Dopaminergic functioning and preschoolers’ theory of mind

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A B S T R A C T

Representational theory of mind (RTM) development follows a universal developmental timetable whereby major advances in reasoning about mental representations occur between the ages of 3 and 5 years old. This progression appears to be only absent in the case of specific neurodevelopmental impairments, such as autism. Taken together, this suggests that neuromaturational factors may play a role in RTM development. Recent EEG work has shown that one neuromaturational factor pacing this universal developmental timetable is the functional maturation of medial prefrontal cortex. The neurotransmitter dopamine (DA) is thought to play a crucial role in typical frontal lobe development. Therefore, the goal of the present study was to investigate the role that DA may play in RTM development. Ninety-one 48–62-month olds were given a battery of RTM tasks along with EEG measurement. EEG recordings were analyzed for eyeblinks, a reliable indicator of DA functioning, and we calculated their average eyeblinks per minute (EBR). Regression analyses showed that EBR was associated with RTM after controlling for children’s performance on a Stroop-like measure, language ability, gender, and age. These findings provide evidence that DA functioning is associated with RTM in the preschool years, and are discussed with respect to how DA might provide a mechanism that helps to account for both neurobiological and experiential factors that are known to affect the timetable of preschoolers’ RTM development.

Theory of mind is the understanding that human action is motivated by internal mental states such as beliefs, desires, and intentions. In the preschool period, children’s understanding of others’ minds appears to change rapidly. Specifically, children come to explicitly understand that others’ mental states, in particular their knowledge and beliefs, are person-specific representations of the world (Wellman, Cross, & Watson, 2001). This new understanding is sometimes called a “representational theory of mind” (RTM), and is indexed by a canonical battery of tasks, including the false-belief task. Although recent research suggests that the origins of this understanding may be present early in infancy (Onishi & Baillargeon, 2005), children’s ability to recruit these concepts to explain behavior in everyday settings seems to follow a more protracted trajectory. What is perhaps most interesting is that the rapid changes in preschoolers’ RTM development have been observed across cultures with vastly different world views and across multiple variants of the same basic experimental paradigm (Wellman et al., 2001). One exception to this stereotyped developmental time course includes the neurodevelopmental disorder of autism, in which theory-of-mind reasoning is specifically impaired (Baron-Cohen, Leslie, & Frith, 1985).

These findings taken together suggest that the timetable of RTM development may be constrained, at least in part, by neurodevelopmental factors, including perhaps neurochemical ones. The goal of this research is to test this hypothesis by examining the extent to which individual differences in dopaminergic functioning are associated with young children’s theory of mind.

Dopamine (DA) is of primary interest in the present context for several reasons. First, recent electroencephalographic (EEG) research has shown that the functional development of the dorsal medial prefrontal cortex (dMPFC) is a specific neurodevelopmental correlate of preschoolers’ RTM development (Sabbagh, Bowman, Evraire, & Ito, 2009). The dMPFC is rich in DA receptors and lies at the end of the mesocortical dopamine pathway. DA affects cell proliferation in regions that receive DA projections, including the frontal cortex (e.g., Popolo, McCarthy, & Bhide, 2004). Given that cell proliferation is a critical neurodevelopmental process, these findings provide some reason to suspect that DA might play a critical role in the healthy development and functioning of the dMPFC. Thus, we might expect DA to be associated with RTM development in preschoolers.

A second and perhaps more intriguing reason to suspect a role for DA comes from a consideration of the role that DA plays...
in learning. A large body of literature has shown that dopaminergic activity is elicited when animals encounter situations in which their expectations about an event (such as a reward) do not match with what ultimately occurs (Schultz, 2000). It is generally thought that in these cases, dopaminergic activity promotes plasticity necessary for adjusting expectations, and coming to increasingly refined understandings of the causal structure of a given event (Schultz, 2007). This is so intriguing in the present context because one of the most robust findings from the theory of mind literature with young children is that experience plays a critical role in shaping the timetable of theory of mind development in the preschool years. One of the dominant explanations for this role of experience posits that conceptual changes take place as children gradually fine tune their understanding of how mental states affect behavior (e.g., the “theory theory,” Gopnik & Wellman, 1994). These parallels between the processes associated with DA functioning and theory change provide a strong basis for hypothesizing that individual differences in DA functioning may be associated with RTM development in preschool-aged children.

