55 female and 50 male) urban, primarily African American adolescents (mean age = 15.5 years) from low socioeconomic status (SES) families. Approximately 56% ($n = 59$) were prenatally exposed to drugs (heroin and/or cocaine) and 44% ($n = 46$) were not prenatally exposed, but the adolescents were similar in age, gender, race, and SES. Executive functioning, attentional control, working memory, retrospective memory, and overall cognitive ability were assessed by validated performance measures. Executive functioning was also measured by caregiver report. A subset of 52 adolescents completed MRI (magnetic resonance imaging) scans, which provided measures of subcortical gray matter volumes and thickness of prefrontal, parietal, and temporal cortices. Results revealed no differences in PM performance by PDE status, even after adjusting for age and IQ. Executive function, retrospective memory, cortical thickness in frontal and parietal regions, and volume of subcortical regions (i.e., putamen and hippocampus) were related to PM performance in the sample overall, even after adjusting for age, IQ, and total gray matter volume. Findings suggest that variations in PM ability during adolescence are robustly

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related to individual differences in cognitive abilities, in particular executive function and retrospective memory, and brain structure, but do not vary by PDE status.

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Introduction

Prospective memory (PM) is the ability to complete an intended action at a specified future point in time or, more simply, remembering to remember (e.g., Brandimonte, Einstein, & McDaniel, 1996). PM is a multi-phase, complex cognitive ability that includes (a) planning a future activity (intention formation), (b) keeping the intended future event activity in mind (intention retention), (c) initiating the activity (intention initiation), and (d) carrying out the activity according to the previously formed plan (intention execution) (Kliegel, Martin, McDaniel, & Einstein, 2002). An everyday example of PM is remembering to take food out of the oven amid completing other tasks (e.g., making a salad, setting the table, talking on the phone). PM is important for successful daily functioning across the lifespan (Crovitz & Daniel, 1984; Kliegel & Martin, 2003; Terry, 1988).

Although young children are able to complete simple PM tasks (e.g., Ceci & Bronfenbrenner, 1985), age-related improvements have been documented between childhood and adulthood (e.g., Kliegel, Mackinlay, & Jäger, 2008; Wang, Kliegel, Yang, & Liu, 2006; Ward, Shum, McKinlay, Baker-Tweney, & Wallace, 2005; Zimmermann & Meier, 2006; Zöllig et al., 2007). These age-related differences are thought to arise due to environmental and maturational factors, including increased demands placed on individuals (at home, school, and work), increased ability to complete complex cognitive tasks in general, and prolonged development of brain regions supporting PM (Dumontheil, Burgess, & Blake-more, 2008; Kvavilashvili, Messer, & Messer, 2008). The adolescent years may be particularly important in PM development because this period is characterized by (a) significant increases in autonomy (e.g., Osipoff, Dixon, Wilson, & Preston, 2012), (b) improvements in higher order cognitive functions (for a review, see Steinberg, 2005), and (c) continued brain development (particularly of frontal regions; e.g., Gogtay et al., 2004). Indeed, previous research has documented age-related improvements in PM ability during adolescence (e.g., Meacham & Colombo, 1980; Mäntylä, Carelli, & Forman, 2007; Wang et al., 2006, 2011; Zöllig et al., 2007), although exceptions exist (Ward et al., 2005; Zimmermann & Meier, 2006). The current study examined PM during adolescence.

Relations between development of PM and other cognitive abilities

Previous developmental research has shown that age-related improvements in the ability to successfully complete PM tasks are related to the development of at least four different aspects of cognitive functioning: executive functions (e.g., inhibition, cognitive flexibility, planning), controlled attention, working memory, and retrospective memory.

Executive functioning

One study examining PM in 7- to 12-year-old children showed that a large portion of age-related variance in PM task performance could be explained by performance on measures of planning (mapping out a trip to the zoo) and task switching (alternating between two sets of instructions) (Mackinlay, Kliegel, & Mäntylä, 2009; see also Kerns, 2000; Mahy & Moses, 2011; Wang et al., 2006). Similarly, in a study of children (7–10 years), adolescents (13–16 years), and adults (18–21 years), performance on two executive function tasks (self-ordered pointing and Stroop Color Word Interference) predicted PM performance when cognitive demands were high, with better performance on the executive function tasks related to better PM (Ward et al., 2005). These findings suggest that development in executive functioning relates to age-related increases in PM ability.

Controlled attention

The development of attention has also been shown to be related to PM during adolescence. For example, in one study of 13- to 20-year-olds, relations between PM and attention were assessed while participants completed a spatial working memory task (Wang et al., 2011). Specifically, participants were instructed to respond using a button press to PM cues that were presented either outside the area of focal attention (in the form of additional stimuli off to the side of the spatial working memory task) or within the area of focal attention (as a change in background color of the screen on which the spatial working memory task was presented). Developmental differences were observed only for trials in which the cue was presented outside the area of focal attention, suggesting that attentional control may contribute to age-related improvements in PM ability (Wang et al., 2011). Related to these findings, other studies have employed a variety of manipulations that alter attention to PM tasks. These studies show greater benefits of these attentional manipulations for PM performance in adolescents compared with that in young adults (Wang et al., 2006; see also Kerns, 2000; Mattli, Zöllig, & West, 2011; Yang, Chan, & Shum, 2011). Together, these findings suggest that adults' advantage on PM tasks may be related to age-related improvements that facilitate attentional control during tasks and the ability to switch attentional control to other tasks, thereby enhancing PM performance.

Working memory

Studies have also documented a relation between PM and working memory. For example, when intervening tasks require greater use of working memory resources (i.e., higher cognitive load), PM performance has been shown to significantly decrease in children (e.g., Ward et al., 2005). The association between working memory and PM is not solely attributable to age given that significant relations between PM and working memory in 6- to 12-year-old children held even after age was controlled (Kerns, 2000; see also Yang et al., 2011). Little is known about the relation between working memory and PM during adolescence, although the study described previously by Wang and colleagues (2011) suggests that working memory may be important because nonfocal PM cues (in contrast to focal cues) do require working memory in addition to controlled attention.

Retrospective memory

Finally, retrospective memory has been related to successful PM performance during development (e.g., Guajardo & Best, 2000; Wang, Kliegel, Liu, & Yang, 2008; Yang et al., 2011). Specifically, positive correlations have been reported between PM and retrospective memory in 3-, 4-, and 5-year-olds (regardless of load; Wang et al., 2008) and 7- to 12-year-olds (although the pattern of errors on the retrospective memory task differed from that on the PM task; see Yang et al., 2011, for details).

In summary, individual studies have reported associations between PM and (a) executive function, (b) attentional control, (c) working memory, and (d) retrospective memory during childhood and/or adolescence. However, these cognitive functions have not been investigated together in the same study during adolescence. We sought to address this gap by simultaneously examining how PM relates to these abilities in a sample of adolescents.

Neural bases of PM during adolescence

Few studies have examined relations between PM and brain function during adolescence. Most of what is currently known regarding this association comes from electrophysiological studies that have examined neural activity during completion of PM tasks across the lifespan, including adolescence (e.g., Mattli et al., 2011; Zöllig et al., 2007). These studies report age-related differences in behavioral measures of PM and different patterns of neural activity among children, adolescents, and adults. Specifically, event-related potentials (ERPs) generated during trials when PM errors were made appear to be generated from different sources in children/adolescents compared with adults, suggesting that different neural and/or cognitive processes contributed to PM failures in these groups (for details, see Mattli et al., 2011; Zöllig et al., 2007).

