ELSEVIER

Neurobiology of Aging 26 (2005) 1245–1260

NEUROBIOLOGY OF AGING

www.elsevier.com/locate/neuaging

Normal neuroanatomical variation due to age: The major lobes and a parcellation of the temporal region

John S. Allen [a,*], Joel Bruss [a], C. Kice Brown [b], Hanna Damasio [a]

[a] *Human Neuroanatomy and Neuroimaging Laboratory, Department of Neurology, 2RCP, University of Iowa Hospitals and Clinics, 200 Hawkins Dr., Iowa City, IA 52242, USA*
[b] *Lone Tree Biostatistics, LLC, Lone Tree, IA, USA*

Received 5 June 2004; received in revised form 1 May 2005; accepted 1 May 2005

Abstract

We used high-resolution MRI to investigate gray and white matter aging in the major lobes of the cerebrum (frontal, parietal, temporal, occipital) and the major sectors of the temporal lobe (temporal pole, superior temporal gyrus, infero-temporal region, parahippocampal gyrus, amygdala, hippocampus). Subjects included 87 adults between the ages of 22 and 88 years. Regions of interest were hand-traced on contiguous 1.5 mm coronal slices. For the cerebrum in general, gray matter decreased linearly with age, resulting in a decline of about 9.1–9.8% between the ages of 30 and 70 years, and a decline of 11.3–12.3% by the age of 80. In contrast, white matter volume increased until the mid-50s, after which it declined at an accelerated rate. At 70 years, white matter volume was only 5.6–6.4% less than at 30 years, but by age 80, a cubic regression model predicted that the decrease would be 21.6–25.0%. Multivariate analyses indicate that the frontal gray matter was most strongly associated with age, while occipital gray and white matter were least associated. Reduction in volume in the hippocampus was best modeled by a cubic regression model rather than a linear model. No sex differences in aging were found for any regions of interest.

Keywords: White matter; Gray matter; MRI; Hippocampus; Amygdala; Frontal lobe; Parietal lobe; Temporal lobe; Occipital lobe; Volumetrics

1. Introduction

Over the years, the relationship between age and brain volume has been explored using a variety of different methods. Almost all studies, no matter what the method, confirm the basic observation that as adults get older, their brains become smaller and the sulci visibly increase in size and depth [41]. Autopsy studies indicate that brain weight in both men and women declines by at least 10% between the ages of 25 and 75+ years [10,22,34,47]. Miller et al. [28], in another post-mortem study (in which gray and white matter volumes were determined from fixed sagittal slices taken at 2–3 mm intervals), found that volume decreases at the rate of about 2% per decade following the age of 50. This same study also found that the gray/white ratio declined up to the age of 50, after which it increased, indicating that although overall brain volume remains steady between 20 and 50 years, gray matter volume may be decreasing while white matter volume may be increasing.

Over the past decade, volumetric MRI analyses have added much to our understanding of many aspects of brain aging [6,8,9,43,48,50]. Although different studies have produced some conflicting results, MRI based studies indicate that age-associated brain atrophy does not occur in a uniform manner. For example, age-associated volume reductions have been reported by some to be more pronounced in the frontal lobe compared to other brain regions [9,24], while others have found that the frontal and temporal lobes age at similar rates [3]. The hippocampus may be more sensitive to age effects than the amygdala, cortical gray matter, or basal gray structures [24,39].

Several aging studies have shown that gray and white matter volumes do not change over the life span at the same rate [3,21,24]. Gray matter volume declines throughout adulthood

* Corresponding author. Tel.: +1 319 356 8346; fax: +1 319 356 4505.
E-mail addresses: john-s-allen@uiowa.edu, jsallen38@aol.com (J.S. Allen).

0197-4580/$ – see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.neurobiolaging.2005.05.023

and into old age at a more or less linear rate. In contrast, other studies have shown that white matter volumes actually may increase slowly through adulthood, peaking in volume in the 40–50 year range [3,48]. After 60 years of age, there is a precipitous decline in white matter volume according to Guttman et al. [21]. Although some MRI based studies show that the gray matter decline in women may be slower than in men [6,9,17,31,53], others have not shown significant sex differences in brain aging [5,24,48].