To date there have been no direct investigations of the role that DA might play in RTM reasoning either in children or in adults. However, some intriguing indirect support for a relation between DA and RTM comes from research into clinical disorders associated with dopamine dysfunction. For example, recent evidence suggests that individuals with late stage Parkinson’s disease, a disorder which also involves impaired DA functioning, show deficits in RTM (Péron et al., 2009). Further evidence comes from Savina and Beninger (2007), who investigated RTM performance in schizophrenic patients treated with antipsychotic medication. Atypical antipsychotics (e.g., clozapine, olanzapine) preferentially increase dopaminergic functioning in the medial prefrontal cortex, whereas typical antipsychotics (e.g., haloperidol) do not; risperidone, although classified as an atypical antipsychotic, has an action more like that of typical antipsychotics (Heidbreder et al., 2001). Patients who were taking clozapine or olanzapine had better RTM performance than patients taking typical antipsychotics or risperidone, though the two groups showed no differences on similarly structured control tasks. These findings strongly suggest that DA projections to MPFC may be particularly critical for RTM performance.

The influence of DA on RTM development might be either direct or indirect. For instance, as the literature reviewed above suggests, DA may be important to the development and healthy functioning of relatively circumscribed regions of dMPFC that are associated with young children’s RTM reasoning. In contrast, DA might play an indirect role by affecting the development and functioning of the cognitive support systems that are known to affect RTM development. One cognitive support system that is of special interest in this regard is children’s executive functioning (EF) skills. Children’s performance on one class of EF tasks, sometimes called response-Conflict executive functioning (RC-EF) tasks, is highly correlated with performance on RTM tasks (Carlson & Moses, 2001). Furthermore, there is some evidence that aspects of executive functioning are associated with DA. Infants, toddlers and preschool-aged children who have low DA because of a dietary treatment for phenylketonuria (PKU) show specific impairment on EF tasks in comparison to control groups (Diamond, 2001 for a review). Also, in typically developing children allelic variants of DA-related genes (e.g., DRD4, COMT) are associated with RC-EF task performance such that those with a genetic predisposition to more available DA perform better on the tasks (Diamond, Biandri, Fossella, & Gehlbach, 2004). Thus, we included a battery of RC-EF tasks in our study to help establish whether DA is directly or indirectly associated with RTM development.

There are several well-established batteries of tasks for measuring individual differences in young children’s RTM and RC-EF performance. However, measures of individual differences in DA functioning are less prominent. For the present study, we used children’s eyeblink rates (EBR) as an unobtrusive way of measuring functional DA activity. EBR is governed by activity in the ventromedial caudate nucleus, part of the striatum (Taylor et al., 1999). The caudate nucleus, like the dMPFC, receives DA projections from the ventral tegmental area (VTA), though the projections to the caudate come along the mesolimbic rather than the mesocortical pathway. Most important, a number of studies using both human and other animal models have shown that experimental manipulations designed to affect levels of DA also positively affect EBR—namely, as available DA increases (for example, through the introduction of DA agonists), EBR also increases (Blin, Masson, Azulay, Fondarai, & Serratrice, 1990; Elsworth et al., 1991; Kleven & Koek, 1996). Moreover, researchers have used the EBR technique to characterize individual differences in DA functioning in developmental disorders in which dopaminergic functioning is impaired, including Attention Deficit Hyperactivity Disorder (ADHD; Konrad, Gauggel, & Schurek, 2003), and childhood onset schizophrenia (Caplan & Guthrie, 1994). Thus, EBR is a reliable indirect online measure of DA functioning in children.

The present study set out to investigate the relation between DA and RTM using a sample of archival data collected in our lab from mid-2006 to early 2007. The archival sample consisted of 60 typically developing 4-year olds for whom we had behavioral measures of their RC-EF and RTM skills, as well as resting (i.e., baseline, task-independent) EEG data. The resting EEG data was collected in a manner quite similar to the manner in which other researchers have collected EBR data (e.g., Dreisbach et al., 2005; Müller et al., 2007). Included in the recording montage were leads below and above both eyes (i.e., infraorbital and supraorbital, respectively). These pairs show characteristic sharp high amplitude waves of opposite polarity when a subject blinks (see Fig. 1), thereby allowing us to identify the number of blinks across the resting EEG recording session. We hypothesized that individual differences in EBR would be positively correlated with preschoolers’ RTM performance, thereby providing indirect evidence that DA functioning of typically developing children may play a role in RTM development. Of particular interest was whether this relation was direct, or mediated by a common relation with RC-EF.
1. Methods

1.1. Participants

Sixty typically developing children participated in two testing sessions. Although no systematic demographic data were collected, participants were drawn from predominantly Caucasian, middle-class communities in Kingston, Ontario and surrounding areas. Participants received $15 and a small toy at the end of the first session, and a $10 gift certificate to Chapters Bookstore and another small toy at the end of the second session. The two study sessions occurred within 2 weeks of each other. Participants’ age in months was calculated from their birth date at the time of the first session. All participants were born within 2 weeks of their original due date.