Relations between PM and brain structure during adolescence are also relatively unexplored. A comprehensive review of the development of rostral prefrontal cortex (PFC), or Brodmann area 10, suggests that this region likely supports processes of integration or coordination such as PM

(Dumontheil et al., 2008). However, this link was not examined empirically in this report. Relations between event-based PM ability and changes in cortical thickness following moderate to severe traumatic brain injury (TBI) have been examined in children and adolescents (7–17 years; McCauley et al., 2010). Specifically, structural measures acquired 3 months post-injury showed that significant thinning in multiple brain regions in the left hemisphere (dorsolateral and inferior prefrontal cortex, anterior and posterior cingulate, temporal lobe, fusiform, and parahippocampal gyri) and the right hemisphere (dorsolateral, inferior, and medial prefrontal cortex, cingulate, and temporal lobe) was negatively correlated with PM performance (i.e., greater thinning was associated with poorer PM performance; see McCauley et al., 2010, for details).

Although these findings are based on a sample of children and adolescents with brain injury, they are in line with studies in typical adults that have related brain structure (Gordon, Shelton, Bugg, McDaniel, & Head, 2011) and function (i.e., positron emission tomography [PET] and magnetic resonance imaging [MRI]; see Burgess, Gonen-Yaacovi, & Volle, 2011, for a review) to PM, suggesting that PM relies on multiple brain regions. Relations between PM and prefrontal cortex are prominent in the adult literature (i.e., Brodmann area 10; Burgess, Quayle, & Frith, 2001; Burgess et al., 2011; Kliegel, McDaniel, & Einstein, 2008; Okuda et al., 2007; Reynolds, West, & Braver, 2009); however, robust associations with parietal regions (e.g., precuneus; Burgess et al., 2001, 2011; Martin et al., 2007; Reynolds et al., 2009) and temporal regions (including hippocampus; e.g., Gordon et al., 2011) have also been documented.

Finally, prefrontal, parietal, and temporal cortices have also been shown to be related to the other cognitive abilities that play a role in the development of PM; for example, prefrontal cortex plays a role in executive function and working memory, parietal regions play a role in retrospective and working memory, and temporal regions are known to be a key area for retrospective memory (Alvarez & Emory, 2006; Gheiti & Bunge, 2012; Gottlieb & Snyder, 2010; Owen, McMillan, Laird, & Bullmore, 2005). Given these previous associations and the fact that brain development continues throughout the adolescent years (Giedd et al., 1999; Gogtay et al., 2004; Paus, 2005), we sought to examine relations between PM performance and brain structure as measured via MRI.

PM in special populations

PM relies on multiple cognitive systems and neural networks; as such, individual differences in performance may arise from experiences that affect cognitive or brain development. For instance, impairments in PM have been demonstrated in children and/or adolescents with neurodevelopmental disorders such as autism (Farrant, Boucher, & Blades, 1999; Jones et al., 2011), schizophrenia (Kumar, Nizamie, & Jahan, 2008), and acquired traumatic brain injury (TBI; Kinsella et al., 1996; McCauley et al., 2010; Tay, Ang, Lau, Meyyappan, & Collinson, 2010) and those who use substances known to affect brain development (e.g., alcohol: Heffernan & O'Neill, 2012; cigarettes: Heffernan, O'Neill, & Moss, 2012; cannabis: Bartholomew, Holroyd, & Heffernan, 2010).

Our group is conducting a longitudinal study examining the effects of prenatal drug exposure (PDE) on the neurocognitive and social development of adolescents from urban low-income environments (Nair, Black, Ackerman, Schuler, & Keane, 2008; Schuler, Nair, Black, & Kettinger, 2000). Previous research suggests that PDE and its associated risk factors have small but persistent effects on the development of cognitive abilities during childhood and adolescence (for reviews, see Ackerman, Riggins, & Black, 2010; Buckingham-Howes, Berger, Scaletti, & Black, 2013). PDE interferes with the development of monoaminergic neurotransmitters (i.e., dopamine, norepinephrine, serotonin) involved in multiple cognitive systems (Mayes, 1999). Animal models exploring these effects show consistent deficits in executive function, attention, and memory systems (Gabriel & Taylor, 1998; Gendle et al., 2003). Although effects of PDE in humans are also influenced by the complex environments that often accompany parental drug use, effects in some cognitive domains (e.g., cognitive control, behavior regulation, language, memory) and the neural regions that support these abilities have been reported across studies, even when environmental factors are statistically controlled (Ackerman et al., 2010; Buckingham-Howes et al., 2013).

Previous reports from our sample have shown differences in attention (Ackerman et al., 2008) and retrospective memory (Riggins et al., 2012) in children and adolescents with a history of PDE and a

non-exposed community comparison group. These findings suggest that differences in cognitive abilities that relate to PM may result from PDE and its associated environment. Thus, a final goal of this study was to investigate whether PDE influences PM.

The current investigation

The current study examined PM during adolescence, which has been shown to be a time of continued development in PM ability. Because individual differences in PM have been shown to arise as a function of a variety of conditions that affect cognitive and neural development, our first hypothesis was that adolescents with a history of PDE would perform more poorly than non-exposed adolescents from the same community on a PM task. Previous research suggests age-related improvements in PM are related to other cognitive abilities, including executive function, attentional control, working memory, and retrospective memory. Thus, our second hypothesis was that PM would be related to four previously identified aspects of cognitive function (executive function, attentional control, working memory, and retrospective memory) during adolescence. Finally, associations between PM and cognitive ability are likely driven by reliance on overlapping neural substrates such as regions in prefrontal, parietal, and temporal lobes. Our third hypothesis was that PM would relate to measures of brain structure in subcortical, frontal, parietal, and temporal regions.

Method

Participants

Participants were part of a longitudinal study designed to examine the effects of PDE and social and environmental risk factors on the neurocognitive, social, and psychological development of adolescents. Women and their infants ($N = 265$) were recruited shortly after giving birth between February 1992 and July 1995 at a university hospital serving a largely urban African American population for a randomized controlled trial of a home-based intervention for substance-abusing women and their infants (Nair, Schuler, Black, Kettinger, & Harrington, 2003). Eligibility criteria included prenatal drug exposure (cocaine/heroin), gestational age of more than 32 weeks, birth weight of more than 1750 g, and no congenital or medical problems requiring admission to the neonatal intensive care unit. Infants and their caregivers were followed for evaluations through middle childhood and were recontacted for follow-up during adolescence. Recruitment and follow-up procedures are described in detail elsewhere (Schuler et al., 2000). The current analyses focus on data collected during adolescence.

