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Structural brain development between childhood and adulthood: Convergence across four longitudinal samples

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ABSTRACT

Longitudinal studies including brain measures acquired through magnetic resonance imaging (MRI) have enabled population models of human brain development, crucial for our understanding of typical development as well as neurodevelopmental disorders. Brain development in the first two decades generally involves early cortical grey matter volume (CGMV) increases followed by decreases, and monotonic increases in cerebral white matter volume (CWMV). However, inconsistencies regarding the precise developmental trajectories call into question the comparability of samples. This issue can be addressed by conducting a comprehensive study across multiple datasets from diverse populations. Here, we present replicable models for gross structural brain development between childhood and adulthood (ages 8–30 years) by repeating analyses in four separate longitudinal samples (391 participants; 852 scans). In addition, we address how accounting for global measures of cranial/brain size affect these developmental trajectories. First, we found evidence for continued development of both intracranial volume (ICV) and whole brain volume (WBV) through adolescence, albeit following distinct trajectories. Second, our results indicate that CGMV is at its highest in childhood, decreasing steadily through the second decade with deceleration in the third decade, while CWMV increases until mid-to-late adolescence before decelerating. Importantly, we show that accounting for cranial/brain size affects models of regional brain development, particularly with respect to sex differences. Our results increase confidence in our knowledge of the pattern of brain changes during adolescence, reduce concerns about discrepancies across samples, and suggest some best practices for statistical control of cranial volume and brain size in future studies.

Introduction

The human brain continues to develop structurally between childhood and adulthood, as evident from longitudinal studies using structural MRI (Aubert-Broche et al., 2013; Dennison et al., 2013; Ducharme et al., 2015; Lebel and Beaulieu, 2011; Lenroot et al., 2007; Sowell et al., 2004; Tamnes et al., 2013; Urošević et al., 2012; Vijayakumar et al., 2016; Wierenga et al., 2014b). Many of these studies report similar overall changes, but substantial inconsistencies in the developmental trajectories of structural brain measures have also been noted in previous reports (Ducharme et al., 2015; Mills and Tamnes, 2014; Walhovd et al., 2016). While the potential impact of quality control procedures (Ducharme et al., 2015), or software used to estimate brain measures (Walhovd et al., 2016), on structural brain developmental trajectories have been investigated, no study has yet attempted to replicate developmental trajectories across multiple longitudinal samples. As accurate population models of human brain development are crucial for our understanding of typical development as well as neurodevelopmental disorders, it is essential that our models are replicable across diverse samples.

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Characterizing the developmental trajectories of gross brain structures is essential not only for understanding basic processes of brain development, but also for informed analysis considerations. Comparative structural MRI studies of brain development are often confronted with the question as to whether to "normalize" brain measures by controlling for differences in cranial or brain size – intracranial volume (ICV) or whole brain volume (WBV) – between participants (O'Brien et al., 2011). This is an important consideration for studies describing changes in specific brain structures across development, to ensure that observed regional effects are independent of global size changes. By controlling for cranial or brain size, researchers can be more confident that the differences observed between participants (or across time) are not due to overall cranial or brain size differences between individuals (or over time), but instead reflect differences in the specific structure of interest (Sanfilipo et al., 2004). It is not clear from the available literature whether absolute changes in regional brain volumes, or changes in these structures relative to cranial/brain size, are more important and relevant for the understanding of the developing brain. This may be particularly important to ascertain for volumes of structures that do not directly correlate with cranial or brain size, where the decision whether or not to correct for cranial or brain size in the analyses can affect both the results and their interpretation (O'Brien et al., 2011).

The present study analyzed four separate datasets collected in three different countries in an attempt to replicate gross brain developmental trajectories. Using a team science approach and open collaboration framework to improve replication, the aim of this study was to test two simple but fundamental questions that are highly relevant and yet unresolved issues in the developmental neuroimaging field: 1) How do gross brain volumes develop between childhood and early adulthood? 2) How does accounting for global measures of ICV or WBV affect developmental trajectories?