For analysis, three children were excluded because they failed to complete the full task battery. Two additional children were excluded because performance on a standardized language measure suggested possible language delays. Finally, one other child was excluded because the number of blinks during EEG recording was greater than 2.5 standard deviations above the sample mean number of blinks. Blinks this excessive are likely indicative of eye irritation during EEG recording and are therefore not interpretable for the purposes of the study. Thus, the final sample consisted of 54 children (19 boys and 35 girls). Ages ranged from 48 months to 62 months ($M = 53.78$, $SD = 3.67$).

2. Measures and materials

2.1. Rocket ship/swirling line video

During EEG recording, and thus the period in which we measured children’s EBR, participants watched a 6-min video that had two alternating components, each lasting 30 s: a still picture of a rocket ship, and a clip of a green line that swirled in concentric circles (alternating clockwise and counter-clockwise in direction each time the clip appeared). The video began with a clockwise swirling line clip.

2.2. Behavioral tasks

The full details for the behavioral tasks can be found in their primary references. Here, we provide a brief description of each task and how it was scored for purposes of analyses. Measures consisted of four theory-of-mind tasks and three executive functioning tasks.

2.2.1. Theory-of-mind battery

Knowledge Access (Pillow, 1989; Wellman & Liu, 2004). Children were asked what they thought might be inside a closed drawer and then were shown the contents. A new character, Tiger, was introduced who had not seen the contents of the drawer and the child was asked, “Does Tiger know what is in the drawer?” (Range: 0/1).

False-belief Contents (Hogrefe, Wimmer, & Perner, 1986). Children were shown a familiar sweets box (i.e., a Smaritces box) and asked what they thought was inside. After responding, that they thought it was Smarties, the box was opened and children were shown that it was actually crayons inside. The box was then closed and a new character introduced who had not seen inside of the box. Children were asked, “What does Monkey think is in the box? Smarties or crayons?” (Range: 0/1).

False-belief Location Change Task (Wimmer & Perner, 1983). Children were asked where one puppet thought her plane was after it was moved in her absence. Children passed the task if they answered that the puppet would look for her plane in its original location (i.e., where it was before it was moved) (Range: 0/1).

Appearance-Reality: Rock (Flavell et al., 1986). Children were shown an object that looked like one thing but was then revealed to be another (i.e., a sponge that was painted to look like a rock). Children passed the task if they correctly answered what the object looked like (i.e., a rock), even after they were shown what the object was in reality (i.e., a sponge) (Range: 0/1).

2.3. Executive functioning task battery

Grass/Snow Stroop (Carlson & Moses, 2001). Children were instructed to point to a green coloured card when the experimenter said “snow” and to a white coloured card when the experimenter said “grass”. The final score was the proportion (%) of correct responses over 16 trials. Sometimes children made multiple responses on a single trial, but only their first responses were scored (Range: 0–100).

Dimensional-Change Card Sort (Carlson & Moses, 2001; Frye, Zelazo, & Palfai, 1995). Children were instructed to sort cards that varied on two dimensions: color (red and blue), and shape (boats and rabbits). First, children were instructed to sort the cards according to shape (i.e., boats in one basket, rabbits in the other). Then, they were asked to switch and sort the cards according to colour (i.e., red in one basket, blue in the other). Children were given a score based on the number of post-switch sorts that clearly demonstrated they were sorting by the second dimension (Range: 0–3).

Less is More (Carlson, Davis, & Leach, 2005). Children were shown two trays: one containing a large amount of candy (i.e. five jelly beans) and one containing a small amount of candy (i.e. two jelly beans). Children were told that when they pointed to a tray that those candies would be given to a puppet, Naughty Monkey, and the child would receive the candy in the other tray for themselves. On each trial, children received a score of 0 if they pointed to the tray with the larger amount, a score of 1 if they hovered over the larger amount but then pointed to the tray with the smaller amount, and a score of 2 if they pointed to the smaller amount right away. Scores were summed across 16 consecutive trials and then converted to a score out of 100 (Range: 0–100).

