

Structural Magnetic Resonance Imaging of the Adolescent Brain

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ABSTRACT: Magnetic resonance imaging (MRI) provides accurate anatomical brain images without the use of ionizing radiation, allowing longitudinal studies of brain morphometry during adolescent development. Results from an ongoing brain imaging project being conducted at the Child Psychiatry Branch of the National Institute of Mental Health indicate dynamic changes in brain anatomy throughout adolescence. White matter increases in a roughly linear pattern, with minor differences in slope in the four major lobes (frontal, parietal, temporal, occipital). Cortical gray matter follows an inverted U-shape developmental course with greater regional variation than white matter. For instance, frontal gray matter volume peaks at about age 11.0 years in girls and 12.1 years in boys, whereas temporal gray matter volume peaks at about age 16.7 years in girls and 16.2 years in boys. The dorsal lateral prefrontal cortex, important for controlling impulses, is among the latest brain regions to mature without reaching adult dimensions until the early 20s. The details of the relationships between anatomical changes and behavioral changes, and the forces that influence brain development, have not been well established and remain a prominent goal of ongoing investigations.

KEYWORDS: magnetic resonance imaging (MRI); adolescence; gray matter; white matter

INTRODUCTION

It comes as no surprise to parents of teens that the brain of an 8 year old is different than the brain of a 13 year old. Yet to pin down these differences in a scientific way has been elusive. Nature has gone to great extremes to protect this most vital organ. It is wrapped in a leathery case, surrounded by a protective moat of fluid, and completely encased in bone. This has shielded the brain from falls or attacks from predators, but it has also shielded the brain from scientists. Even after the availability of X rays or CT scans, the study of the healthy teen brain remained indirect, because such techniques use ionizing radiation, which ethically precludes their use in non-ill populations.

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Magnetic resonance imaging (MRI) has changed that. It provides exquisitely accurate pictures of the living, growing brain without the use of ionizing radiation and has helped launch a new era of adolescent neuroscience. In addition to anatomical images, MRI can also be used to assess brain function. It does so by capitalizing on different magnetic properties of oxygenated versus nonoxygenated hemoglobin.

This chapter focuses on the first type of MRI—looking at the changing anatomy of the brain during the teen years.

METHODS

The data for this chapter are derived from an ongoing longitudinal pediatric brain MRI study being conducted at the Child Psychiatry Branch of the National Institute of Mental Health. To date, the sample of healthy youths consists of 329 scans from 95 males and 66 females, with MRI scans and neuropsychological testing acquired at approximately 2-year intervals.

Once the images are acquired, they are analyzed by a variety of automated and manual tracing techniques through collaboration with several imaging centers throughout the world. Further details of the testing and screening of this sample and the methods of image analysis have been published elsewhere.¹⁻⁴

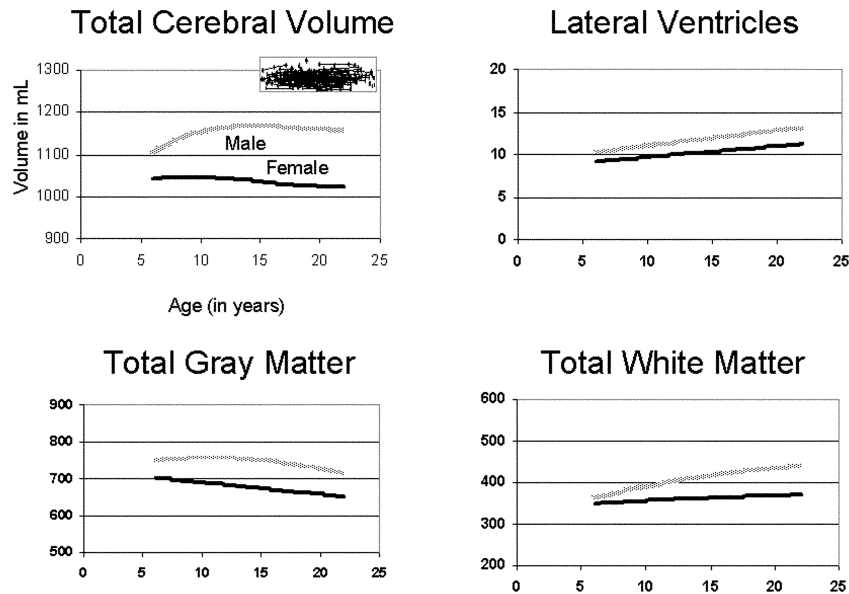


FIGURE 1. Total size of the brain.

