Neural Correlates of Reward Processing in Typical and Atypical Development

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Abstract
Atypically developing children including those born preterm or who have autism spectrum disorder can display difficulties with evaluating rewarding stimuli, which may result from impaired maturation of reward and cognitive control brain regions. During functional magnetic resonance imaging, 58 typically and atypically developing children (6–12 years) participated in a set-shifting task that included the presentation of monetary reward stimuli. In typically developing children, reward stimuli were associated with age-related increases in activation in cognitive control centers, with weaker changes in reward regions. In atypically developing children, no age-related changes were evident. Maturational disturbances in the frontostriatal regions during atypical development may underlie task-based differences in activation.

Keywords
reward, autism spectrum disorder, preterm birth, brain development, functional MRI

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social and reward-type stimuli in autism spectrum disorder has come from functional MRI studies reporting hypoactivation within the mesocorticolimbic circuitry in response to both social and monetary rewards in school-age children, adolescents, and adults with autism spectrum disorder.\(^1\)\(^2\)\(^3\)\(^4\)\(^5\)\(^6\)\(^7\)\(^8\)\(^9\)\(^10\)\(^11\)\(^12\)\(^13\)\(^14\)\(^15\)\(^16\)\(^17\)\(^18\)\(^19\)\(^20\)\(^21\)\(^22\)\(^23\)\(^24\)\(^25\)\(^26\)\(^27\) indicating little developmental change with age in this population.

Affective and behavioral disturbances prevalent in children with autism spectrum disorder are also seen in children born very preterm,\(^19\) and premature birth is a risk factor for the development of autism.\(^20\)\(^21\) Although the underlying pathology remains unknown, it is hypothesized that a combination of perinatal and postnatal factors can lead to the disruption of the frontal lobe and striatal development in preterm-born children, which can result in some autism spectrum disorder behavioral phenotypes. Structural imaging studies have related alterations in affective behavioral processing to emotion and reward-related brain regions and their underlying white matter fiber pathways in children and adolescents born preterm.\(^22\)\(^23\)\(^24\) Furthermore, behavioral studies with infants\(^22\) and young children (2-3 years) born preterm have reported that they are impaired in their ability to associate value with stimuli perceived as rewarding by typically developing children. In a study with young children born preterm examining executive functioning, using a delayed alternation task demonstrated that preterm-born children chose unrewarded stimuli more so than term-born children, indicating that the preterm-born children were impaired in their ability to learn reward associations.\(^25\) However, information on how preterm-born children process reward information during childhood remains unknown.

Although evidence from functional and structural neuroimaging studies has suggested abnormalities within the reward system in atypically developing children and adolescents, it is unclear how these regions mature functionally, especially in relation to cognitive control centers. The present functional MRI study addressed the development of reward and cognitive control brain regions during typical and atypical development. The participant groups included typically developing children (6-12 years) and atypically developing children (with autism spectrum disorder or born preterm) of comparable ages. Data were combined from children with autism spectrum disorder and those born preterm, as both populations exhibit deficits in reward processing that may be associated with impaired frontal–striatal development. The data from the atypically developing group were contrasted with those obtained from the typically developing group for better understanding of the development of reward-related processes. Children participated in a set-shifting task where they received positive feedback in the form of monetary reward stimuli. It was hypothesized that atypically developing children, both children with autism spectrum disorder and those born preterm, would demonstrate hypoactivation in reward centers including the medial prefrontal cortex and striatum throughout childhood, accompanied by little developmental change in cognitive control regions such as the anterior cingulate cortex and lateral prefrontal cortex.

Methods

Participants

Twenty-six children diagnosed with autism spectrum disorder were recruited through the Autism Research Unit at The Hospital for Sick Children (Toronto, Canada) and diagnosed by clinician experts supported by a research reliable Autism Diagnostic Observation Schedule–Generic\(^26\) and Autism Diagnostic Interview–Revised.\(^27\) The children with autism were all verbal and high functioning (IQ > 80) and were all born at term. Although the children with autism spectrum disorder were term-born, specific birth data were not collected.

Thirty-one preterm-born children were recruited through the neonatal follow-up clinic at The Hospital for Sick Children. All children were born at <32/40 weeks’ gestational age (mean = 27.4 weeks) and had no significant brain injury detected or significant medical difficulties during the neonatal period. The Autism Diagnostic Observation Schedule and Autism Diagnostic Interview–Revised were not administered to the children born preterm.