Peabody Picture Vocabulary Task (PPVT) (Dunn & Dunn, 1997). Children’s performance on RTM tasks is highly correlated with their language ability (see e.g., Astington & Jenkins, 1999) and so we chose to include a measure of receptive vocabulary in the present study, namely the PPVT. In this task, children were shown a series of picture sets. An experimenter said a word that corresponded to one of four pictures on the page, and children were asked to point to the picture of that word. There were 9 sets in total and 12 different words to identify in each set. Each successive set increased in difficulty level. As soon as participants made seven errors within a set, the task ended. Participants’ scores were calculated as the item number of the most difficult correctly identified word minus the total number of errors they made along the way (Range: 0–108).

2.4. EEG recording

Electrophysiological data was recorded from the scalp with a 128-channel Geodesic Sensor Net (EGI, Eugene, OR). The net consisted of 128 carbon electrodes knitted into an elastic geodesic tension structure that when applied, distributes electrodes evenly over the scalp. Each electrode is positioned relative to the vertex electrode in a geodesic montage that stretches around the sphere of the head. EEG activity at all channels was recorded in reference to the vertex electrode (Cz), sampled at 500 Hz, and digitally filtered between 0.01 and 200 Hz (time constant = 1 s). EEG was recorded continuously throughout the video, and any necessary electrode readjustments were made during swirling line segments only. Impedances were maintained below 30 kΩ throughout recording.

2.5. Eyeblink measurements

Eyeblink measurements for each participant were calculated as the number of eyeblinks occurring over the total EEG recording session (i.e. number of blinks per minute—EBR). Time segments for large periods of excessive noise were flagged and subtracted from the total time, as it was not possible to reliably identify eye-
blinks within these noisy sections. Eyeblink rates were calculated as the number of eyeblinks divided by the total duration of useable time for each participant. All participants had greater than 3.5 min of noise-free data. Only the infraorbital and supraorbital electrode pairs over each eye (Left: channels 127, 26 and Right: channels 126, 8) were used for eyeblink measurements. Data from these channels were filtered using a 20 Hz low-pass filter. To identify candidate eyeblinks we first performed an algorithmic search of the relevant channels for instances where waveforms diverged from one another 100.00 μV or more for less than 400 ms. Candidate eyeblinks were then visually inspected by a coder to ensure that they took the form of characteristic opposing high amplitude waves and that these waves occurred in at least three of the four orbital channels. A second independent coding of the eyeblinks from 25% of the sample yielded an inter-rater correlation of .96.

2.6. Procedure

The present study was part of a larger investigation into neurodevelopmental correlates of children’s social-cognitive development. In addition to the RTM and RC-EF batteries described above, the larger study included a number of additional tasks that were not analyzed in the present study including structured role playing activities, measures of pretense understanding and measures of pre-RTM theory of mind understandings. Because of the large battery of tests, participants came to an on-campus laboratory for a number of 1.5-h sessions. Informed consent was obtained at the outset of both sessions. The study was approved by the Queen’s University Research Ethics Board and follows the regulations set out in the Declaration of Helsinki.

2.6.1. Session 1

Participants’ EEG was recorded at the outset of the first time session. Electrophysiological data (EEG) was recorded from the scalp using the geodesic sensor net.

Participants sat in a chair while the net was applied and adjusted to ensure correct placement and good contact between the electrodes and the scalp. Net placement and adjustment took approximately 10–15 min.

Following net application, participants were photographed for later evaluation of correct net placement. Participants were then prepared to watch the video described above. Children were informed that they could look anywhere on the screen during the swirling line segments but that during rocket ship segments, they were to look directly at the rocket ship. They were encouraged to do their best to remain still throughout the procedure. The lights were dimmed for optimal video viewing, and parents were allowed to remain in the room with their child. Both parent and child were asked to try to remain quiet throughout the recording session. After EEG recording, the net was removed. The entire process (i.e., instructions, EEG recording, net removal) took approximately 10 min.

Following EEG collection, children sat down at a child-sized table in a quiet room with a female experimenter and were given a first round of behavioral tasks in the following order with the following durations: (1) False-belief Contents (3 min), (2) Knowledge Access, (3 min) and (3) Grass/Snow Stroop (7 min).

