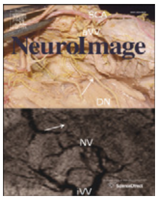
NeuroImage 59 (2012) 1023–1027

Contents lists available at SciVerse ScienceDirect

NeuroImage

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



Correlation among body height, intelligence, and brain gray matter volume in healthy children

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ARTICLE INFO

Article history:
Received 4 January 2011
Revised 27 July 2011
Accepted 29 August 2011
Available online 10 September 2011

Keywords:
Body height
Intelligence quotient
Gray matter
Children
Voxel-based morphometry

ABSTRACT

A significant positive correlation between height and intelligence has been demonstrated in children. Additionally, intelligence has been associated with the volume of gray matter in the brains of children. Based on these correlations, we analyzed the correlation among height, full-scale intelligence quotient (IQ) and gray matter volume applying voxel-based morphometry using data from the brain magnetic resonance images of 160 healthy children aged 5–18 years of age. As a result, body height was significantly positively correlated with brain gray matter volume. Additionally, the regional gray matter volume of several regions such as the bilateral prefrontal cortices, temporoparietal region, and cerebellum was significantly positively correlated with body height and that the gray matter volume of several of these regions was also significantly positively correlated with full-scale intelligence quotient (IQ) scores after adjusting for age, sex, and socioeconomic status. Our results demonstrate that gray and white matter volume may mediate the correlation between body height and intelligence in healthy children. Additionally, the correlations among gray and white matter volume, height, and intelligence may be at least partially explained by the effect of insulin-like growth factor-1 and growth hormones. Given the importance of the effect of environmental factors, especially nutrition, on height, IQ, and gray matter volume, the present results stress the importance of nutrition during childhood for the healthy maturation of body and brain.

Introduction

The famous aphorism, *mens sana in corpore sano* (i.e., “a sound mind in a sound body”) is as relevant today as in the time of Juvenal. Insofar as intelligence is an indication of a healthy brain and height is an indicator of a healthy body, the high correlation between IQ and height seen in children (Tuvemo et al., 1999; Wheeler et al., 2004) and young adults (Humphreys et al., 1985; Teasdale et al., 1989) suggests parallel development of the two measures. Moreover, growth velocity was associated with IQ in a longitudinal study (Lundgren et al., 2001). Thus, it is suggested that taller stature is associated with higher IQ.

To explain the correlation between height and IQ, we hypothesized that brain structure may mediate the relationship in that several recent studies have shown a significant positive correlation between brain regional gray matter volume and IQ (Frangou et al., 2004; Haier et al., 2004; Shaw et al., 2006; Wilke et al., 2003). Specifically, several gray matter regions are significantly correlated with IQ, including the prefrontal cortex (Shaw et al., 2006), orbitofrontal cortex (Frangou et al., 2004), cingulate gyrus (Frangou et al., 2004; Wilke et al., 2003), and cerebellum (Frangou et al., 2004). Additionally, it is plausible that regional gray matter volume may mediate the correlation between height and IQ because the main environmental determinant of height is nutrition (Silventoinen, 2003) and because differences in breakfast dietary habits affect not only IQ, but also gray matter volume in healthy children (Taki et al., 2010). Although revealing the correlation among height, IQ, and gray matter volume is important from the perspective of developing a healthy lifestyle, including a sound diet, in children, the correlation among body height, intelligence, and gray matter volume has not yet been clarified.

Therefore, the purpose of this study was to analyze whether a significant correlation between the gray and white matter volumes of the brain and body height existed using brain magnetic resonance imaging (MRI) in 160 healthy children aged 5–18 years of age. In addition, we also analyze the correlation between regional gray and white matter volume and full-scale IQ in the same subjects, and compare the two results to check whether there are overlapping regions that show

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doi:10.1016/j.neuroimage.2011.08.092

significant correlation with height and also significant correlation with full-scale IQ. We collected brain magnetic resonance (MR) images, full-scale IQ scores, verbal IQ (vIQ) scores, and performance IQ (pIQ) scores. Correlations between regional gray and white matter volume and body height, and between regional gray and white matter volume and IQ were analyzed by applying voxel-based morphometry (VBM), which is an established automated neuroimaging technique that enables global analysis of brain structures without a priori identification of a region of interest so that it is not biased toward any specific brain region, thereby permitting the identification of potential structural differences or abnormalities in the brain (Ashburner and Friston, 2000). Therefore, we used VBM to conduct an unbiased search for relationships between brain structure and height or IQ.