A total of 34 typically developing children were recruited for the study (19 males, 15 females; mean age: 9.57 ± 1.87 years; range: 6.39-12.75 years). Children were screened for developmental delay and were all term-born (>37 weeks’ gestation).

Any children with learning disabilities or neurological or medical disorders (other than autism spectrum disorder) were not included; none of the children were taking medication and had sensory and/or motor dysfunction or standard contraindications for MRI. The study was approved by the research ethics board of Hospital for Sick Children, and written informed consent was obtained from parents and informed assent from the children.

Behavioral Assessments

Cognitive ability (IQ) was measured using the Full-4 Wechsler Abbreviated Scale of Intelligence\(^28\) for all participants except 1 from the autism spectrum disorder group who had received a recent assessment using the Wechsler Intelligence Scale for Children IV.

Experimental Task

Prior to the scanning session, participants were familiarized with the experimental task and stimuli. Children performed several practice trial sets until they demonstrated that they understood the task. The stimulation protocol required a 2-alternative forced choice between compound stimuli of 2 dimensions (dimension 1: color of clown fish, dimension 2: type of aquatic plant; Figure 1A). Colorful fish and plant stimuli were designed to engage the children to ensure adequate task performance.

The participants viewed the stimuli through magnetic resonance-compatible liquid crystal display (LCD) goggles. Children’s responses were recorded via 2 keypads, placed under the right and left index fingers, respectively, and connected to a computer running Presentation software (Neurobehavioral Systems, Berkeley, California).

At the start of each scanning run, children were shown all possible targets (ie, yellow fish in front of a tall green plant; Figure 1A), each lasting 1 second, with a string of “X”s above to represent the text that would later appear to indicate the target. This was followed by a fixation cross for 20 seconds followed by an explicit instructional cue that was presented for 1 second. The instructional cue was an image of the target stimulus that depicted a particular exemplar from one of the dimensions (eg, blue fish). A trial stimulus followed the cue, which
consisted of 2 compound stimuli (eg, left: blue fish in front of a plant; right: a red fish in front of a plant; Figure 1B), 1 on either side of the screen. The task was to indicate the compound stimulus (ie, blue fish in front of a plant) that included the target stimulus by pressing 1 of 2 buttons with their left or right index finger, corresponding with the left or right side of the screen. Trials were repeated 3 to 4 times, until a new target stimulus was presented (set shift). After each trial, the participant was given feedback on whether they were correct or incorrect, by means of a gold coin (correct) or an X (incorrect). The participants were periodically informed on the total gold coins accumulated in their piggy bank, which was used as the primary reward stimulus.

The relevant dimension of the target stimulus (eg, blue fish or tall green plants) always appeared in the foreground for a set of trials. The session comprised 3 scanning runs of 10 sets that contained 3 to 4 trials. Each trial lasted 3 seconds, including a blank screen buffer if the child responded before the 3 seconds had elapsed. If the child did not respond, the trial was considered incorrect.

Each trial was followed by feedback that informed the child whether the response was correct or incorrect, by means of a gold coin (correct) or an X (incorrect). Once the child responded consistently to the cue (3 or 4 consecutive correct responses), either an intradimensional or an extradimensional shift of the stimuli occurred; the intradimensional or extradimensional shifts were randomly assigned. An intradimensional shift involved a 1-dimensional change in the target stimulus (eg, from blue fish target to yellow fish target). An extradimensional shift meant a multidimensional change in the target stimulus (eg, from blue fish target to green plant target). Each time a shift occurred, the participant was shown a new cue, which gave them the new target stimulus. Participants were periodically given an update on the total accumulated number of gold coins in their “piggy bank” that was used as the primary reward stimulus in the analysis. The piggy bank was presented a maximum of 6 times during a single scanning run.