2.6.2. Session 2

The second laboratory session consisted solely of behavioral tasks administered as in the first session in the following order: (1) False-belief Location (3 min), (2) Dimensional-Change Card Sort (5 min), (3) Appearance-Reality Rock (3 min), (4) Less is More (8 min), and (5) PPVT (15–20 min).

3. Results

Composite scores for RTM and RC-EF were first calculated. The RTM composite score was calculated by averaging participants’ performance on the False-Belief Location task, the Appearance-Reality Rock task, the Knowledge Access task and the False-Belief Contents task. The RC-EF composite score consisted of averaging participants’ z-scores on the Grass/Snow Stroop task, the Less is More task, and the Dimensional-Change Card Sort task. Similar procedures for creating such aggregates have been followed by other researchers, namely Carlson and Moses (2001). Eyeblink rates were calculated as the number of blinks per minute, averaged across both the rocket ship and swirling line portions of the video.

3.1. Descriptive analyses

3.1.1. RC-EF battery

Children’s performance in the RC-EF battery is summarized in Table 1. RC-EF performance was surprisingly good for children in this age range: 14.8% of the participants performed perfectly on all of the RC-EF tasks, and the remainder of the data were highly negatively skewed. The one RC-EF task that showed greater variance in performance was the Grass/Snow Stroop task. Comparisons of mean performance were made with results of previously published studies using this age range (e.g., Carlson et al., 2005; Carlson & Moses, 2001). Performance on the Card Sort measure was 15% higher here than in Carlson and Moses (2001), and performance on the Less is More task was 8% higher. Further, we did not find evidence for a strong positive correlation between RC-EF and age that is typically seen for children in this age range, \( r(52) = .21, p = .12 \), though an age correlation was found for the Grass/Snow Stroop task, \( r(52) = .28, p = .04 \). Together these findings suggest that RC-EF performance may have been a bit higher in the present sample than what is typical, which may limit variability and thus the extent to which we are able to detect relations between RC-EF and the other variables of interest.

Significant or near significant gender differences were found on both the RC-EF battery, \( t(52) = 1.94, p = .056 \); and the individual measure of Grass/Snow Stroop performance, \( r(52) = 3.28, p = .002 \), with females out performing males. Therefore, in all focal analyses gender was included as a covariate.

3.1.2. RTM battery

Children’s performance on the RTM tasks is also summarized in Table 1. Here, the overall performance of children was in line with what would typically be expected of children in this age group. Mean performance on each of the tasks was similar to data reported in past studies using similar age ranges (e.g., Carlson & Moses, 2001).

<table>
<thead>
<tr>
<th>Behavioral task</th>
<th>Range</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grass/Snow Stroop</td>
<td>0–100</td>
<td>79.90</td>
<td>26.52</td>
</tr>
<tr>
<td>Less is more</td>
<td>0–100</td>
<td>80.85</td>
<td>25.72</td>
</tr>
<tr>
<td>Dimensional change card sort</td>
<td>0–3</td>
<td>2.26</td>
<td>1.26</td>
</tr>
<tr>
<td>RC-EF composite z-score</td>
<td>−2.23–87</td>
<td>.11</td>
<td>.71</td>
</tr>
<tr>
<td>False-belief location</td>
<td>0–1</td>
<td>.71</td>
<td>.46</td>
</tr>
<tr>
<td>Appearance reality rock</td>
<td>0–1</td>
<td>.66</td>
<td>.48</td>
</tr>
<tr>
<td>Knowledge access</td>
<td>0–1</td>
<td>.72</td>
<td>.45</td>
</tr>
<tr>
<td>False-belief contents</td>
<td>0–1</td>
<td>.49</td>
<td>.50</td>
</tr>
<tr>
<td>RTM composite score</td>
<td>0–1</td>
<td>.64</td>
<td>.35</td>
</tr>
<tr>
<td>PPVT</td>
<td>47–92</td>
<td>75.54</td>
<td>11.09</td>
</tr>
<tr>
<td>EBR</td>
<td>.17–18.44</td>
<td>7.14</td>
<td>4.27</td>
</tr>
</tbody>
</table>

RC-EF: response-conflict executive functioning; RTM: Representational theory of mind; PPVT: Peabody Picture Vocabulary Test; EBR: Eyeblink rate; SD: standard deviation
Sabbagh, Moses, & Shiverick, 2006; Sabbagh, Xu, Carlson, Moses, & Lee, 2006). Correlation analyses showed that RTM performance was associated with age $r(52) = .45$, $p = .001$, to roughly the same extent as in other studies, thereby providing confidence that RTM development was typical within the sample.