Two non-exposed community comparison (CC) samples with no evidence of PDE were recruited from the university primary care clinic at the 5-year time point and the early adolescent time point (at approximately 14 years of age). Medical records were reviewed to identify children born in the university hospital during the same period as children in the PDE group; drug testing of new mothers and newborns was mandatory at that time. Participants had negative mother and infant toxicology screens and no evidence of drug use during pregnancy. CC children were in the care of their biological mothers and had no serious developmental or congenital problems. Participants were recruited to be similar to the PDE group on child's age, gender, and race as well as maternal education level at the birth of the target child and age of first pregnancy (Ackerman et al., 2008; Schuler & Nair, 2001).

Both the PDE and CC participants were contacted during early adolescence and recruited for additional assessments. One assessment took place during early adolescence, which was conducted from January 2007 to March 2010, and another took place during mid-adolescence, which was conducted from July 2008 to February 2011. In addition, an associated neuroimaging study was conducted in between these visits from August 2007 to July 2008. A total of 105 adolescents (PDE = 59, CC = 46) completed the mid-adolescence assessment (approximately 15.5 years of age), which is the focus of the current report. Of the original PDE sample, 22% were retained during mid-adolescence. A retention analysis demonstrated that there were no significant differences between this sample and the sample lost to follow-up on maternal education, age at first pregnancy, receipt of public assistance (Women,

Infants, and Children [WIC], medical assistance, public housing, Aid to Families with Dependent Children [AFDC], and/or food stamps) or child gender, birth weight, neonatal abstinence syndrome severity, or prenatal exposure to tobacco or alcohol. A subset of 52 adolescents (PDE = 28, CC = 24) were eligible and agreed to participate in an associated neuroimaging study (see below for details). The demographic characteristics of the participants who participated in the scan were similar to those of the full sample.

Procedures

PDE was assessed at delivery through positive mother or infant toxicology screen, maternal self-report, and/or notation in the mother's chart (Schuler et al., 2000). In the current PDE sample, 17% of infants were exposed to cocaine, 7% were exposed to heroin, and 32% were exposed to both cocaine and heroin. The use of other drugs (i.e., tobacco and alcohol) was present in both groups. In the PDE group, 53% were also prenatally exposed to alcohol and 78% to tobacco. In the CC group, 13% were prenatally exposed to alcohol and 20% to tobacco.

Data included in the current report were collected during three separate visits. The first was during early adolescence (average age = 14.2 years, $SD = 1.2$) during which caregivers and adolescents completed comprehensive protocols, including questionnaires and cognitive tasks. The second was an associated neuroimaging study (average age = 14.4 years, $SD = 1.25$; see below for details). The third was during mid-adolescence (average age = 15.5 years, $SD = 1.1$) during which participants completed questionnaires and cognitive tasks, including a PM task that required them to remember various tasks throughout the visit (this task is described in further detail below). Occasionally, participants were not able to complete all tasks due to time constraints. Sample sizes for each task are indicated below (range = 97–105). Participants with data missing for a particular analysis were excluded from that analysis, which resulted in small variations in sample sizes.

Approximately 68% of eligible participants agreed to participate and completed a neuroimaging protocol, which took place after the early adolescence assessment and approximately 1 year before the mid-adolescence visit ($M = 380$ days, $SD = 134$, range = 77–794). This protocol included both structural and functional MRI scans; only results from the former are reported here. Exclusionary criteria for the neuroimaging protocol included metal on or in the body, medications shown to interfere with neuroimaging, history of claustrophobia, pregnancy, substance or medication use the day of the scan, tattoos less than 6 weeks old, neurologic disorders, and brain injuries. There were no differences between groups in delay between the initial visit and scan ($p = .70$). The study was approved by the institutional review boards at the University of Maryland–Baltimore and the National Institute on Drug Abuse's Intramural Research Program. Informed consent was obtained from caregivers, and assent was obtained from all participants. Examiners were blinded to participant drug exposure status at every phase of the study.

Measures

Prospective memory

During the mid-adolescence assessment, a PM task modified from the Memory for Future Intentions Task was administered (Raskin, 2004; Woods, Moran, Dawson, Carey, & Grant, 2008). The items on this PM task were designed to measure adolescents' ability to engage in PM throughout the day while completing other tasks they might experience in other settings such as in school. At the beginning of the laboratory session, participants were told that they would be tested on their ability to remember activities and carry them out. They were instructed that after the experimenter performed a specific action (i.e., clapped his or her hands, snapped his or her fingers, or knocked on the table) or after a given amount of time passed (i.e., 2 or 15 min), they were to write down a specific item on a notecard (e.g., name of a teacher, favorite color, name of their school, favorite TV show, their initials). A total of 5 trials were administered throughout the laboratory session in a set order (Table 1). For example, in Trial 1, the examiner would say, "When I snap my fingers, write the name of a teacher who knows you well on a notecard." In this example, the examiner would keep track of the time and snap his or her fingers at the appropriate time. During the delay interval, participants completed

Table 1

Prospective memory trials administered throughout the laboratory session.

| Trial | Prospective memory instruction | Cue type ^a |
|----------|---|-----------------------|
| Practice | "In 2 minutes, draw a smiley face." | Time |
| Trial 1 | "When I snap my fingers, write the name of a teacher who knows you well." [2 min] | Event |
| Trial 2 | "When I clap, write your favorite color." [15 min] | Event |
| Trial 3 | "After 2 minutes, write the name of your school." | Time |
| Trial 4 | "After 15 minutes, write your favorite TV show." | Time |
| Trial 5 | "When I knock on the table, write your initials." [2 min] | Event |

^a During time-based cues, participants kept track of time; during event-based cues, the experimenter kept track of time.

questionnaires and other non-memory cognitive assessments. Participants earned 1 point for performing the correct action and 1 point for the correct time (± 1 min). After completion of this trial, participants completed additional neurocognitive tests and questionnaires until the examiner introduced the next PM trial. Before the administration of the first trial, participants were given a practice trial and practice adding 2 to 5 min to the current time to ensure understanding of the task and mathematical abilities. The primary dependent measure of interest was the proportion of recall points achieved (out of 5) and was available for 102 participants. Of the original sample, 3 participants did not complete all trials due to time constraints during the session and were excluded from analyses examining differences in performance on measures at the individual trial level (e.g., performance on event- vs. time-based trials).

Executive function

Delis–Kaplan Executive Functioning System Color–Word Interference Test. During the mid-adolescence assessment, participants completed the Delis–Kaplan Executive Functioning System's (D-KEFS) Color–Word Interference Test, which assesses higher level cognitive functions, including executive function. The Color–Word Interference Test is based on the classic Stroop task and measures participants' ability to inhibit verbal responses to generate a conflicting response of naming dissonant ink colors in which words are printed. In Trial 1, participants named the dissonant ink color of the printed words. In Trial 2, participants read the color word. In Trial 3, participants named the dissonant ink color. In Trial 4, participants switched back and forth between naming the dissonant ink color and reading the words. The fourth trial measured inhibition and cognitive flexibility (Delis, Kaplan, & Kramer, 2001). Behavioral measures of executive function as measured by the D-KEFS were available for 103 participants.

