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Modeling brain tissue volumes over the lifespan: quantitative analysis of postmortem weights and in vivo MR images

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Abstract

Normative measurements of brain gray matter and white matter tissue volumes across the lifespan have not yet been established. The purpose of this article was to use mathematical modeling and analytical functions to demonstrate the growth trajectory of gray matter and white matter from age 0 to age 90. For each gender, brain weight functions were generated by utilizing existing autopsy data from 4400 subjects. Brain gray matter, white matter and lateral ventricular volumes were measured from 39 MR volumes of normal individuals. These were converted to weight by multiplying the tissue volumes by the specific gravity of that tissue. White matter volumes were described by a saturating exponential function, and the gray matter volume function was calculated by subtracting the white matter weight function from the brain weight function. For each gender, equations were generated for white matter and gray matter volumes as a function of age over the lifespan.

Keywords: Brain weight; Gray matter; White matter

1. Introduction

Brain tissue is composed of gray matter, which contains cell bodies (neurons), and white matter, which contains nerve fibers (axons) surrounded by a myelin sheath. MR imaging has provided a tool to quantitate these tissue volumes and several studies have shown brain cerebral spinal fluid (CSF), gray matter and white matter volumes for different populations over different ages [1–10]. However, normative measurements of brain gray matter and white matter tissue volumes across the lifespan have not yet been established. Greater knowledge of structural brain development might lead to further understanding of the relationship between anatomic structure and neurological function, as well as provide a means to evaluate brain pathology. The purpose of this article was to use mathematical modeling and analytical functions to demonstrate the growth trajectory of gray matter and white matter from age 0 to age 90.

2. Methods

2.1. Functions for brain weight from autopsy data

Dekaban [11] obtained over 4400 autopsy reports from multiple hospitals in the Washington DC area between the years 1964 and 1973. These reports were from people who ranged from newborn to over 86 years of age. The brains were separated from the spinal cord just below the decussation of the pyramids and immediately weighed with the cerebral ventricles unopened and the leptomeninges intact. The autopsies were performed within 30 h of death and the brains were without pathological evidence of neurological disease. After stratifying the data by gender, Dekaban [11] sorted the brain weights into 23 groups based on age. Tables with the number of subjects, age ranges, mean brain weights and brain weight standard deviations were reported for each group.

For Dekaban's Groups 1–3 (ages 0 to 1.1 years), we used multiple linear regression with indicator variables and

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ANOVA to determine that the values for male and female brain weights were coincident and could be described with a linear function [12]. For Dekaban's Groups 5–22 (ages 3 to 83), mean brain weights were fit with a least-squares gamma function described by Starmer and Clark [13]. The best-fit linear and gamma functions were combined to create a piecewise function for brain weight from age 0 to age 90. The piecewise function for male brain weight (MBW), in kilograms, is as follows:

$$\begin{aligned} &\text{for age} \le 1.58,\ \mathrm{MBW}(\text{age}) = 0.5297 \times \text{age} + 0.344 \\ &\text{for age} > 1.58, \mathrm{MBW}(\text{age}) = 1.134 \times \text{age}^{0.1068} \\ &\qquad \times exp\left(-\frac{\text{age}}{252.3}\right) \end{aligned} \tag{1}$$

where age is in years. The piecewise function for female brain weight (FBW), in kilograms, is as follows:

$$\begin{aligned} &\text{for age} \le 1.18, \mathrm{FBW}(\text{age}) = 0.5297 \times \text{age} + 0.344 \\ &\text{for age} > 1.18, \mathrm{FBW}(\text{age}) = 0.955 \times \text{age}^{0.1357} \\ &\qquad \times exp\left(-\frac{\text{age}}{212.1}\right) \end{aligned} \tag{2}$$

where age is in years. Fig. 1 illustrates Eq. (1) and Eq. (2) and the brain weight data from Dekaban [11].