**Magnetic Resonance Imaging Data Acquisition**

Participants underwent functional neuroimaging at the research-dedicated MRI suite at The Hospital for Sick Children. Participants were scanned on a 1.5-T MRI scanner (GE Signa Excite, Waukesha, Wisconsin), using an 8-channel array head coil. Anatomical images were obtained using a 3-dimensional fast spoiled gradient echo (FSPGR) sequence, producing volumes of T1-weighted axial slices with voxels = 0.9375 mm × 0.9375 mm, slice thickness of 1.5 mm, repetition time (TR) = 9 milliseconds. Following the anatomical sequences, children completed 3 functional scanning runs using a 2-dimensional spiral in/out sequence, producing 183 volumes of T2*-weighted axial slices, with voxels of 3.75 mm × 3.75 mm, a slice thickness of 5 mm, TR = 2 seconds, and lasted a total duration of 6 minutes.

**Functional MRI Data Preprocessing and Statistical Analysis**

Standard preprocessing included skull stripping the anatomical images followed by linear registration to a template in the standardized space.
of the Montreal Neurological Institute. Three volumes at the beginning of each functional run were excluded from the analysis, allowing for the blood oxygen level dependent (BOLD) signal to achieve an equilibration state. Functional images were then motion and slice time corrected, aligned to individual anatomical images, and spatially smoothed at 10 mm FWHM (full width at half maximum) using a Gaussian blurring kernel and scaled to percentage change.

Postprocessing of functional MRI data was achieved using Analysis of Functional NeuroImages software (version 2011_12_21_1014). Data were analyzed using an event-related design, whereby each time period that contained the reward stimulus (piggy bank) was modeled as a regressor. The event-related protocol was operationalized to be the piggy bank time image shown 3 to 6 times within the scanning run (variable depending on task performance; maximum of 6 piggy banks × 3 scanning runs = 18 stimuli). All other events (including unsuccessful trials) were modeled as baseline in the analysis.

Regressors were convolved with a canonical hemodynamic response function and modeled using a gamma variate function. A general linear model was computed, and the overall model fit was assessed using an F statistic. An analysis of covariance was used for the group by age analysis. For each subject, a general linear model was computed, and the overall model fit was assessed using an F statistic. An analysis of covariance was used for the group by age analysis. For each subject, a general linear model was computed, and the overall model fit was assessed using an F statistic. Thus, the total data set included 58 children, 29 per group.

**Behavioral Data**

All participants included in the analyses completed the task with high accuracy, with no significant differences evident between groups ($P = .52$). The typically developing children correctly answered 92.7\% of trials, and the autism spectrum disorder group also answered the majority of trials correctly (91\%) as did the group of children born preterm (92\%). Given that the behavioral performance was comparable between the experimental groups, and the hypotheses regarding the brain imaging was the same for atypically developing groups of children (autism spectrum disorder and preterm), the subsequent functional MRI data were combined for these participants.

**Functional Neuroimaging Data**

*Typically developing children.* Typically developing children showed age-related effects in response to the reward stimuli in a whole brain analysis in the right inferior frontal gyrus, right middle frontal gyrus, bilateral cingulate gyri, left insula, and putamen. The full list of clusters and corresponding Montreal Neurological Institute coordinates are shown in Table 2. Comparable results were found when controlling for IQ.

*Atypically developing children.* The whole brain analysis in the atypically developing children revealed a significant activation
peak in the orbitofrontal cortex. Deactivations were found in the anterior cingulate cortex, middle cingulate cortex, and caudate; see Table 3 for a complete list of foci.

The ROI analyses (directed search) further verified these results, revealing activation in the orbitofrontal cortex and deactivations in the anterior cingulate cortex and middle frontal gyrus. The full list of clusters from the ROI analyses is shown in Table 3. Results remained similar when including IQ as a covariate.

Typically versus atypically developing children. The whole brain analysis found significant activation, greater in the typically developing children, in the right insula, bilateral cingulate and middle frontal gyri, right medial frontal gyrus, and left precentral gyrus. The full list of activation clusters for this analysis is shown in Table 4.

A directed search in our a priori regions of interest (ROIs) verified significantly larger activations in the control children in the right anterior cingulate cortex and lateral middle frontal gyr. The ROI analysis of the striatum further revealed activation in the caudate. The full list of activation clusters for the ROI analysis is shown in Table 4.