Behavior Rating Inventory of Executive Function. During the mid-adolescence assessment, participants' caregivers completed the Behavior Rating Inventory of Executive Function (BRIEF), which is an 86-item questionnaire that assesses executive function behaviors in youths in both home and school environments. The questionnaire produces several scales that measure aspects of executive functioning. Caregivers were provided with statements such as "My child acts upset by a change in plans" and "My child is impulsive" and were asked how each statement describes their child on a Likert-type scale consisting of 1 (*never*), 2 (*sometimes*), and 3 (*often*). Scores were summed and converted to *t* scores with a mean of 50. The BRIEF provides two broad indexes, the behavioral regulation and meta-cognition indexes, and an overall global executive composite, which have excellent internal consistency (Cronbach's alphas = .94, .96, and .97, respectively; Gioia, Isquith, Guy, & Kenworthy, 2000). Cronbach's alphas for the current sample were .96, .96, and .98 for the PDE group and .91, .95, and .95 for the CC group, respectively; combined Cronbach's alpha levels were .95, .96, .96. Caregiver ratings of executive function were available for 100 participants.

Attention

At the early adolescence assessment, participants completed the Continuous Performance Test II (CPT), which is a sustained attention assessment tool administered on a computer and is useful as a screener for attention problems (Conners, 2004). One letter at a time was presented on the screen

at varying intervals of 1, 2, and 4 s, and respondents pressed the space bar for every letter presented except “X.” Letters were presented in six blocks, with three sub-blocks each containing 20 letter presentations. The entire task took approximately 14 min to complete. Split-half reliability for all CPT variables ranged from .73 to .95. The CPT has high sensitivity to distinguishing between ADHD (attention deficit/hyperactivity disorder) clinical and nonclinical comparison groups. Commission and omission errors were used in analyses. Commission errors occurred when participants pressed the space bar on trials when the letter “X” was presented. Omission errors occurred when participants failed to press the space bar on trials containing non-“X” letters. Measures of attention were available for 103 participants.

Working memory

At the mid-adolescence assessment, participants completed the Cambridge Neuropsychological Test Automated Battery's Spatial Working Memory task (CANTAB-SWM), which is a language-independent neurocognitive assessment battery administered using a touch-screen computer. The Spatial Working Memory task was administered to measure the ability to retain spatial information and manipulate remembered items in working memory. A number of boxes were presented on the screen. Participants completed 3 practice trials with three boxes each and then completed a series of trials increasing in difficulty from four to eight boxes. One blue token was hidden in one of the boxes. Participants opened each box until it was found and then placed the blue token in a column on the right side of the screen. Then, avoiding the box that had contained the blue token, participants were instructed to search for the next blue token, which might be hidden in any of the previously empty boxes. The process was repeated until a blue token was found in every box. Performance was measured by the number of errors made during each trial. Errors were counted when participants opened a box where a blue token had already been found (Cambridge [Cognition, 2006](#)). This measure of working memory ability was available for 103 participants.

Retrospective memory

At the mid-adolescence assessment, participants completed the California Verbal Learning Test-Children's Version (CVLT-C), which measures strategies and processes involved in learning and recalling verbal material. In this task, participants were asked to remember a shopping list of 15 items (List A). For the first 5 trials, the same list was read to participants, and they were asked to recall words from the list after each presentation. A second list (List B) was then presented, and participants were asked to recall as many words from this list as possible. Then, participants were asked to list items from List A. The 15 words on List A were categorized as fruits, clothing, or toys, and participants were given cues based on these categories to elicit words from List A (e.g., “Tell me things to wear”). This assessment resulted in measures of immediate recall (List A-Trial 1), learning (List A-Trial 5), and proactive interference (List B and percentage change from List A-Trial 1 to List B-Trial 1) ([Delis, Kramer, Kaplan, & Ober, 1994](#)). This measure was available for 97 participants.

General intelligence

At the early adolescence assessment, an estimate of general intellectual ability (IQ) was obtained using the Vocabulary and Matrix Reasoning subtests from the Wechsler Abbreviated Scale of Intelligence (WASI). The Vocabulary subtest measures word knowledge, verbal concept formation, and fund of knowledge. The Matrix Reasoning subtest measures visual information processing and abstract reasoning skills ([Wechsler, 1999](#)). IQ was available for 102 participants.

Anatomical MRI

Between the early and mid-adolescence assessments, a 3-T Siemens Allegra scanner was used to acquire a whole-brain oblique axial T1-weighted structural image (MPRAGE) for anatomical evaluation (1-mm³ isotropic voxels: TR [repetition time] = 2.5 s; TE [time to echo] = 4.38 ms; FA [flip angle] = 80°). Cortical reconstruction and volumetric segmentation was performed using the FreeSurfer image analysis suite (<http://surfer.nmr.mgh.harvard.edu>). The technical details of the FreeSurfer pipeline are described in prior publications ([Dale, Fischl, & Sereno, 1999](#); [Dale & Sereno, 1993](#); [Desikan et al., 2006](#); [Fischl & Dale, 2000](#); [Fischl, Liu, & Dale, 2001, 2004b](#); [Fischl, Sereno, & Dale, 1999a](#);

Fischl, Sereno, Tootell, & Dale, 1999b; Fischl et al., 2002; Fischl et al., 2004a; Han et al., 2006; Jovicich et al., 2006; Reuter, Rosas, & Fischl, 2010; Segonne, Pacheco, & Fischl, 2007; Segonne et al., 2004; Sled, Zijdenbos, & Evans, 1998). FreeSurfer morphometric procedures have been demonstrated to show good test–retest reliability across scanner manufacturers and across field strengths (Han et al., 2006).

A total of 14 bilateral regions of interest (ROIs) were selected from frontal, parietal, and temporal regions that approximate areas that have been previously shown to be related to PM (Burgess, Dumontheil, & Gilbert, 2007; Gordon et al., 2011; Umeda, Nagumo, & Kato, 2006). The dependent measure for subcortical regions (hippocampus, caudate, and putamen) was gray matter volume (e.g., Gordon et al., 2011) and for cortical regions (parsopercularis, parsorbitalis, parstrangularis, superior frontal, caudal/rostral anterior cingulate, precuneus, rostral middle frontal, frontal pole, parahippocampus, and entorhinal) was cortical thickness (see McCauley et al., 2010, for a similar approach during adolescence) based on the Desikan–Killiany atlas (see Desikan et al., 2006, for details). Because measures of gray matter volume of cortical regions have also been used in the adult literature (e.g., Gordon et al., 2011), we included analyses of these in the online [supplementary material](#). Of the 52 participants who participated in the imaging study, 47 (22 CC and 25 PDE) had both PM and imaging data.

General analytic approach

First, differences between the PDE and CC groups' performance on the cognitive assessments (including PM, executive function, attention, working memory, and retrospective memory) and measures of brain structure were examined. Second, relations between PM and other cognitive abilities were examined using correlations conducted between PM and each task. Multivariate analyses were also conducted to examine which measures accounted for the greatest variance in PM ability and included both traditional least-squares regression and a general monotone model (GeMM; Dougherty & Thomas, 2012). GeMM is a semi-parametric statistical algorithm that models the data at the rank-order level (using Kendall's tau). The advantage of GeMM is that linear relations are not assumed or required, and it is less affected by extreme scores or nonlinearities in the data, which may be important because the PM task consisted of 5 trials and previous research has not yet verified interval properties of the dependent measures. GeMM uses a model selection procedure based on the Bayesian information criterion (BIC), with preference given to models with smaller values of BIC. For reference, a BIC of zero corresponds to the null model (Dougherty & Thomas, 2012). In short, the GeMM analysis serves as a complementary test to the traditional least-squares model and will provide additional support for any observed effects. Finally, relations between PM and brain structure were examined for the subset of participants for whom MRI data were available using a similar correlational approach to that used with the cognitive assessments. To retain maximal variability in the data, raw scores were used as dependent measures in all analyses. Analyses were not corrected for multiple comparisons (for justification, see Perneger, 1998; Rothman, 1990; Saville, 1990).