Methods

Subjects

All subjects were healthy Japanese children included in the Japanese database of normal pediatric brain MRIs. They were recruited in the following manner. First, we distributed 29,740 advertisements summarizing this study to kindergartens, elementary, junior high, and high schools in Miyagi Prefecture in Japan. Then, the 1423 parents of subjects with an interest in this study contacted us by mail. Next, we mailed both child and parent versions of detailed information concerning this study to the parents. Finally, 776 parents and subjects who were willing to participate in this study re-contacted us by mail. Subjects with histories of malignant tumors, head trauma with a loss of consciousness lasting more than 5 min, developmental disorders, epilepsy, psychiatric diseases, or claustrophobia were excluded from the study by a preliminary telephone interview, a mail-in health questionnaire, or an oral interview. We collected brain MR images from 291 subjects in the order in which we received notification of their intention to participate in the project. Trained examiners also collected data on intelligence quotients (IQ) by administering the Japanese version of the Wechsler Adult Intelligence Scale-Third Version (WAIS-III) (Fujita et al., 2006) to subjects who were at least 16 years of age and the Japanese version of the Wechsler Intelligence Scale for Children-Third Edition (WISC-III) (Azuma et al., 1998) to subjects who were younger than 16 years of age. We calculated the full-scale, verbal, and performance IQs on the WAIS/WISC for each subject. We also collected data on body height and weight from subjects using height and weight scales. Data on body height and weight were also collected from the subjects. We calculated the body-mass index (BMI) of the participants by dividing weight in kilograms by the square of height in meters. Data regarding the family's socioeconomic status was collected from each subject's parent(s) by asking about each family's annual income. Annual income data were collected using the following discrete variables: annual income below 20,000 US dollars (the currency exchange rate was set at one US dollar equals 100 yen), 1; 20,000–40,000 US dollars, 2; 40,000–60,000 US dollars, 3; 60,000–80,000 US dollars, 4; 80,000–100,000 US dollars, 5; 100,000–120,000 US dollars, 6; and ≥120,000 US dollars, 7. The final sample consisted of 160 participants (78 boys, 82 girls). The ages of the subjects ranged from 5.6 to 18.4 years. The characteristics of each group are shown in Table 1. Written informed consent was obtained from each subject and his/her parent(s) prior to MR image scanning after a full explanation of the purpose and procedures of the study was provided according to the Declaration of Helsinki (1991). Approval for these experiments was obtained from the institutional review board of Tohoku University.

Image acquisition

All images were collected using a 3-T Philips Intera Achieva scanner. Using a Magnetization Prepared Rapid Gradient Echo (MPRAGE) sequence, three dimensional high-resolution T1-weighted structural images (240 × 240 matrix, TR = 6.5 ms, TE = 3 ms, TI = 711 ms, FOV = 24 cm, 162 slices, 1.0-mm slice thickness, scan duration = 8 min, 3 s.) were collected.

Table 1
Characteristics of subjects.

	Boys ($n = 78$)	Girls ($n = 82$)	P
Age [years], (mean ± SD, range)	10.6 ± 2.81, 5.6–16.6	11.0 ± 2.96, 5.8–18.4	0.478[a]
Height [cm], (mean ± SD, range)	141.2 ± 16.66, 111.0–173.4	139.5 ± 14.55, 114.0–172.8	0.487[a]
Weight [kg], (mean ± SD, range)	36.8 ± 12.64, 18.5–68.6	36.0 ± 12.51, 10.8–72.3	0.661[a]
Full-scale IQ, (mean ± SD, range)	104.9 ± 14.07, 77–137	100.7 ± 11.54, 71–128	0.040 [a]
Verbal IQ, (mean ± SD, range)	105.0 ± 14.69, 67–143	101.1 ± 13.58, 67–134	0.084[a]
Performance IQ, (mean ± SD, range)	103.5 ± 14.78, 71–136	100.0 ± 11.23, 80–129	0.088[b]

[a] Student's *t*-test.
[b] Welch's *t*-test.

Image analysis

VBM with Diffeomorphic Anatomical Registration using Exponentiated Lie algebra (DARTEL) (Ashburner, 2007) was conducted for the image analysis. After image acquisition by MRI, all T1-weighted MR images were analyzed using Statistical Parametric Mapping 8 (SPM8) (Wellcome Department of Cognitive Neurology, London, UK) in Matlab (Math Works, Natick, MA, USA). First, the "New Segmentation" algorithm from SPM8 was applied to every T1-weighted MR image to extract tissue maps corresponding to gray matter, white matter, and cerebrospinal fluid (CSF). This algorithm, which is an improvement over the "Unified Segmentation," (Ashburner and Friston, 2005) uses a Bayesian framework to iteratively perform the probabilistic tissue classifications and transform the spatial deformations into normalized space. Although we were interested only in the probabilistic tissue segmentation at this point, the new Bayesian segmentation and warping algorithm, which includes an improved set of tissues priors (Ashburner and Friston, 2009) for regularization, increased the robustness and accuracy of the segmentation compared with that of previous standard VBM algorithms. That step allowed us to obtain probability maps of the three aforementioned types of tissue for every subject and to precisely assign them to a common space. Next, these segmented tissue maps were used to create a custom, more population-specific template using the DARTEL template creation tool (Ashburner, 2007), which estimates the best set of smooth deformations on the basis of every subject's tissues to create a common average, applies the deformations to create a new average, and then reiterates the process until convergence is achieved. The smoothness and reversibility of the deformation are obtained from the diffeomorphic property of DARTEL's transformations and ensure the accuracy of the mapping between the two spaces. The template space was matched to the Montreal Neurological Institute (MNI) space using an affine-only registration, which enabled us to match our images' custom coordinate space to the more standard MNI space (Bergouignan et al., 2009). The affine registration is a 12-parameter registration (Ashburner et al., 1997). At the end of that process, each subject's gray matter map was warped by applying its corresponding smooth and reversible deformation parameters to the custom template space and then to the MNI standard space. We also computed the group-wide means and variance of all images to quickly confirm the accuracy of the process. The major advantage of creating a population-specific template for registration of the tissues is to limit the amount of stretching each image experiences during the necessary step of spatial normalization. Next, the warped gray