The mean BOLD percentage signal change in response to the reward stimuli was extracted from the anterior cingulate cortex, medial prefrontal cortex, and lateral prefrontal cortex. The data extracted from the anterior cingulate cortex in the typically developing population showed a positive trend with age and revealed a peak in activation at 10 years of age (Figure 2). The activation extracted from the anterior cingulate cortex in the atypically developing population showed an opposite effect with BOLD signal decreased at older ages. In the lateral

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**Table 2. Within-Group Analysis: Age Effects Associated With Reward Stimuli in Typically Developing Children.**

| Brain Region                       | Side | Cluster Size | X    | Y    | Z    | t Value | P Value |
|-----------------------------------|------|--------------|------|------|------|---------|---------|
| **Global search**                 |      |              |      |      |      |         |         |
| Activation                        |      |              |      |      |      |         |         |
| Frontal lobe                      |      |              |      |      |      |         |         |
| Lateral prefrontal cortices       |      |              |      |      |      |         |         |
| Inferior frontal gyrus            | R    | 9            | 30   | 22   | 24   | 3.9     | .001    |
| Primary motor cortices            |      |              |      |      |      |         |         |
| Precentral gyrus                  | L    | 27           | −32  | −16  | 34   | 4.2     | .001    |
|                                 | L    | 5            | −38  | −6   | 40   | 3.9     | .001    |
| Medial prefrontal cortices        |      |              |      |      |      |         |         |
| Superior/middle frontal gyrus     | R    | 14           | 24   | 12   | 40   | 4.2     | .001    |
| Parietal lobe                     |      |              |      |      |      |         |         |
| Postcentral gyrus                 | L    | 53           | −22  | −30  | 56   | 4.5     | .001    |
|                                 | R    | 25           | 26   | −32  | 66   | 4.8     | .001    |
| Precuneus                         | L    | 25           | −26  | −48  | 30   | 4.5     | .001    |
| Angular gyrus                     | R    | 19           | 30   | −54  | 34   | 4.6     | .001    |
| Inferior parietal lobule          | R    | 5            | 32   | −38  | 26   | 4.0     | .001    |
| Limbic lobe                       |      |              |      |      |      |         |         |
| Cingulate gyrus                   | L    | 9            | −20  | −4   | 42   | 4.2     | .001    |
|                                 | R    | 5            | 16   | 14   | 44   | 4.1     | .001    |
| Insula                            | L    | 15           | −26  | −30  | 16   | 4.3     | .001    |
| Temporal lobe                     |      |              |      |      |      |         |         |
| Middle temporal gyrus             | L    | 6            | −58  | −50  | −8   | 3.9     | .001    |
|                                 | R    | 5            | 46   | −4   | −24  | 4.1     | .001    |
| Hippocampus                       | L    | 10           | −36  | −20  | −12  | 4.6     | .001    |
| Occipital lobe                    |      |              |      |      |      |         |         |
| Middle occipital gyrus            | L    | 35           | −30  | −76  | 6    | 4.5     | .001    |
| Lingual gyrus                     | L    | 64           | −16  | −80  | −16  | 4.7     | .001    |
|                                 | R    | 25           | 10   | −86  | −12  | 4.3     | .001    |
|                                 | R    | 8            | 20   | −78  | −16  | 3.9     | .001    |
| Inferior occipital gyrus          | L    | 5            | −32  | −78  | −10  | 3.9     | .001    |
| Basal ganglia and thalamus        |      |              |      |      |      |         |         |
| Putamen                           | R    | 134          | 28   | −8   | 20   | 5.1     | .001    |
|                                 | L    | 17           | −26  | −16  | 14   | 4.1     | .001    |
| Thalamus                          | R    | 22           | 26   | −32  | 16   | 4.4     | .001    |
| Cerebellum                        |      |              |      |      |      |         |         |
| Culmen (cerebellum)               | L    | 7            | −10  | −52  | −18  | 3.8     | .001    |

Abbreviations: L, left; R, right.

*Within-group analysis (typically developing children): Age-related activation in response to viewing rewarding stimuli. Coordinates are listed in MNI space (Montreal Neurological Institute space, Collins et al29). Medial–lateral (X), anterior–posterior (Y), and superior–inferior (Z) stereotaxic coordinates (mm) are relative to midline (positive values are right, anterior, and superior). Results are based on a random-effects analysis.
prefrontal cortex, the typically developing population exhibited a much greater increase in activation with age compared to the neurodevelopmental population (Figure 2). In the medial prefrontal cortex, a similar analysis that found trends of increased and decreased activation was associated with older ages in the typically and atypically developing population, respectively. Results did not change when IQ was included as a covariate.