Results

Demographic comparison

Differences between the PDE and CC groups were evaluated for the following variables: gestational age, birth weight, age at the mid-adolescence assessment, IQ, gender, food security, grade in school, living with biological mother, caregiver's age at mid-adolescence visit, caregiver IQ, and prenatal exposure to substances other than cocaine and heroin (e.g., alcohol, tobacco) (see [Table 2](#)). Results revealed that adolescents in the PDE group had lower birth weights than adolescents in the CC group (2806 vs. 3463 g), were older at the mid-adolescence assessment than the CC group (15.68 vs. 15.23 years), were less likely than the CC group to be living with their mothers (68% vs. 100%), had older caregivers than the CC group (48.8 vs. 39.7 years), and were exposed more often to alcohol and tobacco during the prenatal period than the CC group. No differences were found between groups in gestational age, IQ, gender, food security, grade in school, or caregiver IQ.

Table 2

Comparison of demographic information between groups.

| Demographics | PDE | CC | Group difference |
|-------------------------------|------------------|------------------|--|
| At birth | | | |
| Gestational age (weeks) | 38.52 (2.49) | 39.16 (1.41) | $t(94) = 1.44, p = .15, d = -0.32$ |
| Birth weight (g) | 2806.36 (528.60) | 3463.59 (628.70) | $t(98) = 5.66, p < .001, d = 1.13$ |
| Adolescence | | | |
| Age (years) | 15.68 (1.13) | 15.23 (1.01) | $t(103) = -2.16, p = .03, d = -0.42$ |
| IQ (standard score) | 90.47 (33.30) | 94.76 (34.29) | $t(102) = 0.65, p = .52, d = -0.13$ |
| Gender | 49% male | 46% male | $t(103) = 0.35, p = .73, d = 0.06$ |
| Food security | 21.1% (high) | 35.6% (high) | $\chi^2(102) = 5.03, p = .17, r = .22$ |
| Grade in school (range) | 7th–12th grades | 7th–12th grades | $\chi^2(103) = 7.55, p = .18, r = .27$ |
| Living with biological mother | 68% | 100% | $t(100) = 5.08, p < .01, d = 1.71$ |
| Caregiver | | | |
| Caregiver age (years) | 48.8 (9.8) | 39.7 (6.3) | $t(103) = -5.46, p < .001, d = -1.10$ |
| Caregiver IQ (full scale) | 85.37 (13.80) | 89.40 (12.60) | $t(102) = 1.53, p = .13, d = 0.30$ |
| Exposure to other substances | | | |
| Alcohol | 53% | 13% | $t(103) = -4.57, p < .001, d = -0.90$ |
| Tobacco | 78% | 20% | $t(103) = -7.23, p < .001, d = -1.42$ |

Note. Bold indicates significant difference ($p < .05$). Comparison includes only adolescents who participated in the mid-adolescent time visit where the prospective memory measure was collected.

Differences between PDE and CC groups on cognitive tasks and measures of brain structure

Group differences in PM, executive function, working memory, attentional control, and retrospective memory were evaluated using analyses of covariance (ANCOVAs) controlling for IQ and age at the mid-adolescence assessment. This approach was taken to ensure that any observed effects would not be driven by the observed age difference between the groups or effects of cognitive ability in general (Table 3).

Prospective memory

Between-group analyses revealed no differences between the PDE and CC groups on PM recall (see Table 3). In addition, there were no differences between groups on any subtype of the PM task (e.g., event- vs. time-based PM, 2- vs. 10-min delay) (all $ps > .13$). Across all adolescent participants, performance on PM recall varied from 12.5% to 100% accuracy. Performance for event-based PM was better than that for time-based PM, and performance on 2-min delay trials was better than that on 15-min delay trials (see Table 3). Bayesian analysis revealed Bayes factors ranging from 2.84 to 6.28, with all measures of PM supporting the null hypothesis that there were no differences between the PDE and CC groups.

Other cognitive measures

Analyses revealed significant differences between the PDE and CC groups on executive function abilities, as indexed by caregiver report (BRIEF; see Table 3). Adolescents with a history of PDE had higher scores (poorer executive function) compared with CC adolescents for all three indexes of the BRIEF: Behavior Regulation subscale, Metacognition subscale, and Global score ($ps < .05$). No differences between groups were found for the other cognitive measures (i.e., CANTAB-SWM, D-KEFS, CPT, or CVLT-C). Bayes factors for the behavioral measure of executive function (D-KEFS), controlled attention (CPT), working memory (CANTAB-SWM), and retrospective memory (CVLT-C) support the null hypothesis. However, Bayes factors for the caregiver-reported measure of executive function provide weak support for group differences (see Table 3).

Brain structure

Group differences in brain structure were evaluated using ANCOVAs controlling for total gray matter and age at time of the scan to ensure that any observed effects were not the result of total brain size or general maturation related to age. Analyses revealed significant differences between the PDE

Table 3

Average participant scores on all cognitive tasks.

| | PDE [mean (SD)] | CC [mean (SD)] | Group difference | Bayes factor |
|---------------------------------|-----------------|----------------|--|--------------|
| Prospective memory | | | | |
| Recall | 75.5 (20.0) | 78.7 (14.0) | $F(1, 97) = 1.13, p = .29, \eta^2 = .01$ | 3.82 |
| Time-based | 51.8 (37.2) | 56.1 (30.2) | $F(1, 97) = 0.76, p = .38, \eta^2 = .01$ | 4.55 |
| Cue-based | 89.4 (17.7) | 90.6 (18.2) | $F(1, 97) = 0.17, p = .69, \eta^2 < .01$ | 6.00 |
| 2-min delay | 83.4 (22.8) | 88.6 (18.0) | $F(1, 97) = 1.77, p = .19, \eta^2 = .02$ | 2.84 |
| 15-min delay | 62.1 (27.0) | 61.1 (26.4) | $F(1, 97) = 0.07, p = .79, \eta^2 < .01$ | 6.28 |
| Executive function (D-KEFS) | | | | |
| Inhibition condition | 8.2 (3.3) | 8.9 (2.7) | $F(1, 98) = 1.45, p = .23, \eta^2 = .02$ | 3.01 |
| Cognitive flexibility condition | 8.8 (3.2) | 8.6 (2.8) | $F(1, 98) = 0.08, p = .79, \eta^2 < .01$ | 6.28 |
| Executive function (BRIEF) | | | | |
| Behavior regulation | 57.3 (13.2) | 51.3 (8.7) | $F(1, 95) = 5.98, p = .02, \eta^2 = .06$ | 0.41 |
| Metacognition | 58.4 (10.9) | 53.0 (9.3) | $F(1, 95) = 5.43, p = .02, \eta^2 = .05$ | 0.53 |
| Global | 58.5 (12.2) | 52.6 (8.8) | $F(1, 95) = 6.35, p = .01, \eta^2 = .06$ | 0.35 |
| Attentional control (CPT) | | | | |
| Commissions | 52.0 (8.4) | 54.2 (11.1) | $F(1, 98) = 0.16, p = .68, \eta^2 < .01$ | 6.35 |
| Omissions | 55.7 (14.6) | 54.8 (17.2) | $F(1, 98) = 0.06, p = .81, \eta^2 < .01$ | 6.05 |
| Working memory (CANTAB-SWM) | | | | |
| Eight box errors | 24.6 (11.0) | 25.2 (11.1) | $F(1, 98) = 0.10, p = .75, \eta^2 < .01$ | 6.21 |
| Retrospective memory (CVLT-C) | | | | |
| A 1–5 | 48.1 (11.0) | 49.3 (9.2) | $F(1, 92) = 0.18, p = .68, \eta^2 < .01$ | 5.84 |
| A 1 | 0.19 (0.96) | 0.05 (0.80) | $F(1, 92) = 1.14, p = .29, \eta^2 = .01$ | 3.73 |
| B | −0.78 (0.94) | −0.55 (0.87) | $F(1, 92) = 1.26, p = .26, \eta^2 = .01$ | 3.53 |
| % Change A to B | −0.99 (1.20) | −0.59 (1.10) | $F(1, 92) = 2.45, p = .12, \eta^2 = .03$ | 2.04 |