To address the first of our two questions, we focused on characterizing how ICV and WBV as well as gross regional brain volumes, namely cortical grey matter volume and cortical white matter volume, change across development in each of our longitudinal samples. In order to control for potential confounds that could be introduced by differences in automated software (Walhovd et al., 2016), or quality control procedures (Ducharme et al., 2015), we processed, quality-controlled, and analyzed these four datasets using the same methods. Controlling for these factors ensured we could more confidently assess the potential impact of sample differences and certain statistical decisions on these developmental models. We hypothesized that both ICV, WBV, and regional brain volumes would show continued development through adolescence, and that, having standardized the analysis methods, there would be broad similarities in the developmental trajectories seen across the four samples.

To investigate our second question, we examined how controlling for ICV or WBV affects the developmental trajectories of two major regional brain measures: cortical grey matter volume (CGMV) and cerebral white matter volume (CWMV). We assessed the effects of controlling for ICV or WBV on the developmental trajectories of these brain volumes using two different methods previously used in the published literature: (i) *the proportional method*: where the regional brain volume of interest is divided by ICV or WBV leaving a proportional value and (ii) *the covariate method*: where shared variance with ICV or WBV is accounted for by regression statistics through the inclusion of ICV or WBV as a covariate in the developmental model. These two methods of controlling for total cranial/brain size were applied to the age-only developmental models as well as models incorporating age and sex variables to characterize what can happen to developmental trajectories and sex comparisons when investigations use these methods, as has been done previously in the aging and disease literature (Pintzka et al., 2015; Sanfilipo et al., 2004). Given our first hypothesis that ICV and WBV would show dynamic changes across this time-period, we hypothesized that incorporating ICV or WBV using the proportional or the covariate method would have differing effects on the modelled trajectories of our regions of interest. We further expected that incorporating measures of ICV or WBV in models incorporating sex would modulate the effect of sex on model fit, since many of the sex differences seen in regional brain volumes are thought to be attributed to differences in boys having, on average, larger brain volumes as compared to girls (Giedd et al., 2012).

Table 1
Participant demographics for each sample. Mean (standard deviation), age and interval between scans are given in years. The table describes the total number of scans included in each sample, and the number of scans each study participant undertook (2–6 scans).

	NIH Child Psychiatry Branch			University of Pittsburgh		
	All	Female	Male	All	Female	Male
N	33	10	23	73	41	32
Age mean (SD)	15.8 (5.5)	16.6 (5.8)	15.4 (5.3)	13.3 (1.4)	12.9 (1.3)	13.9 (1.3)[a]
Age range	7.0–29.9	8.1–29.5	7.0–29.9	10.1–16.2	10.1–15.9	11.4–16.2
N scans	136	42	94	146	82	64
2 scans	–	–	–	73	41	32
3 scans	13	4	9	–	–	–
4 scans	7	2	5	–	–	–
5 scans	9	2	7	–	–	–
6 scans	4	2	2	–	–	–
Interval	4.1 (2.3)	4.1 (2.0)	4.0 (2.4)	2.2 (0.4)	2.2 (0.4)	2.1 (0.4)
	Neurocognitive Development			Braintime		
	All	Female	Male	All	Female	Male
N	76	37	39	209	112	97
Age mean (SD)	15.2 (3.6)	15.1 (3.5)	15.4 (3.7)	15.7 (3.8)	15.5 (3.6)	15.9 (3.9)
Age range	8.2–21.9	8.4–21.8	8.2–21.9	8.0–26.6	8.2–24.8	8.0–26.6
N scans	152	74	78	418	224	194
2 scans	76	37	39	209	112	97
3 scans	–	–	–	–	–	–
4 scans	–	–	–	–	–	–
5 scans	–	–	–	–	–	–
6 scans	–	–	–	–	–	–
Interval	2.6 (0.2)	2.7 (0.2)	2.6 (0.2)	2.0 (0.1)	2.0 (0.1)	2.0 (0.1)

[a] Age difference between sexes (by design, see Supplementary material for details).