Discussion

Using functional MRI, activation in brain regions involved in cognitive control and reward-based processing using monetary reward stimuli was examined in typically developing children, those with autism and those born preterm. Performance was comparable between groups; however, brain activation in response to reward stimuli differed significantly between typically and atypically developing children. In typically developing children, reward stimuli evoked increased activation in the medial prefrontal cortex, striatum, lateral prefrontal cortex, and dorsal anterior cingulate cortex, and was associated with older ages. In contrast, atypically developing children only showed activation in the orbitofrontal cortex. Activation in other reward and cognitive control centers was absent or showed no activation changes in atypically developing children across the age range. Comparable between-group behavioral performance accompanied by differential changes in activation in the prefrontal cortices suggests alterations in processing of reward stimuli.

Maturation of Cognitive Control Neural Systems

Recent functional MRI studies highlight nonlinear developmental changes in the activation of cognitive control regions. Many studies report age-related increases in frontal, parietal, temporal, striatal, and cerebellar cortices, which are thought to reflect age-related integration of control systems. A developmental functional MRI study of sustained attention in a continuous performance task in a large sample of 70

Table 3. Within-Group Analysis: Age Effects Associated With Reward Stimuli in Atypically Developing Children.

| Brain Region                  | Side | Cluster Size | X    | Y    | Z    | t Value | P Value |
|-------------------------------|------|--------------|------|------|------|---------|---------|
| **Global search**             |      |              |      |      |      |         |         |
| Activation                   |      |              |      |      |      |         |         |
| Frontal lobe                  |      |              |      |      |      |         |         |
| Medial Prefrontal Cortices    |      |              |      |      |      |         |         |
| orbitofrontal cortex          | R    | 5            | 2    | 30   | −20  | 4.0     | .001    |
| Deactivation                  |      |              |      |      |      |         |         |
| Frontal lobe                  |      |              |      |      |      |         |         |
| Motor Cortices                |      |              |      |      |      |         |         |
| precentral gyrus              | R    | 16           | 48   | 0    | 46   | −4.4    | .001    |
|                             | L    | 9            | −34  | −16  | 50   | −4.0    | .001    |
| Supplementary motor area      | L    | 7            | 0    | −18  | 50   | −4.3    | .001    |
| Occipital Lobe                |      |              |      |      |      |         |         |
| Lingual gyrus                 | R    | 34           | 4    | −80  | −14  | −4.9    | .001    |
| Parietal Lobe                 |      |              |      |      |      |         |         |
| Angular gyrus                 | R    | 24           | 50   | −68  | 36   | −4.6    | .001    |
| Inferior parietal lobule      | L    | 11           | −50  | −54  | 38   | −4.1    | .001    |
| Limbic Lobe                   |      |              |      |      |      |         |         |
| Anterior cingulate cortex     | R    | 16           | 2    | 8    | 38   | −4.2    | .001    |
| Middle cingulate cortex       | L    | 24           | −10  | −26  | 46   | −4.6    | .001    |
| Cingulate gyrus               | R    | 8            | 12   | −8   | 46   | −4.2    | .001    |
|                             | L    | 5            | −16  | −14  | 34   | −3.9    | .001    |
| Caudate                       | R    | 6            | 14   | 4    | 26   | −4.1    | .001    |
| Temporal Lobe                 |      |              |      |      |      |         |         |
| Fusiform gyrus                | R    | 7            | 44   | −36  | −10  | −4.3    | .001    |
| **Directed search**           |      |              |      |      |      |         |         |
| Anterior cingulate cortex     | R    | 16           | 2    | 8    | 38   | −4.2    | .001    |
| Middle cingulate cortex       | L    | 2            | −10  | −2   | 40   | −3.7    | .001    |
| Prefrontal cortices lateral   |      |              |      |      |      |         |         |
| Middle frontal gyrus          | L    | 4            | −26  | 16   | 50   | −3.9    | .001    |
| Medial                        |      |              |      |      |      |         |         |
| Orbitofrontal cortex          | R    | 5            | 2    | 30   | −20  | 4.0     | .001    |

Abbreviations: L, left; R, right.