Note. Group differences were evaluated using ANCOVAs controlling for age and IQ. CANTAB-SWM, Spatial Working Memory task from the Cambridge Neuropsychological Test Automated Battery; BRIEF, Behavioral Rating Inventory of Executive Function; CVLT-C, California Verbal Learning Test–Children's Version; CPT, Conners' Continuous Performance Task. Standard scores are presented for means and standard deviations when available to facilitate comparison with other samples. Bold indicates significant difference.

and CC groups in left and right hippocampal volume only, $F_s(1, 48) = 12.91$ and $8.54, p_s \leq .01, \eta^2_s = .23$ and $.15$, respectively. Hippocampal volume (mm^3) in both the left and right hemispheres was larger in the PDE group (left: $M = 4046.71, SD = 409.68$; right: $M = 4081.25, SD = 381.31$) compared with the CC group (left: $M = 3810.88, SD = 327.61$; right: $M = 3877.42, SD = 346.46$). This finding has been reported previously (Riggins et al., 2012). A marginal difference in thickness was observed in rostral middle frontal cortex in the right hemisphere, $F(1, 48) = 3.49, p = .07, \eta^2 = .08$. Rostral middle frontal gyrus was thicker in the PDE group ($M = 2.64, SD = 0.13$) compared with the CC group ($M = 2.55, SD = 0.13$) (see also [supplementary material](#) for analyses of cortical volume). Bayesian analyses supported these findings with Bayes factors of 0.02, 0.13, and 0.75, suggesting group differences for left hippocampus, right hippocampus, and right rostral middle frontal cortex, respectively.

Relations between PM and cognitive ability

Because analyses on all but one of the cognitive measures revealed no differences between the PDE and CC groups, all subsequent analyses were conducted with the groups combined (analyses of PDE and CC groups separately are available in the [supplementary material](#) but are largely consistent with the combined group findings). To examine relations between PM and other cognitive abilities, partial correlations controlling for age at the mid-adolescence assessment were conducted examining relations between PM recall and (a) general cognitive abilities (IQ), (b) executive function performance (D-KEFS), (c) caregiver report of executive function (BRIEF), (d) working memory (CANTAB-SWM), (e) attentional control (CPT), and (f) retrospective memory (CVLT-C) (see [Table 4](#)).

Consistent with previous research (e.g., Yang et al., 2011), PM recall was marginally related to IQ, $r(99) = .19, p = .06$. To ensure specificity in observed relations between PM and cognitive abilities, IQ was added as a covariate in all subsequent analyses along with age.

Table 4

Partial correlations between prospective memory and other cognitive measures controlling for age and IQ.

| | <i>r</i> | <i>p</i> |
|-------------------------------|----------|----------|
| Executive function (D-KEFS) | | |
| Inhibition | –.28 | .01 |
| Inhibition-switching | –.32 | .001 |
| Executive function (BRIEF) | | |
| Behavior regulation | –.18 | .08 |
| Metacognition | –.22 | .03 |
| Global | –.22 | .04 |
| Attentional control (CPT) | | |
| Commissions | –.08 | .46 |
| Omissions | –.10 | .33 |
| Working memory (CANTAB-SWM) | | |
| Eight box errors | –.20 | .06 |
| Retrospective memory (CVLT-C) | | |
| A 1–5 | .43 | .001 |
| A 1 | .25 | .02 |
| B | .24 | .02 |
| % Change A to B | .06 | .57 |

Note. CANTAB-SWM, Spatial Working Memory task from the Cambridge Neuropsychological Test Automated Battery; BRIEF, Behavioral Rating Inventory of Executive Function; CLTV-C, California Verbal Learning Test– Children's Version; CPT, Conners' Continuous Performance Task. Bold indicates significant difference.

Results from these analyses revealed that PM recall was related to both measures of retrospective memory and executive function. Specifically, better performance on the PM task was associated with better retrospective memory and better executive function ability. No relations were observed between PM and attentional control or working memory.

Finally, to determine which variables of interest (age, group membership, general cognitive abilities, executive function performance, caregiver report of executive function, working memory, attentional control, and retrospective memory) accounted for unique variance in PM, we modeled the data using both traditional least-squares regression and GeMM (Dougherty & Thomas, 2012; see “General analytic approach” section in Method). To reduce multicollinearity, one measure from each cognitive task was selected based on the largest correlation value from the previous analysis. The Global score on the BRIEF and the switching condition of the D-KEFS were not correlated, $r(98) = .07$, $p = .52$; thus, both were included in the regression, resulting in eight predictors (see Table 5). Correlations among other predictors ranged from .01 to .45.

Table 5

Summary of regression analysis predicting PM recall.

| | <i>R</i> ² | <i>F</i> | β | <i>t</i> |
|-----------------------------|-----------------------|----------|---------|----------|
| Model | .30 | 4.14* | | |
| Exposure group (PDE or CC) | | | –0.07 | –0.64 |
| Age | | | 0.14 | 1.35 |
| IQ | | | 0.12 | 1.20 |
| D-KEFS inhibition-switching | | | –0.13 | –1.21 |
| BRIEF global | | | –0.20 | –2.03* |
| CPT omissions | | | –0.01 | 0.92 |
| CANTAB-SWM | | | –0.01 | 0.93 |
| CVLT-C A 1–5 | | | 0.36 | 3.27* |

Note. CANTAB-SWM, Spatial Working Memory task from the Cambridge Neuropsychological Test Automated Battery; BRIEF, Behavioral Rating Inventory of Executive Function; CLTV-C, California Verbal Learning Test–Children's Version; CPT, Conners' Continuous Performance Task.

* $p < .05$.