No significant gender differences in performance were found on the RTM battery, $r(52) = .10$, $p = .92$.

Although RC-EF task performance was near ceiling in the present sample, this did not prevent us from detecting the usual robust relation between the RC-EF and RTM aggregates, $r(52) = .43$, $p = .001$. This pattern was replicated, though less powerfully, when considering the relation between RTM performance and performance on the Grass/Snow Stroop task alone, $r(52) = .37$, $p = .006$. This also suggests that Grass/Snow Stroop performance may provide a reasonable and potentially preferable measure of children’s executive functioning, at least in the current sample.

3.1.3. PPVT

Children’s performance on the PPVT task is summarized in Table 1. All children included in the present sample scored within the normative range. As would be expected, PPVT performance was positively correlated with age, $r(52) = .281$, $p = .04$. No significant gender differences were found, $p > .90$.

3.1.4. EBRs

EBRs were calculated separately for the swirling line and rocket ship portions of the data. EBRs during the swirling line portion were positively skewed and leptokurtic, whereas during the rocket ship segments they were normally distributed. Participants blinked significantly more during the rocket ship (still photo) ($M = 9.86$, $SD = 5.83$) than swirling line ($M = 4.57$, $SD = 3.55$) portions of the video, $t(53) = 8.62$, $p < .001$. However, despite these differences, the two measures of EBR were highly correlated with one another, $r(52) = .62$, $p < .001$. Thus, the focal analyses used a measure of EBR collapsed across both segment types to create a more stable and reliable measure. This aggregate was not significantly correlated with age, $r(52) = -.20$, $p = .14$, and no significant gender differences were detected, $r(52) = .34$, $p = .73$.

3.2. Focal analyses

Our main question of interest was whether EBR was significantly related to RTM performance, and whether that relation was independent of common associations with other factors known to be associated with RTM, DA or both.

For our focal analyses, we ran two sets of multiple regressions: one predicting RTM from EBR, RC-EF, age, gender, and PPVT, and one predicting RC-EF from EBR, RTM, age, gender, and PPVT. The first regression, predicting RTM performance from age, gender, PPVT, overall RC-EF and EBR yielded a significant model, $F(5, 46) = 7.36$, $p < .001$, which was able to explain 44% of the variance in RTM. Age, PPVT, and EBR were significant independent predictors of RTM. Despite an initially significant zero-order correlation, RC-EF was only marginally predictive of RTM in the regression. Notably, EBR was the strongest predictor of RTM performance, once the variance associated with age, RC-EF and PPVT was accounted for (see Fig. 2 and Table 2). This same regression was run again, this time using just Grass/Snow Stroop performance as the measure of RC-EF. The pattern of findings from the regression was essentially the same as when the RC-EF aggregate was used, except that Grass/Snow Stroop was not a significant predictor in the full model.

For the second set of regressions, we predicted RC-EF performance from EBR, RTM, age, gender, and PPVT. When considering the RC-EF aggregate, we found that only PPVT was a significant independent predictor of RC-EF, despite an overall significant model,
yses would attenuate the relationships found between EBR, RTM and RC-EF.

The number of useable segments was not correlated with EBR, \( r(53) = -0.119, p = 0.39 \), nor with RTM performance, \( r(53) = 0.101, p = 0.47 \). Including the number of useable segments in all of the regression analyses described above did not change the results. The number of segments was not a significant independent predictor of either RTM or RC-EF performance, \( p's > 0.11 \). This suggests that task engagement does not account for the relation between EBR and RTM.

### 4. Discussion

The primary goal of the present study was to assess the possibility that individual differences in children’s RTM abilities are associated with indirect indices of DA functioning after relevant factors are statistically controlled. Results clearly showed that EBR was a strong unique predictor of children’s RTM performance, thereby providing indirect support for our notion that DA is a key neurodevelopmental factor affecting RTM development.

These findings dovetail with other research connecting dopamine and representational theory of mind in autistic and schizophrenic populations. Both autism and schizophrenia have been associated with indirect indices of DA functioning after relevant factors are statistically controlled. Results clearly showed that EBR was a strong unique predictor of children’s RTM performance, thereby providing indirect support for our notion that DA is a key neurodevelopmental factor affecting RTM development.

