Beyond age and gender: Relationships between cortical and subcortical brain volume and cognitive-motor abilities in school-age children

Melissa M. Pangelinan, Guangyu Zhang, John W. VanMeter, Jane E. Clark, Bradley D. Hatfield, Amy J. Haufler

© 2010 Elsevier Inc. All rights reserved.

Introduction

Historically, the development of cognitive and motor skills in typically developing children has been studied and discussed separately, with only a few notable exceptions (McGraw, 1943; Piaget and Inhelder, 1969). However, there is growing evidence that these two domains are fundamentally interrelated across development (Diamond, 2000; Rosenbaum et al., 2001). Indeed, recent research suggests that these skills are not only interrelated at the behavioral level but may also rely on the development of similar cortical and subcortical neural structures (Davis et al., 2010; Diamond, 2000). Support for this notion comes primarily from children with developmental disorders such as attention deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD), dyslexia, and developmental coordination disorder (DCD) (Davis et al., 2009; Gilger and Kaplan, 2001; Piek and Dyck, 2004). Although these studies provide a basis for a relationship between cognitive and motor skills at the level of brain and behavior, evidence from developmental disorders may not hold true for typically developing children. Thus, the purpose of the current study is to address this knowledge gap by examining the trajectory of cortical and subcortical brain development with respect to both cognitive and motor skills in typically developing children.

Evidence from clinical populations has served as the basis for recent studies investigating the interrelation of cognitive and motor skills. In particular, children with developmental disorders such as ADHD and ASD, which are characterized predominantly as cognitive (attention) and socio-emotional (affective) disorders, respectively, also exhibit impaired motor functions. This includes: poor handwriting and fine motor skills (Fuentes et al., 2009; Racine et al., 2008), difficulties planning movements (Ellason et al., 2004; Hughes, 1996; Rinhearht et al., 2001), and poor gross motor coordination (Leary and Hill, 1996; Miyahara et al., 1997; Pitcher et al., 2003). Consistent with these behavioral deficits, children with ADHD and ASD have been found to have structural abnormalities in brain regions that mediate both cognitive and motor circuits, including: subdivisions within the frontal cortex (Carper and Courchesne, 2000; Mostofsky et al., 2002),...
To address these knowledge gaps, a subset of the original dataset which consisted of 172 prepubescent typically developing children between the ages of 6 and 13 years was analyzed using linear mixed regression models to characterize global (total gray and white matter) and regional volumes (frontal gray and white, parietal gray and white, cerebellum, caudate, putamen, and globus pallidus), intelligence, executive function (spatial working memory), and visuomotor skill with respect to age and gender effects. Subsequent analyses allow for the investigation of relationships above and beyond the well-established effects of age and gender on cortical and subcortical brain volumes (De Bellis et al., 2001; Lenroot et al., 2007; Reiss et al., 1996; Sowell et al., 2002) as well as behavior (Waber et al., 2007). This approach enables unique relationships between brain and behavior to emerge, which might otherwise be obscured by age and gender effects. We hypothesized that generalized intelligence and executive function (spatial working memory) would be positively related to the volume of the cerebellum and basal ganglia, in addition to fronto-parietal cortical development. We also hypothesized that visuomotor skill development would be positively related to fronto-parietal cortical brain development. Moreover, at the level of behavior, cognitive ability (intelligence and executive function) would be positively related to visuomotor ability.

Materials and methods

The purpose of the NIH MRI Study of Normal Brain Development (funded by the National Institute of Child Health and Human Development, the National Institute on Drug Abuse, the National Institute of Mental Health, and the National Institute of Neurological Disorders and Stroke) was to provide a large, longitudinal public database (Pediatric MRI Data Repository) of demographic, behavioral, and anatomical brain data from healthy infants, children, and adolescents (Brain Development Cooperative Group and Evans, 2006). The list of participating sites and a complete listing of the study investigators may be found at [http://www.bic.mni mcgill.ca/nihcpd/info/participating_centers.html](http://www.bic.mni mcgill.ca/nihcpd/info/participating_centers.html). All procedures for the secondary analyses were approved by the Institutional Review Board (IRB) at the University of Maryland and in accordance with the NIH MRI Study of Normal Brain Development data access procedures. The testing procedures including the exclusion criteria, sample demographics, data acquisition parameters, MRI data processing, and performance of the full sample on the behavioral tasks have been reported previously (Brain Development Cooperative Group and Evans, 2006; Waber et al., 2007). For the current study, participant demographics, telephone screening, physical and neurological exam, pubertal status, segmented MRI volumes, as well as the behavioral performance on cognitive and motor tasks were obtained from the Pediatric MRI Data Repository (data release 2).