In this report, we present the results of an MRI study of the effects of age on gray and white matter volumes of the major cerebral lobes (frontal, temporal, parietal, and occipital) and of the major sectors of the temporal lobe (temporal pole, superior temporal gyrus, infero-temporal region, parahippocampal gyrus, amygdala, and hippocampus). A total of 87 subjects (43 men, 44 women), between the ages of 22 and 88 years, were included in this cross-sectional analysis. This study constitutes a novel contribution to the MRI brain aging literature in that it provides a high-resolution and comprehensive (manual tracing of regions of interest on contiguous 1.5 mm slices of non-resized brains) assessment of regional volumetric changes in a relatively large subject group.

2. Methods

2.1. Subjects

Subjects were 43 men (mean age = 49.4 years, S.D. = 20.8, range 22–88) and 44 women (mean age = 47.0 years, S.D. = 16.7, range 23–74) (see Table 1 for age distributions). All were right-handed (assessed by the Oldfield–Geschwind handedness inventory; mean score = 95, S.D. = 11) with no left-handedness in first degree relatives, healthy, and with no history of neurological or psychiatric illness. Older subjects (greater than 60 years) were assessed by interview on a case-by-case basis for general health status and medication usage. None had a clinical history of heart disease, hypertension, diabetes, or any other common age-associated disease. All brain MRIs were screened for the presence of visible pathology. All subjects gave informed consent in accordance with institutional and federal rules.

Table 1
Age distribution of subjects

Age (years)	No. of men	No. of women
20–29	12	11
30–39	5	6
40–49	6	6
50–59	3	8
60–69	9	11
70–79	5	2
80–89	3	0
Total	43	44

2.2. Image acquisition

Thin cut T1-weighted MR images were obtained in a GE Signa scanner operating at 1.5 T, using the following protocol: SPGR/50, TR 24, TE 7, NEX1, matrix 256×192, FOV 24 cm. We obtained 124 contiguous coronal slices, 1.5 or 1.6 mm thick and interpixel distance 0.94 mm. The slice thickness was adjusted to the size of the brain so as to sample the entire brain, while avoiding wrap artifacts. Three individual datasets were obtained for each brain during each imaging session. These were coregistered and averaged post hoc using automated image registration (AIR 3.03, UCLA [52]), to produce a single data set, of enhanced quality with pixel dimensions of 0.7 mm in plane and interslice spacing of 1.5 mm between planes [23].

All brains were reconstructed in three dimensions using Brainvox [16], an interactive family of programs designed to reconstruct, segment, and measure brains from MR acquired images. An automated program, extensively validated against human experts [18], was used to segment the images into the three primary tissue types (white, gray, CSF). Before tracing regions of interest (ROIs), brains were realigned, but *not resized*, along a plane running through the anterior and posterior commissures (i.e., the AC-PC line). This realignment limited right–left rotation, and ensured that coronal slices used in the tracing of ROIs were perpendicular to a uniformly and anatomically defined axis of the brain in all subjects.

2.3. Regions of interest

Regions of interest were traced by hand on contiguous coronal slices of the realigned brain. Anatomical landmarks were identified and marked on the surface of 3D reconstructions. The parcellation of the major lobes (frontal, temporal, parietal, and occipital) was based on a scheme modified from [40]; see [1,2] for a very detailed description of the parcellation method and tracing conventions (Fig. 1). Gray and white matter volumes of the insula and cingulate gyrus are excluded from the volumes of the major lobes; gray matter volumes of the basal ganglia, claustrum, and thalamus are also excluded. The cerebellum and brain stem were excluded from all tracings. Although the ROIs were traced separately in the two hemispheres, the volumes of the two hemispheres are combined in this analysis.

The parcellation of the temporal lobe and its subregions was as follows (Fig. 1). Parcellation of the *temporal lobe* itself is described in detail in [1,2]. In brief, the superior boundary of the temporal lobe is formed by the Sylvian fissure (SF), which is followed to its most posterior extension. In cases where the SF splits into two branches, the branch that extends most posteriorly is followed (this is almost always the superior branch). The superoposterior boundary of the temporal lobe is defined by a line drawn on the lateral surface of the hemisphere, which connects the end of the SF to a plane that separates the occipital lobe from the rest of the cerebrum; the inferoposterior boundary is defined by this