We also found some evidence that EBR was related to some aspects of executive functioning in children, specifically the Grass/Snow Stroop measure, though our evidence was weaker here due to an apparent ceiling effect in the RC-EF measures. There is plenty of evidence to suggest that response-conflict executive functioning is related to dopamine (e.g., Diamond, 2001; Diamond et al., 2004). Specifically, the catechol-O-methyl transferase (COMT) gene contributes to the rate at which DA is degraded in the central nervous system. Polymorphisms of COMT that would be associated with more available DA (i.e., the Met-Met variant) have been shown to predict greater performance on tasks requiring inhibition and conflict negotiation such as the Wisconsin Card Sort Task in adults (Bruder et al., 2005; Egan et al., 2001; Lipsky et al., 2005) and a directional Stroop task in children (Diamond et al., 2004). Allelic variation on the COMT gene predicts the greatest amount of variance in cognitive performance in paradigms with a relatively simplistic conflict or reversal component similar to the tasks included in the present battery (Bilder, Volavka, Lachman, & Grace, 2004). Additionally, ADHD has been associated with both abnormalities in dopaminergic functioning (Konrad et al., 2003) and impaired executive functioning (Barbary, 1997). Taken together with the present study’s findings, this suggests that dopaminergic functioning is associated with RC-EF skill.

Perhaps the most intriguing findings came from the multiple regression analyses in which RTM performance was predicted from a host of control variables, and the focal factors of EBR and RC-EF. In these analyses, we found that EBR was a robust predictor of RTM when the other variables were statistically controlled. This finding is interesting for at least two reasons. First, this pattern of findings suggests that the relation between EBR and RTM is not attributable to the common relations that each of these variables might have with executive function or language. Second, the fact that RC-EF and RTM were both associated with DA functioning independent of relevant control variables raises the question of whether the well-established ontogenetic association between RC-EF and RTM may be attributable, at least in part, to their common association with DA. The most common explanation for the relation between RC-EF and RTM is that RTM tasks have inherent RC-EF demands. On this view, developing some modicum of RC-EF skill is a precursor to expressing understanding of RTM in standard tasks, such as the ones used in the present study (see e.g., Moses, 2001). This simple story has recently been challenged on several points (see Benson & Sabbagh, 2009 for a review), and the current findings challenge these claims even further. Specifically, our findings raise the possibility the concurrent relation between RTM and RC-EF may be epiphenomenal—the two are related less because of apparent similarities in their task demands and more because they each rely to a similar extent on dopaminergic functioning. This finding is broadly consistent with previous research on the neurobiological bases of RTM and RC-EF; these two skills appear to be associated with dis-

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**Table 2**

Results of multiple regression analyses predicting RTM and RC-EF.

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Independent variable</th>
<th>Standardized beta</th>
<th>( t )</th>
<th>Sig.</th>
<th>Zero-order correlation</th>
<th>Partial correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RTM</strong></td>
<td>EBR</td>
<td>0.23</td>
<td>1.78</td>
<td>0.08</td>
<td>0.41</td>
<td>0.25</td>
</tr>
<tr>
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<td>PPVT</td>
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sociable but neighboring regions of the MPFC (see Saxe, Carey, & Kanwisher, 2004), both of which are likely similarly functionally affected by fluctuations in DA.

With respect to limitations, it can be noted that our findings were obtained in a relatively small and relatively homogenous sample, which may raise questions about generalizability. However, this concern is mitigated somewhat by the fact that both RTM and RC-EF were associated with the control variables (age, gender, PPVT) in ways that were consistent with prior research. First, age and PPVT were significant unique predictors of RTM performance as shown in previous studies (Milligan, Astington, & Dack, 2007). Gender was not a significant predictor of RTM, but that too is consistent with the previous research showing that the effect of gender on RTM is typically small and difficult to detect in small samples (Charman, Ruffman, & Clements, 2002). Second, although we had something of a ceiling effect in our RC-EF data that obscured the usual association of this variable with age, we did replicate the typical findings that PPVT and gender were each significant or near significant independent predictors of RC-EF performance (e.g., Carlson & Moses, 2001). These replications of prior findings provide confidence that the present data are commensurate with that reported in the extant literature, and thus bolster the generalizability of the key finding that dopaminergic functioning is a robust unique predictor of RTM skills in preschool children.