Subject selection

A total of 490 observations from 315 children were obtained from the data repository for children between the ages of 6.00 and 12.99 years. Participants visited the laboratory on two occasions: an initial session and follow-up session approximately 2 years later (follow-ups ranged from 1.5 to 2.5 years). On each measurement occasion the children completed physiological screening including: a physical and neurological assessment, the pubertal development scale (Petersen et al., 1988), and provided saliva and urine samples. The children then underwent anatomical MRI scanning and completed a battery of behavioral tests. From the original data set, 172 children were included in the present secondary analysis based on the following additional exclusionary criteria: (1) failing the quality control standards for the MRI data acquisition (for full details see Brain Development Cooperative Group and Evans, 2006); (2) left-handed; (3) full scale IQ<80; (4) history of head injuries or...
measurements at both measurement occasions (1.5
Of the 172 children, 45 (19 males and 26 females) provided complete
one or both measurement occasions for an individual participant.
(

coded on a 4-point scale: 1=not started; 2=barely started; 3=de
growth spurt, body hair, skin changes, breast change, and menarche. Responses were
changes, facial hair, and voice changes. For females the scale assesses the following:
physical development in the following areas for males: growth spurt, body hair, skin

Table 1

<table>
<thead>
<tr>
<th>Gender</th>
<th>One measurement occasion only</th>
<th>Two measurement occasions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Measurement occasion 1</td>
<td>Measurement occasion 2</td>
</tr>
<tr>
<td></td>
<td>Males (N = 49)</td>
<td>Males (N = 19)</td>
</tr>
<tr>
<td></td>
<td>Females (N = 78)</td>
<td>Females (N = 26)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>9.52 (2.05)</td>
<td>8.00 (1.36)</td>
</tr>
<tr>
<td></td>
<td>9.33 (1.87)</td>
<td>8.10 (1.36)</td>
</tr>
<tr>
<td>Full scale IQ</td>
<td>111.35 (13.13)</td>
<td>115.32 (14.31)</td>
</tr>
<tr>
<td></td>
<td>109.97 (11.87)</td>
<td>113.31 (11.67)</td>
</tr>
<tr>
<td>Spatial working memory (# errors)</td>
<td>31.86 (8.25)</td>
<td>36.32 (13.18)</td>
</tr>
<tr>
<td></td>
<td>22.99 (7.97)</td>
<td>33.58 (11.09)</td>
</tr>
<tr>
<td>Pegboard (# pegs both hands)</td>
<td>9.53 (1.86)</td>
<td>8.00 (1.89)</td>
</tr>
<tr>
<td></td>
<td>9.77 (1.95)</td>
<td>8.65 (1.77)</td>
</tr>
<tr>
<td>Total gray matter volume (cm³)</td>
<td>851.31 (55.19)</td>
<td>861.49 (42.68)</td>
</tr>
<tr>
<td></td>
<td>774.27 (62.15)</td>
<td>803.87 (74.40)</td>
</tr>
<tr>
<td>Total white matter volume (cm³)</td>
<td>492.70 (26.18)</td>
<td>482.05 (28.79)</td>
</tr>
<tr>
<td></td>
<td>438.59 (48.65)</td>
<td>432.06 (45.17)</td>
</tr>
<tr>
<td>Frontal gray matter volume (cm³)</td>
<td>289.70 (22.18)</td>
<td>290.85 (18.54)</td>
</tr>
<tr>
<td></td>
<td>261.48 (21.95)</td>
<td>271.64 (26.35)</td>
</tr>
<tr>
<td>Frontal white matter volume (cm³)</td>
<td>177.01 (22.02)</td>
<td>173.19 (11.80)</td>
</tr>
<tr>
<td></td>
<td>156.76 (18.48)</td>
<td>154.46 (16.35)</td>
</tr>
<tr>
<td>Parietal gray matter volume (cm³)</td>
<td>149.05 (13.04)</td>
<td>150.38 (9.61)</td>
</tr>
<tr>
<td></td>
<td>136.21 (14.15)</td>
<td>142.64 (17.05)</td>
</tr>
<tr>
<td>Parietal white matter volume (cm³)</td>
<td>95.94 (11.06)</td>
<td>93.40 (7.68)</td>
</tr>
<tr>
<td></td>
<td>85.02 (11.34)</td>
<td>85.11 (11.71)</td>
</tr>
<tr>
<td>Cerebellum matter volume (cm³)</td>
<td>138.64 (10.46)</td>
<td>140.73 (11.48)</td>
</tr>
<tr>
<td></td>
<td>127.46 (11.68)</td>
<td>130.05 (8.98)</td>
</tr>
<tr>
<td>Caudate Volume (cm³)</td>
<td>11.68 (0.92)</td>
<td>12.15 (0.67)</td>
</tr>
<tr>
<td></td>
<td>10.94 (0.98)</td>
<td>11.33 (1.03)</td>
</tr>
<tr>
<td>Putamen volume (cm³)</td>
<td>11.03 (1.45)</td>
<td>11.57 (1.03)</td>
</tr>
<tr>
<td></td>
<td>10.35 (1.02)</td>
<td>10.42 (0.99)</td>
</tr>
<tr>
<td>Globus pallidus (cm³)</td>
<td>2.47 (0.32)</td>
<td>2.52 (0.34)</td>
</tr>
<tr>
<td></td>
<td>2.52 (0.34)</td>
<td>2.48 (0.29)</td>
</tr>
<tr>
<td></td>
<td>2.75 (0.29)</td>
<td>2.75 (0.29)</td>
</tr>
<tr>
<td></td>
<td>2.43 (0.30)</td>
<td>2.43 (0.30)</td>
</tr>
</tbody>
</table>