*Within-group analysis (atypically developing children): Age-related activation in response to viewing rewarding stimuli. Coordinates are listed in MNI space (Montreal Neurological Institute space, Collins et al. 29). Medial–lateral (X), anterior–posterior (Y), and superior–inferior (Z) stereotaxic coordinates (mm) are relative to midline (positive values are right, anterior, and superior). Results are based on a random-effects analysis.
Table 4. Between-Group Analysis: Age Effects Associated With Reward Stimuli Between Typically Versus Atypically Developing Children.

| Brain Region                      | Side | Cluster Size | X   | Y   | Z   | t Value | P Value |
|-----------------------------------|------|--------------|-----|-----|-----|---------|---------|
| **Global search**                 |      |              |     |     |     |         |         |
| **Activation**                    |      |              |     |     |     |         |         |
| Frontal lobe                      |      |              |     |     |     |         |         |
| Primary motor cortices            |      |              |     |     |     |         |         |
| Precentral gyrus                  | L    | 83           | −30 | −24 | 62  | 4.3     | .001    |
| Precentral gyrus                  | L    | 12           | −52 | −6  | 38  | 3.8     | .001    |
| Precentral gyrus                  | L    | 10           | −48 | −10 | 50  | 3.9     | .001    |
| Precentral gyrus                  | L    | 5            | −44 | −14 | 54  | 3.8     | .001    |
| **Medial prefrontal cortices**    |      |              |     |     |     |         |         |
| Medial frontal gyrus/superior     | R    | 14           | 12  | 38  | 44  | 4.0     | .001    |
| Superior frontal gyrus            | R    | 9            | 18  | −6  | 58  | 4.0     | .001    |
| **Lateral prefrontal cortices**   |      |              |     |     |     |         |         |
| Middle frontal gyrus              | L    | 185          | −28 | 10  | 44  | 4.4     | .001    |
| Superior frontal gyrus            | L    | 17           | −22 | 40  | 30  | 4.1     | .001    |
| Middle frontal gyrus              | R    | 6            | 24  | 58  | 26  | 3.7     | .001    |
| **Parietal lobe**                 |      |              |     |     |     |         |         |
| Paracentral lobule                | R    | 33           | 4   | −16 | 50  | 4.0     | .001    |
| Precuneus                         | L    | 53           | −2  | −72 | 22  | 4.0     | .001    |
| Postcentral gyrus                 | L    | 49           | −36 | −24 | 48  | 4.3     | .001    |
| Inferior parietal lobule          | L    | 24           | −28 | −22 | 32  | 4.2     | .001    |
| **Occipital lobe**                |      |              |     |     |     |         |         |
| Lingual gyrus                     | R    | 187          | 10  | 88  | −12 | 5.4     | .001    |
| Cuneus/calcarine gyrus            | L    | 79           | −22 | −76 | −14 | 5.4     | .001    |
| Middle occipital gyrus/cuneus     | R    | 20           | 2   | −84 | 6   | 3.9     | .001    |
| **Limbic lobe**                   |      |              |     |     |     |         |         |
| Insula                            | R    | 225          | 30  | 6   | 24  | 4.3     | .001    |
| Cingulate gyrus                   | R    | 50           | 14  | 14  | 44  | 4.2     | .001    |
| Cingulate gyrus                   | L    | 21           | −16 | 12  | 42  | 4.4     | .001    |
| Cingulate gyrus                   | L    | 14           | −16 | −14 | 36  | 4.3     | .001    |
| Cingulate gyrus                   | R    | 9            | 22  | −14 | 28  | 3.7     | .001    |
| Cingulate gyrus                   | L    | 5            | −6  | −18 | 28  | 3.8     | .001    |
| **Middle cingulate cortex**       |      |              |     |     |     |         |         |
| Cerebellum                        | R    | 12           | 4   | 6   | 38  | 3.7     | .001    |
| **Temporal lobe**                 |      |              |     |     |     |         |         |
| Middle temporal gyrus             | R    | 15           | 38  | −52 | 0   | 4.4     | .001    |
| **Directed search**               |      |              |     |     |     |         |         |
| Anterior cingulate cortex         | R    | 12           | 4   | 6   | 38  | 3.7     | .001    |
| **Prefrontal cortices**           |      |              |     |     |     |         |         |
| Medial                             | R    | 2            | 24  | 58  | 26  | 3.7     | .001    |
| Superior medial gyrus             | R    | 2            | 12  | 40  | 44  | 3.8     | .001    |
| Lateral                            | R    | 37           | −26 | 14  | 44  | 4.1     | .001    |
| Superior frontal gyrus            | R    | 11           | −36 | 2   | 42  | 4.1     | .001    |
| Superior frontal gyrus            | L    | 7            | −22 | 40  | 30  | 4.1     | .001    |
| Middle frontal gyrus              | R    | 7            | 24  | 34  | 44  | 3.8     | .001    |
| Middle frontal gyrus              | R    | 2            | 16  | 38  | 44  | 3.7     | .001    |
| Striatum                          | R    | 4            | 26  | 58  | 26  | 3.6     | .001    |
| Caudate                           | R    | 28           | 14  | −8  | 20  | 3.8     | .001    |