2.2. Calculating brain weight from MR images

Three-dimensional T1-weighted volumes of normal individuals who served as control subjects in other studies done at our institution [14,15] were analyzed to obtain volumes of the lateral ventricles, brain gray matter and brain white matter. All of the control subjects were healthy without history of head trauma, meningitis or substance abuse. The image volumes were acquired on 1.5-T GE Signa scanners (GE Medical Systems, Milwaukee, WI, USA) using a standard quadrature birdcage transmit/receive head coil and a T1-weighted spoiled gradient recalled sequence. There were 39 three-dimensional (3-D) volumes from 18 males (9 to 57 years) and 21 females (9 to 50 years). Of these 39 MR volumes, 18 were obtained from longitudinal scans 6 years apart. The T1-weighted 3-D volumes were processed with the methods described in Riddle et al. [15]. In summary, the acquired image volumes were converted to 1-mm isotropic volumes with trilinear interpolation, inhomogeneities were corrected with N3 from MIPAV [16] and the brains were extracted from the 3-D volumes. Intensity thresholds between gray matter and white matter were automatically determined with fuzzy C-means from MIPAV [16], and thresholds between CSF and gray matter were manually selected by viewing sagittal slices through the lateral ventricles with ImageJ [17]. Based on these CSF–gray matter thresholds, 3-D CSF masks were created. Lateral ventricular volumes were determined by manually drawing regions of interest around the lateral ventricles in the CSF masks.

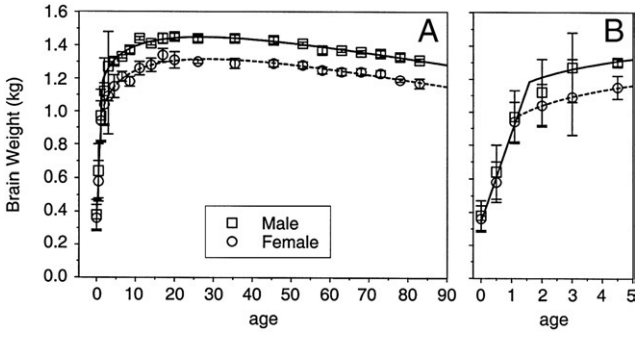

Fig. 1. (A) illustrates the piecewise brain weight functions [Eq. (1) and Eq. (2)] and the brain weighs from Dekaban [11]. The error bars indicate Dekaban's [11] standard deviations. The age scale is expanded in (B) to better show the first 5 years.

The volume measurements were converted to weight by multiplying the tissue volumes by the specific gravity of that tissue. Specific gravity is the density of a substance divided by the density of water, and the specific gravity of CSF was considered to be 1.00. Harper et al. [18] measured the specific gravity of gray matter and white matter from the brains of 26 control subjects who were without head injury or pathological evidence of neurological disease. The average specific gravity for gray matter was 1.0326 and the average specific gravity for white matter was 1.0404. Courchesne et al. [5] used a specific gravity of 1.0365 for both gray matter and white matter, which is, interestingly, the mean of Harper's gray matter specific gravity and white matter specific gravity. Since the autopsy brains were weighed with the cerebral ventricles unopened, MRI brain volumes were converted to brain weight (BW) in kilograms with the following equation:

$$\begin{aligned} \mathrm{BW} = {} & V_{\mathrm{LV}} \times 0.001 + V_{\mathrm{GM}} \times 0.0010326 + V_{\mathrm{WM}} \\ & \times 0.0010404 \end{aligned} \tag{3}$$

where V_{LV} is the volume of the lateral ventricles in cubic centimeters (cm^3), V_{GM} is the volume of the brain gray matter in cubic centimeters and V_{WM} is the volume of brain white matter in cubic centimeters.

3. Results

3.1. Calculated brain weights

For the MR studies done at our institution, brain weights were calculated with Eq. (3) and the gray matter, white matter and lateral ventricle volumes. The difference between the calculated brain weight [Eq. (3)] and the brain weight function [Eq. (1) or Eq. (2)] was determined for each MR volume. The standard error of estimate (Se) for the brain weight functions is the standard deviation of these differences [19]. If the calculated brain weights [Eq. (3)] fit the brain weight functions [Eq. (1) or Eq. (2)], then the average of the differences should approach 0. Table 1 contains the number of subjects, average of the differences