neurological deficits; (5) learning disability, including attention deficit hyperactivity disorder (ADHD) or enrollment in special education; and, (6) puberty development scale score 1.5–2 ("barely started puberty"). Data from each measurement occasion were subjected to these criteria and may result in the loss of data from one or both measurement occasions for an individual participant.

Table 1 presents the sample characteristics for the current analysis. Of the 172 children, 45 (19 males and 26 females) provided complete measurements at both measurement occasions (1.5–2 years between measurements). The rest of the children either provided complete initial measurement but did not have a complete data set for the follow-up (70 children—21 males and 49 females) or vice versa (57 children—28 males and 29 females). The resulting statistical analysis for each dependent measure included 217 observations. Within subject associations, when applicable, were determined using the participant identification number and were accounted for by specifying the correlation structure for repeated measures.

Behavioral measures

The NIH MRI Study of Normal Brain Development consisted of performance measures from a battery of neuropsychological assessments (intelligence, verbal learning/fluency, executive function, fine motor dexterity, and academic skills). For the purpose of the current study, the following assessments were selected among the larger set of available neuropsychological measures. General intelligence was assessed with the Wechsler Abbreviated Scales of Intelligence (WASI—Wechsler, 1999) Full Scale IQ and comprised of performance on the following subtests: vocabulary, block design, similarities, and matrix reasoning. Spatial working memory was selected to represent one aspect of executive function and was assessed by the Cambridge Neuropsychological Test Automated Battery (CANTAB—CenNeS, 1998) spatial working memory task (SWM—total number of errors). For this computerized task, children were asked to sequentially point to boxes on the screen to determine which box contains a blue square without pointing to the same box twice. The number of return errors within and between trials is recorded. The Purdue Pegboard (Gardner and Broman, 1979) bimanual task (number of pegs placed with both hands together) was selected as a measure of visuomotor ability and manual dexterity. For this task, children are asked to place as many pegs as possible into the board using both hands simultaneously within 30 s. The raw scores for each of these behavioral measures were obtained from the data repository for each child.