ANATOMICAL CHANGES IN THE TEEN BRAIN

Total Brain Volume

The total size of the brain is already approximately 90% of its adult size by age six years (FIG. 1). This is counterintuitive to anyone who has seen a child trying to wear an adult’s hat. The discrepancy is accounted for by the fact that head circumference does change throughout childhood (approximately, 2.0 inches in boys and 1.9 inches in girls from ages 4 to 18 years),⁵ but the increase is due mostly to an increase in skull thickness not brain size.⁶

In our sample, male brains are approximately 12% larger on average than those of females. This difference remains statistically significant, even when controlling for height and weight. Of course, gross size of structures may not reflect sexually dimorphic differences in neuronal connectivity or receptor density. Given the myriad parameters influencing brain size, size alone should not be interpreted as imparting any sort of functional advantage or disadvantage.

Although the total size of the brain remains relatively stable across the ages of 6 to 20 years the various subcomponents of the brain undergo dynamic changes.

On an MRI image white matter, gray matter, and fluid have different signal strength, and these different tissue types are often used to categorize different brain structures or regions.

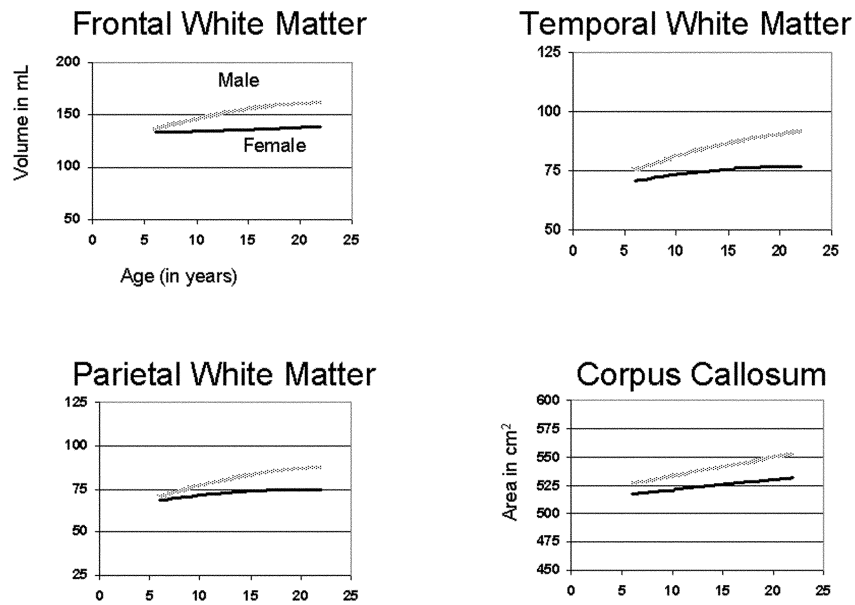


FIGURE 2. White matter in brain relative to age.

White Matter

Regional Volumes of White Matter

On MRI scans white matter indicates myelinated axons. Myelination is the result of oligodendrocytes wrapping neuronal axons in a fatty sheath that speeds up transmission between neurons—up to 100 times the speed of unmyelinated neurons. The greater speed of neuronal processing may facilitate cognitive complexity and the ability to adeptly combine information from multiple sources.

The amount of white matter in the brain generally increases throughout childhood and adolescence (see FIG. 2). The white matter increases are roughly linear, and the slope of increase is approximately the same in the four major lobes of the brain (frontal, temporal, parietal, and occipital).

Myelinated axons can be (1) *projectional*, connecting the brain to the spinal cord; (2) *associational*, connecting one type of brain part to another; or (3) *commissural*, connecting similar parts of the brain in the left and right hemispheres. A relatively new type of MRI called Diffusion Tensor Imaging (DTI) may help discern these different types of white matter connections.

The corpus callosum (CC) comprises the third type of myelinated axons, and is by far the most conspicuous white-matter component of the brain. It consists of approximately 180 million myelinated axons⁷ connecting similar parts of the left and right cerebral hemispheres. The connections generally take the shortest route, so a certain topography of the brain is preserved on the CC, with anterior sections consisting of fibers connecting frontal brain areas, middle sections connecting middle cortical areas, and posterior sections connecting posterior cortical areas. There is some controversy as to just how tightly these spatial relationships of the cortex are maintained in the CC, but for some of the areas studied, such as the somatosensory regions, the spatial representation is highly preserved.^{8,9}