An open question concerns the specific nature of the relation between RTM and dopaminergic functioning. Individual differences in dopaminergic functioning are influenced by both tonic and phasic factors. Tonic levels of DA are associated with single regularly spaced action potentials in dopaminergic neurons that release DA into the extracellular space (Chergui, Suaud-Chagny, & Gonon, 1994; Goto, Otani, & Grace, 2007). Tonic DA then has functional consequences for phasic DA release. Phasic bursts of 2-6 action potentials release DA non-linearly into the extracellular space in response to behaviorally relevant cues (Chergui et al., 1994; Goto et al., 2007). In the present study we used eyelink rate as a measure of available dopamine. To our knowledge, EBR measurements are unable to separate tonic and phasic DA; EBR is responsive only to the amount of DA available at the ventromedial caudate nucleus, which involves both tonic and phasic processes.

At this point, a case can be made for a role for both tonic and phasic DA in theory of mind development. Tonic levels of DA may be important developmentally for establishing the neural architecture that we know is involved in later RTM reasoning. Animal studies have shown that DA is important for cell proliferation and generation within the fetal cortex (Popolo et al., 2004). Children who will later show more advanced RTM may have more well developed dMPFC due to the influence of early DA. Stable genetic factors, such as COMT, have been hypothesized to play a role in establishing cortical tonic DA levels (Bilder et al., 2004), and this stability could help explain how the effects of fetal DA continue to have an impact on behavior during the preschool period.

In comparison, phasic DA release has been theorized to be an important factor in promoting cognitive flexibility. As outlined in the introduction, a wealth of research has focused on the role that responsive DA signaling plays in detecting occasions in which predictions about the world do not match with the true ensuing state of affairs (see e.g., Schultz, 2007). For several theories of DA functioning, a key tenet is that DA promotes the neural plasticity necessary to flexibly update representations of goals and expectations in response to feedback from the environment (Montague, Hyman, & Cohen, 2004). This phasic dopamine release is believed to enhance the reception of new information and promote flexible cognitive control (Miller & Cohen, 2001). What is perhaps most intriguing about this hypothesis in the present context is that it dovetails well with both theoretical and empirical work that has emphasized the role of relevant experiences in shaping the emergence of RTM. Several experiential factors have been shown to affect the trajectory of RTM development including early parent–child talk about mental states (e.g., Ruffman, Slade, & Crowe, 2002), number of older siblings (e.g., Perner, Ruffman, & Leekam, 1994), and socio-economic status (Pears & Moses, 2003). These factors are typically thought to affect the development of RTM by causing children to reflect on their current (and, in young children, un-adultlike) conceptualizations of mind, and then change those conceptualizations in light of the incoming evidence (see e.g., Carpendale & Lewis, 2004). It could be that DA plays a central role in this everyday cognitive development, by promoting the plasticity necessary to flexibly update conceptualizations of how mental states cause human behavior.

In conclusion, our goal was to investigate the possibility that indirect measures of individual differences in DA functioning might be associated with children’s RTM development. Our findings provided support for this hypothesis by showing that EBR was associated with preschoolers’ RTM development when relevant variables were statistically controlled. From the outset, we focused on DA because the frontal regions that have been shown to be important for RTM development are primary targets of DA projections through mesocortical DA pathways. One intriguing speculation is that DA represents a relatively “endogenous” factor affecting the timetable of RTM development. By endogenous, we mean that the variability boundaries on DA functioning are shaped, at least in part, by a limited set of shared, heritable genetic factors. Insofar as DA affects RTM, then these endogenous factors that affect DA may also constrain RTM development. The identification of candidate endogenous factors affecting RTM reasoning is important, given the cross-cultural similarities in the ontogenetic timetable of RTM reasoning, and the specificity with which it can apparently be affected in certain developmental disorders (such as autism). Of course, we would not wish to say that DA itself represents a purely endogenous factor, given that functioning of the DA system is likely to be influenced by experiential as well as genetic factors. Nor would we wish to argue that DA is the only such neurochemical factor affecting theory of mind development, particularly given that DA functioning can be affected by a number of other factors, such as serotonin (see Kapur & Remington, 1996), and oxytocin (Baskerville & Douglas, 2008). Nonetheless, these findings take us a step further in understanding how neurobiological factors might affect neuromaturational events that set the stage for the typical ontogenetic course of critical social-cognitive achievements. Future research should be aimed at better understanding what role DA might play in RTM development during the preschool period, and possibly during other developmental epochs in which children’s social-cognitive understanding appears to undergo dramatic changes.

Acknowledgements

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References