MRI acquisition/analysis and measures

The NIH Study of Normal Brain Development collected whole brain MRI using 1.5 T General Electric or Siemens Medical Scanners with 1.2 mm slice thickness, 1 mm in-plane resolution. T1-weighted images were acquired using an RF-spoiled gradient echo with a 22–25 ms repetition time, 10–11 ms echo time, 30° excitation angle, 180° refocusing pulse, and 256 anterior-posterior field of view. T2-weighted and proton-density weighted images were acquired using a fast/turbo spin echo, repetition time of 3500 ms, 90° excitation angle, effective echo time of 12–17 ms, and 256 mm anterior-posterior field of view. Centralized data processing performed on the data by the Brain Development Cooperative Group involved the following procedures: image corrections for image intensity non-uniformity, spatial normalization using Automated Non-linear Image Matching and Anatomical Labeling (ANIMAL), and tissue classification using Intensity—Normalized Stereotaxic Environment for Classification of Tissues (INSECT), and automatic surface parameterization (Constrained Laplacian-based Automated Segmentation with Proximities Algorithm—CLASP). The combination of ANIMAL, INSECT, and CLASP provided enhanced classification and segmentation of the pediatric volumes.

Consistent with the evidence regarding the neural substrates for the behavioral dependent measures of interest, the following segmented volumes (in cm³) were obtained from the data repository for each child: (1) total gray matter, (2) total white matter, (3) frontal gray matter, (4) frontal white matter, (5) parietal gray matter, (6) parietal white matter, (7) cerebellum, (8) caudate, (9) putamen, and (10) globus pallidus.

Statistical analysis

Previous studies have reported age and gender differences in these brain volumes (De Bellis et al., 2001; Lenroot et al., 2007; Reiss et al., 1996; Sowell et al., 2002) and behavioral measures (Waber et al., 2007). Thus, the brain volumes and behavioral measures were subjected to a two-level statistical analysis—the first to account for age and gender effects and the second to examine the relationships
between the brain volumes and behavior above and beyond the first-level effects. For the first level analysis, we employed linear mixed effects modeling (also known as random effects models). This type of analysis is ideal for data sets consisting of multiple measurement points (i.e., repeated measures) with missing data and/or irregular intervals between measurements. This statistical approach is consistent with those employed in recent developmental investigations of longitudinal MRI data (Lenroot et al., 2007; Shaw et al., 2008; Tiemeier et al., 2010). Although higher order models (quadratic, cubic) were tested, linear models were most appropriate (parsimonious) for the age range examined presently (6.00–12.99 years). Thus, each dependent variable of interest was modeled as:

\[ Y_{ij} = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \gamma_i + \epsilon_{ij} \]

where:

- \( Y_{ij} \) observed MRI volume or behavioral variable for individual \( i \) at time \( j \).
- \( \beta_0, \beta_1, \) and \( \beta_2 \) regression coefficients
- \( X_1 \) and \( X_2 \) age and gender
- \( \gamma_i \) is the random intercept for subject \( i \), with \( \gamma_i \sim \mathcal{N}(0, \sigma^2) \)
- \( \epsilon_{ij} \) residuals, with \( \epsilon_{ij} \sim \mathcal{N}(0, \sigma^2) \), \( \epsilon_{ij} \) and \( \epsilon_{il} \) are independent.

In this equation \( \beta_0 \) is the intercept parameter, \( \beta_1 \) and \( \beta_2 \) are the slope parameters for age and gender, respectively. This model accounts for within-subject associations due to repeated observations from individuals contributing data at two measurement occasions, and were modeled using the random intercept \( \gamma_i \). This model is equivalent to the linear mixed model with compound symmetric variance-covariance structure.

For the second level analysis, the residuals from each of the linear mixed models were obtained. Given that within-subject associations were controlled for in the first-level model, these conditional residuals are independent of within and between subject factor effects. These conditional residuals were analyzed using Pearson’s correlation to determine associations between the brain volumes and the behavioral (cognitive and motor) variables, above and beyond the effects of age and gender. For all analyses significance levels (\( P \) values) are provided in three categories (\( P<0.05, P<0.01, \) and \( P<0.001 \)).