With the notable exception of marsupials and monotremes, most mammals from insectivores to higher primates have a CC, and it appears to have evolved in parallel with the neocortex.^{10,11} The CC integrates activities of the left and right cerebral hemispheres, such as organizing bimanual motor output¹² and unifying the sensory fields,^{13,14} but is also involved in memory storage and retrieval,¹⁵ attention and arousal,¹⁶ language and auditory functions,¹⁷ and perhaps in the perception of consciousness.¹⁸ Creativity and intelligence are linked to interhemispheric integration,¹⁹ and the more complex the cognitive task, the more critical interhemispheric integration becomes.^{20,21} These functions subserved by the CC continue to improve during childhood and adolescence, highlighting interest in the structural changes shown to progress during that developmental period.²² Further developmental interest stems from CC anomalies reported for several neuropsychiatric disorders of childhood.^{23–30}

In our sample the midsagittal CC size increased on average 1.3% per year. However, when individual children are followed longitudinally, the changes in specific subcomponents of the CC are shown to occur much more dramatically.³¹ The CC changes occur in a front-to-back direction, with the anterior sections reaching adult sizes sooner than the posterior sections. This was somewhat surprising, because in general frontal regions of the brain are thought to mature later.

Another white-matter area that undergoes substantial changes during the teen years is the left arcuate fasciculus, which connects Wernicke’s area (reception of speech) with Broca’s area (production of speech).³²

A postmortem study in 164 psychiatrically normal individuals, ages newborn to 76 years, revealed white matter providing connections between the hippocampus and the frontal cortex was particularly active during the teen years.³³ Speculatively, this may suggest an increasing ability to draw upon memories of past events when making decisions.

Gray Matter

The two major categories of gray-matter subdivision are cortical (on the outer surface of the brain) and subcortical (inside the cortex).

Subcortical Gray Matter

Basal Ganglia. The basal ganglia consist of the caudate, putamen, globus pallidus, subthalamic nucleus, and substantia nigra. The caudate nucleus is currently the only of these structures that we have been able to reliably quantify. The basal ganglia have a central role in control of movement and muscle tone, but are also involved in circuits mediating higher cognitive functions, attention, and affective states.

Caudate volumes decrease during the teen years and are relatively larger in females. This sexual dimorphism is interesting in light of smaller caudate nucleus volumes reported for male predominant disorders, such as ADHD³⁴⁻³⁶ and Tourette’s syndrome.³⁷⁻³⁹

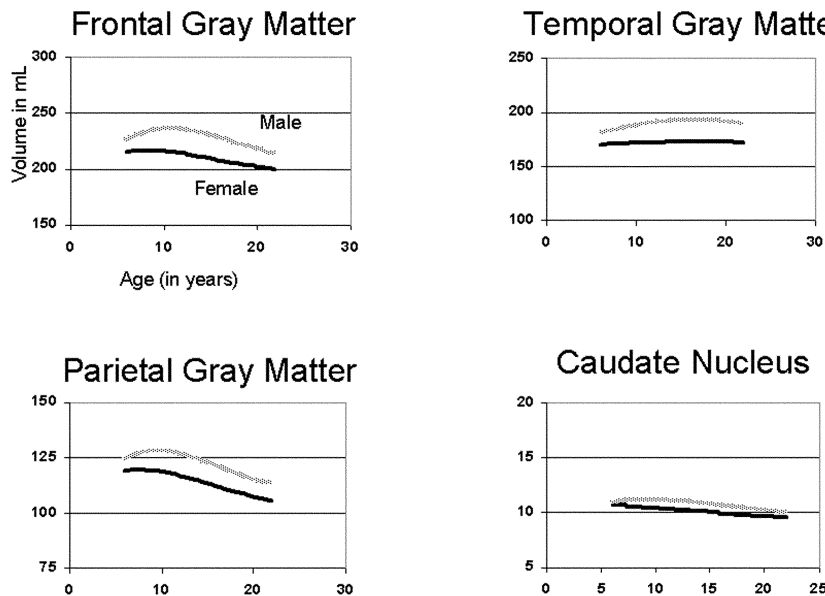


FIGURE 3. Gray matter relative to age.

Amygdala and Hippocampus. The temporal lobes, amygdala, and hippocampus are integral players in the arenas of emotion, language, and memory.⁴⁰ Human capacity for these functions changes markedly between ages 4 and 18,^{41–43} although the relationship between the development of these capacities and morphological changes in the structures subserving these functions is poorly understood.