Abbreviations: L, left; R, right.

Between-group analysis (typically vs atypically developing children): Age-related activation in response to viewing rewarding stimuli in the typically developing population relative to the atypically developing children. Coordinates are listed in MNI space (Montreal Neurological Institute space, Collins et al.29). Medial–lateral (X), anterior–posterior (Y), and superior–inferior (Z) stereotaxic coordinates (mm) are relative to midline (positive values are right, anterior, and superior). Results are based on a random-effects analysis.
children and adults (ages: 10-43 years) showed that progressively stronger recruitment of the ventrolateral prefrontal cortex, superior temporal, and inferior parietal cortices was evident with age, despite comparable task performance. The orbitofrontal cortex, medial prefrontal cortex, and ventral striatum are crucial for reward-related decision-making processes. However, developmental changes in reward systems have been reported inconsistently in the functional MRI literature. Enhanced orbitofrontal cortex activation was reported in children aged 9 to 11 years and adolescents aged 13 to 17 years relative to adults aged 23 to 29 years, despite no between-group differences in performance. The ventral striatum, however, demonstrated heightened activity in adolescents only, relative to adults and children during reward outcome. The authors have suggested that the activation in the striatum in adolescents may reflect an increased sensitivity to rewards in adolescence, related to their higher risk-taking behaviors.

These findings are further supported by evidence suggesting that reward incentives enhance brain activity in typically developing adolescents compared to children and adults. Activity was modulated by the magnitude of the reward in adolescents only in the inferior parietal cortex, basal ganglia, and ventral striatum. In the current study, weak positive changes were seen in reward-processing brain regions in typically developing controls in preadolescence. However, increased activation at older ages was only seen in the orbitofrontal cortex in the atypically developing population. The orbitofrontal cortex has been implicated in motivational aspects of reward processing, especially in relation to saliency and magnitude of reward. Furthermore, in the context of reward paradigms, the orbitofrontal cortex is thought to signal executive functions and to inform goal-directed behavior through its connections with the basal ganglia. Atypically developing children may recruit the orbitofrontal cortex progressively with age in reward-based tasks indexing greater difficulty with assessing saliency of the reward stimuli. Future studies with larger samples are required to validate the role of the orbitofrontal cortex in reward processes. Furthermore, research is needed to better understand sex-based differences in the developmental time courses of activation in central reward regions.
Conclusions

During development, forming reward representations is key to adaptive behavior and learning. Atypically developing children are often impaired in these abilities. In this study, functional activation in reward and cognitive control centers was examined in response to rewarding stimuli in typically and atypically developing children (aged 6-12 years). While performance was comparable between groups, increases and decreases in activation differed significantly, particularly in the frontal lobes. In comparison to typically developing children, children with atypical development showed little activation changes except in the orbitofrontal, which is involved in motivational aspects of reward processing. Activation changes in the orbitofrontal cortex in atypically developing children may indicate a reliance on motivational systems to perform the task. The lack of activation changes at older ages in other reward and cognitive control centers seen in atypically developing children may reflect disturbances in functional maturation of these prefrontal regions, consistent with the frequent deficits in social and reward situations in these children.8,19

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Author Contributions

EGD, ML, and SC analyzed the data. EGD, ML, SC, JS, and MJT wrote the manuscript. KMF and MJT designed the task. KMF acquired the data.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval

Written informed consent was obtained from parents and informed assent from the children.

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