**Results**

**Validation of age and gender effects on cortical and subcortical volumes**

Fig. 1 depicts all brain volumes and behavioral variables of interest with respect to age and gender. Table 2 presents the coefficients (\( \beta \)s) from the first level model with respect to age and gender, as well as the \( t \) and \( P \) values for each measure. Consistent with previous research (Barnea-Goraly et al., 2005; Lenroot et al., 2007; Paus et al., 1999; Reiss et al., 1996), a significant positive relationship was found for age and the volume of total and frontal white matter, parietal white

![Fig. 1. Scatter plots of the brain volumes and behavioral variables with respect to age and gender. Males are depicted as blue circles and females as red crosses. Individuals with two data points are connected with lines (blue for males and red for females). The linear fits for each gender are presented as heavy black lines (solid for males and dashed for females). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)](image-url)
matter, and the cerebellum, while a significant negative relationship was found for parietal gray matter and age (Fig. 1 and Table 2). A significant relationship was found between age and full scale IQ as well as age and pegboard performance (*P < 0.001 for both). No additional significant age effects were found for the other brain volumes or for spatial working memory (*P < 0.05 for all).

Significant gender effects were found for all brain volumes (*P < 0.001 for all), with the exception of the globus pallidus (*P = 0.05). These results confirm previous reports that found that males exhibit greater volumes compared to females for these brain areas (Lenroot et al., 2007; Reiss et al., 1996). There were no significant gender effects for any behavioral variables (*P < 0.05 for all).

Relationships between brain volume and cognitive-motor abilities above and beyond age and gender

In order to determine the unique relationships found between the brain volumes and cognitive-motor abilities, correlations among the residuals based on the first level analysis accounting for age and gender were examined. Table 3 depicts the correlations (correlation coefficients and associated significance levels) between the residual brain volumes and residual behavioral variables.

After accounting for age and gender in both the brain volumes and the behavioral variables, several significant relationships emerged. Specifically, residual full scale IQ was positively related to the residual volumes for total and frontal gray matter, parietal gray, cerebellum, and caudate. Residual IQ was also positively related to the residual volumes for total and frontal gray matter, parietal gray, cerebellum, and the behavioral variables, several significant relationships found between the behavioral variables, several significant relationships found between the behavioral variables, several signifi...
are consistent with volumetric studies across childhood (De Bellis et al., 2001; Lenroot et al., 2007; Reiss et al., 1996; Sowell et al., 2002). In particular, Reiss et al. (1996) reported that males exhibit 11% and 7.5% greater total gray and white matter volume, respectively. Moreover, regionally-specific differences were also reported by Lenroot et al. (2007) in which gender differences were evident in all lobar gray and white matter volumes examined. However, the functional implication and underlying mechanisms that result in gender differences remain unclear.

With respect to the age- and gender-related differences in subcortical volumes, the current results are consistent with Sowell et al. (2002), who found age-related differences in cerebellar volumes, and gender-related differences in both cerebellar and striatal volumes. More recently, Tiemeier et al. (2010) not only found age and gender effects in total cerebellar volume, but also found significant age and gender differences in the inferior posterior region of the cerebellar hemispheres. Importantly, this region of the cerebellum projects to the prefrontal and parietal regions of cortex and is likely associated with higher-order cognitive functions (Middleton and Strick, 1994). Although the volume of the cerebellum was not parsed into constituent regions in the present study, the current findings suggest that developmental changes in cerebellar volume may provide an important substrate for cognitive functions across childhood.

**Cognitive performance and brain volume**

After accounting for age and gender, the volume of the cerebellum and caudate were found to be positively related to IQ. Similarly, the putamen was found to be related to executive function (spatial working memory). These results provide new evidence regarding the role of these subcortical structures in higher-order cognition for typically developing children and are consistent with previous studies in adults (Paradiso et al., 1997) and adolescents (Frangou et al., 2004). A recent study by Lange et al. (2010) examined the relationship between IQ and brain volumes across childhood, but did not find a significant association between IQ and subcortical volumes (including the cerebellum). In contrast, the current study revealed novel relationships between the caudate and cerebellum with IQ in school-aged children only after age and gender were accounted for in the statistical models. Moreover, the current results provide direct evidence for the relationship between the volume of the cerebellum and higher-order cognitive functions in typically developing children, a relationship that was proposed but not previously examined (Tiemeier et al., 2010).