The eight-predictor model based on least-squares regression accounted for 30% of the variation in PM recall, $R^2 = .30$, $F(8, 87) = 4.14$, $p < .001$. Under this model, both retrospective memory ability and caregiver reports of executive function accounted for a significant amount of variance (β s = 0.36 and -0.20 , respectively, $ps < .05$).

Applying GeMM to the data revealed a three-predictor model consisting of age, CVLT-C, and BRIEF as the best-fit model. Fit statistics for this model and the reduced model are provided in Table 6. The majority of the explanatory power is carried by CVLT-C and BRIEF, which is identical to the result in the least-squares model. The inclusion of age, which is justified by BIC, leads to a small but meaningful increase in tau of .052, suggesting that it is also a useful predictor of PM in our sample.

Relations between PM and brain structure

To examine relations between PM and brain structure, partial correlations were conducted between PM recall performance and 14 bilateral ROIs in subcortical, frontal, parietal, and temporal regions controlling for age at scan, age at behavioral assessment, and total gray matter (see Table 7).

Results revealed significant negative relations between PM performance and volume of the left putamen and right hippocampus and significant positive correlations between PM and right pars opercularis, left and right superior frontal cortex, right pars triangularis, right caudal anterior cingulate, right rostral middle frontal cortex, and left and right precuneus (see Fig. 1, Table 7, and supplementary material).

Finally, GLM regressions were conducted to examine the independent relation between PM and the brain areas that showed significant correlations. For these analyses, measures of cortical thickness or subcortical volume served as the dependent measures, and age at scan, total gray matter volume, retrospective memory, executive function, and PM served as the predictor variables. Results revealed that PM was uniquely related ($ps < .05$) to the left putamen and right hippocampal volume and to the right pars triangularis, left and right superior frontal cortex, right caudal anterior cingulate, right rostral middle frontal cortex, and left precuneus thickness. However, PM ability was not uniquely related to right pars opercularis and right precuneus.

Discussion

Three major findings emerged in the current study examining PM during adolescence. First, contrary to our hypothesis, no differences were present in PM performance between adolescents with a history of PDE and the CC group. Second, consistent with our hypothesis, measures of ability in other cognitive domains were related to PM performance. Specifically, performance on both executive function and retrospective memory tasks were related to PM. Third, consistent with our hypothesis, performance on the PM task was related to cortical thickness in frontal and parietal regions and volume of subcortical regions (i.e., putamen and hippocampus). These results are discussed in detail below.

Table 6
Model fit statistics from GeMM analysis.

| Model | BIC _{tau} | tau | R | K | B _{Age} | B _{CVLT} | B _{BRIEF} |
|--------------------|--------------------|-------|------|---|------------------|-------------------|--------------------|
| 3 Predictor models | | | | | | | |
| Age*CVLT*BRIEF | −6.8800 | 0.334 | .510 | 3 | 0.76166 | 0.19323 | −0.0451 |
| 2 Predictor models | | | | | | | |
| Age*CVLT | −4.4587 | 0.273 | .450 | 2 | 0.77808 | 0.22192 | |
| Age*BRIEF | −1.9235 | 0.247 | .307 | 2 | 0.90924 | | −0.0908 |
| CVLT*BRIEF | −5.3231 | 0.282 | .486 | 2 | | 0.81957 | −0.1804 |
| 1 Predictor models | | | | | | | |
| Age | 1.50331 | 0.130 | .168 | 1 | 1 | | |
| CVLT | −5.5402 | 0.237 | .434 | 1 | | 1 | |
| BRIEF | 0.29425 | 0.154 | .252 | 1 | | | 1 |

Note. Beta weights are normalized so that the sum of the absolute values is equal to 1.

Table 7

Partial correlations between prospective memory and measures of brain structure controlling for total gray matter and age at scan and behavioral session.

| Gray Volume/Thickness | Hemisphere | <i>R</i> | <i>p</i> |
|----------------------------|------------|----------|----------|
| Caudate | Left | .05 | .76 |
| | Right | .05 | .75 |
| Putamen | Left | –.32 | .04 |
| | Right | –.17 | .27 |
| Hippocampus | Left | –.13 | .39 |
| | Right | –.33 | .03 |
| Hemisphere | | | |
| Pars opercularis | Left | .29 | .06 |
| | Right | .36 | .02 |
| Pars orbitalis | Left | .21 | .18 |
| | Right | .12 | .45 |
| Pars triangularis | Left | .26 | .09 |
| | Right | .39 | .01 |
| Superior frontal | Left | .40 | .01 |
| | Right | .32 | .03 |
| Caudal anterior cingulate | Left | .11 | .49 |
| | Right | .37 | .01 |
| Rostral anterior cingulate | Left | .02 | .86 |
| | Right | .21 | .18 |
| Rostral middle frontal | Left | .23 | .13 |
| | Right | .31 | .04 |
| Frontal pole | Left | .09 | .57 |
| | Right | .27 | .08 |
| Precuneus | Left | .37 | .01 |
| | Right | .33 | .03 |
| Parahippocampus | Left | .17 | .27 |
| | Right | .18 | .25 |
| Entorhinal cortex | Left | .04 | .81 |
| | Right | .10 | .51 |

Note. Bold indicates $p < .05$.

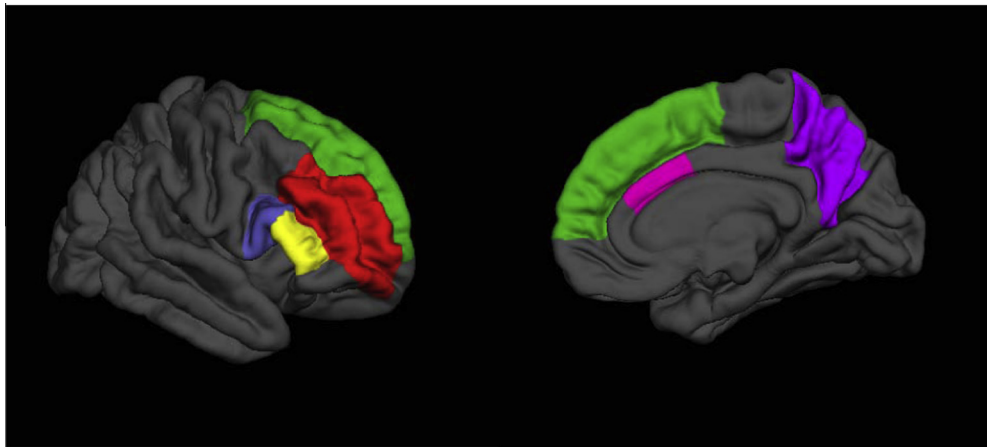


Fig. 1. Cortical regions in the right hemisphere that were significantly correlated with PM performance in the combined sample ($n = 47$) depicted on the template brain from FreeSurfer. Green, superior frontal cortex; red, rostral middle frontal cortex; yellow, pars triangularis; blue, pars opercularis; pink, caudal anterior cingulate; purple, precuneus. Left hemisphere regions (superior frontal cortex and precuneus) and subcortical regions (left putamen and right hippocampus), which were also associated with PM, are not depicted. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Prenatal drug exposure and PM

No differences were observed in PM performance between the PDE and CC groups. Although this was contrary to our hypothesis, previous research suggests that direct effects of PDE on cognitive behavior and brain development are subtle and often attenuated by environmental factors (Ackerman et al., 2010; Buckingham-Howes et al., 2013). Moreover, the PDE and CC groups showed no differences on many of the variables from which indirect effects of PDE are thought to arise (e.g., food security, caregiver IQ), suggesting that the possible influence of these variables was minimal in this sample.