The amygdala and hippocampus have not been quantified for the longitudinal sample. In a previous report from a cross-sectional sample subset of the NIMH sample, amygdala volume increased significantly only in males, and hippocampal volume increased significantly with age only in females.⁴⁴ This pattern of gender-specific maturational volumetric changes is consistent with nonhuman primate studies indicating that the amygdala contains high numbers of androgen receptors⁴⁵ and a smaller number of estrogen receptors,⁴⁶ while the hippocampus contains higher amounts of estrogen receptors.⁴⁷

Influence of estrogen on the hippocampus is further supported by both rodent and human studies. Gonadectomized female rats have a lower density of dendritic spines and decreased fiber outgrowth in the hippocampus, which can be alleviated with hormone replacement.^{47,48} In humans, women with gonadal hypoplasia have smaller hippocampi.⁴⁹ An MRI study of 20 young adults also showed proportionately larger hippocampal volumes in females.⁵⁰

Adolescent behavior is often attributed to “raging hormones,” but it should be noted that although hormones can affect brain structure and function, particularly in the amygdala and hippocampus, they are only part of a larger realm of brain changes influencing adolescent behavior.

Cortical Gray Matter

Early cross-sectional pediatric neuroimaging studies showed a general decrease in the amount of cortical gray matter during childhood, beginning at the earliest ages of the study design, which was often around age 5 years.^{51–54} So it was somewhat of a surprise when data from scans acquired longitudinally, by having people return for scans at approximately two-year intervals, indicated an “inverted U” pattern (see FIG. 3). In further contrast to the linear pattern for white-matter changes, the gray-matter developmental curves differ in the major lobes. For instance, in the frontal lobes, involved in planning, organizing, strategizing, and other “executive” functions, the cortical gray matter reaches its maximal thickness at 11.0 years in girls and 12.1 years in boys.² Temporal lobe cortical gray matter peaks at 16.7 years in girls and 16.2 years in boys. Parietal lobe cortical gray matter peaks at 10.2 years in girls and 11.8 years in boys.

The thickening and thinning of cortical gray matter is thought to reflect changes in the size and complexity of neurons, not a change in the actual number. The increasing size may reflect a process called arborization in which the cells grow extra branches, twigs, and roots, thereby growing “bushier” and making a greater number of connections to other cells. The decreasing amount of gray matter may reflect the process of pruning where certain connections are eliminated.

The forces guiding these processes of arborization and pruning are an area of intense investigation. Genetics, nutrition, toxins, bacteria, viruses, hormones, and many other factors have been shown to have an effect. One hypothesis for the pruning phase is the “use it or lose it” principle, in which those connections that are used

will survive and flourish, whereas those connections that are not used will wither and die. If this hypothesis is correct, the activities of the teen may have a powerful influence on the ultimate physical structure of the brain.

To examine cortical gray matter development with greater regional specificity we examined the change in gray-matter density on a voxel-by-voxel basis in a group of 13 subjects who had each been scanned four times at approximately two-year intervals.⁵⁵ (An animation of these changes is available at <http://www.loni.ucla.edu/~thompson/DEVEL/dynamic.html>).

Cortical-gray-matter loss occurs earliest in the primary sensorimotor areas and latest in the dorsolateral prefrontal cortex (DLPFC) and superior temporal gyrus. The general pattern is for those regions subserving primary functions, such as motor and sensory systems, to mature earliest and the higher-order association areas, which integrate those primary functions, to mature later. For instance, in the temporal lobes the latest part to mature is the superior temporal gyrus/sulcus, which serves as a heteromodal association site integrating memory, audiovisual input, and object-recognition functions (along with prefrontal and inferior parietal cortices).⁵⁶⁻⁵⁸

DISCUSSION

The relatively late development of the DLPFC, not reaching adult levels until the 20s, is intriguing in light of the behavioral data presented elsewhere in this volume. The DLPFC is linked to the ability to inhibit impulses, weigh consequences of decisions, prioritize, and strategize. Speculatively, the DLPFC is still “under construction” for a decade after the throes of puberty and may therefore be related to some of the behavioral manifestations of the teen years. However, direct data on the relationship between the brain changes shown here and behavior changes of the type described for teens has not been established.

In fact, straightforward relationships between volumes of a particular structure and performance on a particular cognitive task are elusive. Even simple tasks eventually involve the majority of brain systems, and the diversity of afferent and efferent connections to the many distinct nuclei of most structures as well as the intricacy of their various neurochemical systems further complicate functional correlates of gross volume size.

In conclusion, brain structure goes through explosive changes during the teen years. The connection between these structural changes and behavioral changes is only beginning to be elucidated.

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