The current findings also provide additional support for the relationship between the striatum (caudate and putamen) and higher-order cognitive functions (IQ and executive function, respectively). The relationship between IQ and the caudate has been reported in one volumetric study in children (Reiss et al., 1996) and is consistent with anatomical studies in non-human primates in which the caudate is involved in “cognitive” cortico-striatal loops and is linked to the dorsolateral prefrontal cortex (Alexander et al., 1986). However, the finding that the putamen volume is related to spatial working memory has not been previously reported in typically developing children. Moreover, this finding appears to be inconsistent with the notion that the putamen is involved in a “motor” cortico-striatal loop, interfacing with the supplementary motor cortex, premotor, primary motor cortex, and somatosensory cortex, and that this loop is distinct from its “cognitive” counterpart (Alexander et al., 1986). However, there is some new evidence from a resting state connectivity study in adults reporting significant positive correlations between the ventral rostral aspects of the putamen with rostral anterior cingulate (BA 32 and BA24) as well as the dorsolateral prefrontal cortex (BA 10) (Di Martino et al., 2008). Functional imaging studies have also reported putamen involvement in executive tasks comparing adults and children. For example, Bunge et al. (2002) found greater activation in the putamen in adults compared to children during No-Go trials and during an Eriksen Flanker task. Similarly, Rubia et al. (2006) also found greater putamen activation during Switch tasks and Simon tasks in adults compared to children. Given that the putamen appears to contribute to components of executive function such as motor inhibition, task switching, and suppression of visual conflict, it is also likely that the putamen also contributes to working memory as in the current study. Thus, it does not appear appropriate to consider the putamen a strictly “motor” structure; the current study provides new support for the notion that the putamen may also contribute to non–motor functions.

In addition to these new subcortical findings, this study confirms relationships between IQ and cortical development (i.e., total and frontal gray matter) that have been previously reported (Shaw et al., 2006). Shaw et al. (2006) observed that children with superior intelligence experienced rapid cortical growth (greater cortical thickness) between 7 and 11 years, while children with average or low intelligence exhibited cortical thinning across this age range. Given that the majority of the children in the present study exhibit high or superior intelligence, the positive correlation between gray matter volume and IQ provide confirmatory evidence. The finding that parietal gray matter and parietal white matter are also related to IQ has not been found previously, but is consistent with the notion that the parietal lobe may interact with the frontal lobes during both cognitive and motor functions. Although the mechanisms underlying the changes in cortical development related to IQ are largely unknown, Shaw et al. (2006) attributed changes in cortical thickness to additional formation of usage-dependent synapses.

**Overlapping behavioral trajectories of cognitive and visuomotor development**

Although the hypothesized relationships between visuomotor ability and brain volumes were not supported, this study sheds new light on the positive relationship between intelligence and visuomotor performance after accounting for the effects of age and gender. This finding supports the notion that cognitive and motor behaviors may be interrelated and potentially mutually influential in the continued development of these abilities across childhood. The relationship between cognitive and motor skills has been previously proposed (Diamond, 2000; Rosenbaum et al., 2001) and is strongly supported by extensive research at both the level of behavior and brain structures in children with developmental disorders. However, only recently has this relationship been examined in typically developing children, and only at the behavioral level (Davis et al., 2010; Martin et al., 2010; Wassenberg et al., 2005). The current study provides additional evidence that relationship found between visuomotor ability and cognition is also present in typically developing children using measures that have not been previously examined (Purdue Pegboard and WASI Full Scale IQ). Since this result emerges after accounting for age and gender, interestingly, it appears that the relationship is already established by 6 years of age regardless of gender. Thus, establishing a child’s trajectory for cognitive and motor skills at a very early age may have broad implications across these two domains and with respect to the child’s continued brain development. This would likely be the case for both typically developing children and for children with developmental disorders.