In addition, there were no differences between the PDE and CC groups on most (i.e., all but one) of the other measures of cognitive abilities. Specifically, there were no differences on performance measures of executive function, attentional control, working memory, or retrospective memory, which differs from previous studies (both in our sample and in other cohorts) that have reported PDE-related differences in attention during childhood (e.g., Ackerman et al., 2008) and retrospective memory during early adolescence (e.g., Betancourt et al., 2011; Riggins et al., 2012). Although many possible explanations exist for the lack of consistency in these findings, one possible explanation is biased attrition in longitudinal investigations. It is possible that those retained longest in longitudinal investigations are the least affected and, thus, significant differences were not observed between the PDE and CC participants who returned for the mid-adolescent assessment. A second possible explanation is that the effects of PDE on cognition decrease with age and dissipated over time (similar to decreased effects of PDE on physical development; e.g., Ackerman et al., 2010; Frank, Augustyn, Knight, Pell & Zuckerman, 2001; cf. Betancourt et al., 2011).

The only significant group difference that emerged on the cognitive tasks was in caregiver-reported difficulties with executive function, with adolescents with a history of PDE having more difficulties. This is particularly interesting because behavioral measures of executive functioning did not show a group difference. The discrepancy between caregiver reports of executive functioning and our behavioral assessment may suggest that differences in executive function exist but were not revealed by the laboratory-based task and only emerge amid the cognitive and social challenges present in daily life.

Group differences in brain structure were restricted to hippocampal volume (bilaterally) and thickness of the right rostral middle frontal cortex (although this failed to meet the conventional statistical threshold). Differences in hippocampal volume from this dataset have been reported previously (see Riggins et al., 2012). Differences in thickness of right rostral prefrontal cortex are novel and are consistent with a previous report on a sample of adolescents with a history of prenatal cocaine exposure (Liu et al., 2013). It is interesting to note that volume of both the right hippocampus and thickness of the right rostral prefrontal cortex were correlated with performance on the PM task. However, given that there were no differences between the groups on PM ability, additional research is needed to understand the consequences of PDE on brain structure and, ultimately, what these differences may mean for complex cognitive behavior such as PM.

Cognitive function and PM

PM was associated with executive functioning (on a behavioral task and through caregiver reports) and retrospective memory individually and in a model that included other measures of cognitive function. These findings suggest interdependence between PM with executive functioning and retrospective memory among adolescents, even after adjusting for general intellectual ability and age. As described in the Introduction, PM is a multi-phase complex ability. Thus, one possible avenue for future research would be to examine whether executive functioning and retrospective memory are related to specific phases or aspects of PM. For example, how these abilities relate specifically to the intention retention and intention initiation subcomponents of PM.

Working memory and attention were not related to PM performance either individually or in a model with other measures of cognitive function. This finding also differs from previous research (e.g., Wang et al., 2006, 2011; Ward et al., 2005). However, these studies suggest that age-related differences in attention and working memory influence PM under conditions where there is high cognitive demand. Therefore, one possible reason for the lack of association in this report is that the task

and design used did not place high enough working memory and attentional demands on participants to yield these effects. Another possible explanation is the difference in task modalities. For example, our working memory measure consisted of a spatial working memory task; however, there was no spatial component to our PM task. Likewise, the attentional control task was visual, and the PM task directions were given verbally. Future research is needed to more fully characterize the effects of working memory and attention on PM performance during adolescence, particularly when task demands are high and within similar domains (e.g., visual, spatial, verbal).

Brain structure and PM

Although previous research in adults has examined relations between brain structure and function and PM (e.g., [Burgess et al., 2011](#); [Gordon et al., 2011](#)), few studies of this nature exist for developmental samples (cf. [McCauley et al., 2010](#)). The current report adds to this area by reporting relations between PM performance and brain structure during adolescence. Results suggested that PM performance was correlated with subcortical and frontal and parietal cortical regions. Consistent with previous findings in adults, PM performance was related to hippocampal volume across the entire sample ([Gordon et al., 2011](#)). In addition, PM performance was also related to thickness in prefrontal and parietal regions, which is consistent with previous research during adolescence ([McCauley et al., 2010](#)). These findings suggest that, similar to research in adults, significant relations can be detected between PM and neural regions that support PM (and other cognitive abilities).

Conclusion

The current study adds important and novel information to the growing body of literature on PM during development. Strengths of the article include a focus on adolescence, consideration of effects of prenatal drug exposure on PM performance, examination of four cognitive abilities that have been previously identified in the literature as relating to PM performance, statistical control of age and IQ to increase specificity of the findings, and examination of relations between PM performance and brain structure. However, there are several limitations of the current work that should be noted. First, findings from the current study are preliminary and should be replicated in another sample because it is unclear how characteristics specific to our sample (e.g., low SES urban adolescents who were primarily African American, group differences between PDE and CC adolescents, high attrition rates) contributed to the results. Findings from the current study should also be extended to examine the influence of other characteristics, such as age or gender, because these characteristics have been shown to influence the effects of PDE (e.g., [Betancourt et al., 2011](#); [Carmody, Bennett, & Lewis, 2011](#)). Second, given the comprehensive nature of this study, PM was one of many abilities assessed. Although this design was advantageous in that it allowed for the comparison of PM performance with other assessments, this design required that the PM task be limited. Thus, the number of trials and different subtypes of PM could not be evaluated (e.g., event- vs. time-based PM). Third, the PM task was administered in the laboratory and might not have been reflective of PM in everyday life. Finally, only one measure of working memory and attention was included in the study. Thus, the lack of significant relations between these measures may have been driven by specific aspects of the task (e.g., difficulty) or parameters available for analysis.

In summary, the current investigation reports that variations in PM ability during adolescence are not related to a history of PDE but are related to individual differences in cognitive abilities and brain structure. Specifically PM was related to both executive function and retrospective memory, which is consistent with previous reports of PM development and its integration with other measures of cognitive function. PM was also negatively related to volume of the putamen and hippocampus and positively related to cortical thickness in frontal and parietal regions. Together, these findings add to the growing body of literature examining the development of PM and factors that may influence this process.

Acknowledgments

The authors thank the participants for their continued contribution to this longitudinal study; Elliott Stein, Kelsey Cacic, and the Neuroimaging Research Branch of the National Institute on Drug Abuse Intramural Research Program (NIDA–IRP) for support with data collection and analysis; Prasanna Nair and the FUTURES team for participant recruitment and testing; and Michael Dougherty, Jeffery Chrabaszcz, and the University of Maryland Design and Statistical Analysis Lab (DASL) for assistance with statistical analysis. This research was funded by National Institutes of Health (NIH) Grants R01 DA07432 (P. Nair), R01 DA021059 (M. M. Black), and ISTAR DA029113 (T. Riggins) and by NIDA–IRP.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.jecp.2014.01.008>.

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