**Conclusions and translational implications**

Taken together, this study demonstrated that cognitive and motor functions are related at both the behavioral and neuroanatomical levels. Although the mechanisms underlying brain development across childhood remain largely unknown, the present results suggest that enriched cognitive or motor experiences may promote behavioral...
improvements across these two domains and may also influence the development of brain structures mediating these functions. Indeed, environmental factors such as engagement in physical and cognitive activities have been found to influence developmental plasticity across the lifespan, and particularly in older adults (Hillman et al., 2008; Kramer and Erickson, 2007; Hertzog et al., 2009). Longitudinal studies are necessary to investigate the efficacy of these types of enriched environments in typically developing children and those with developmental disorders. In particular, it would be interesting to determine if there is a differential effect of fitness (aerobic exercise) training in comparison to motor skill training on anatomical brain development in children with and without development disorders. This line of research would replicate the elegant animal work (Adkins et al., 2006; Black et al., 1990; Kleim et al., 1998) in humans and support the notion of experience-dependent neuronal plasticity mediating cognitive and motor functions in child development. Importantly, these studies are necessary to provide a foundation for different types of brain-based interventions in both typically developing and clinical populations that will have direct implications on academic achievement, physical health, and brain function.

A primary aim of the NIH Study of Normal Brain Development was the creation of developmental trajectories of brain volumes and behavioral performance in typically developing children, which would serve as a means for comparison to those with developmental disorders. One translational implication of the current study is to use these typically developing trajectories to determine if an individual clinical patient appears delayed (i.e., similar to younger typically developing children) or different (i.e., following an altogether different trajectory). Determining whether a patient is developmentally delayed, as opposed to different, is not possible if only age-matched controls are used in comparison to patients and may have drastic consequences on the way that a patient is diagnosed and treated. Moreover, these trajectories provide valuable information for longitudinal characterizations of individual patients’ response to behavioral or pharmacological interventions. For example, it is possible to determine the extent to which an individual’s deficits resolve (e.g., resemble his/her typically developing peers), remain delayed, or remain different.

Study limitations and future directions

This study provides new evidence regarding the relationship between cognitive and motor functions at the level of the brain structure and behavior. However, there were several limitations to the current study which may inform future directions in this research area. First, although puberty status was taken into consideration in the refinement of this dataset using the scores on the Puberty Development Scale, future studies will benefit from using both questionnaires of this type and assessments of hormone levels. This would ensure accurate characterization of children’s puberty status and would provide evidence regarding the effects of hormonal changes on brain development and cognitive–motor behavior. Second, the MRI dataset available consisted of global and lobar volumes. It would be of interest in the future to examine functionally-relevant subregions within these volumes (e.g., dorsolateral prefrontal, anterior cingulate, premotor, primary motor, cerebellar hemispheres or vermis, etc.) and the connections between these subregions (e.g., using diffusion tensor imaging). In doing so, we may determine if cognitive and motor cortical–subcortical loops develop in parallel but with distinct trajectories or if these functional circuits interact across development. Third, given our primary interest in cognitive and motor abilities, future studies would benefit from the use of additional behavioral measures that assess specific aspects of executive control (e.g., Erikson Flanker, Go–NoGo, Stroop, etc.) and detailed assessments of motor skill and coordination (e.g., The Movement Assessment Battery for Children (MABC) or the Bruininks–Oseretsky Test of Motor Proficiency (BOTMP)). In particular, the use of tasks that assess higher-order motor skills, such as those requiring coordination between body/limb segments, goal-directed planning, precise timing, or motor inhibition may demonstrate even greater overlap with the development of cognitive/executive skills.

Acknowledgments

The data set used in the preparation of this manuscript was obtained from the Pediatric MRI Data Repository (data release 2) created by the NIH MRI Study of Normal Brain Development. This multi-site, longitudinal study of typically developing children was conducted by the Brain Development Cooperative Group supported by the National Institute for Child Health and Human Development, National Institute on Drug Abuse, National Institute of Mental Health, and National Institutes of Neurological Disorders and Stroke - contract #s N01-HD023343, N01-MH90002, N01-NS92314, -2315, -2316, -2317, -2319, -2320. This manuscript reflects the views of the authors and may not reflect the opinions or views of the Brain Development Cooperative Group Investigators or the NIH. We would like to thank the Brain Development Cooperative Group for their work on the data collection and processing of the structural MRI. We would also like to thank Dr. Judith Rumsey for her assistance in accessing the data repository. Additional support for the current study was provided by a seed grant from the School of Public Health at the University of Maryland (to AJH) and NIH F31HD612102 (to MMP).

References


