Abstract: Few parents of a teenager are surprised to hear that the brain of a 16-year-old is different from the brain of an 8-year-old. Yet to pin down these differences in a rigorous scientific way has been elusive. Magnetic resonance imaging, with the capacity to provide exquisitely accurate quantifications of brain anatomy and physiology without the use of ionizing radiation, has launched a new era of adolescent neuroscience. Longitudinal studies of subjects from ages 3–30 years demonstrate a general pattern of childhood peaks of gray matter followed by adolescent declines, functional and structural increases in connectivity and integrative processing, and a changing balance between limbic/subcortical and frontal lobe functions, extending well into young adulthood. Although overinterpretation and premature application of neuroimaging findings for diagnostic purposes remains a risk, converging data from multiple imaging modalities is beginning to elucidate the implications of these brain changes on cognition, emotion, and behavior. © 2008 Society for Adolescent Medicine. All rights reserved.

Keywords: Child; Adolescent; Development; MRI; DTI; MT; fMRI; Gray matter; White matter

“A science of the mind must reduce . . . complexities (of behavior) to their elements. A science of the brain must point out the functions of its elements. A science of the relations of mind and brain must show how the elementary ingredients of the former correspond to the elementary functions of the latter.” — William James, The Principles of Psychology, 1890

For most of the 117 years since William James’s formulation of the quest to link biology with behavior, the study of the adolescent brain remained inaccessible. Wrapped in a tough leathery membrane, surrounded by a protective moat of fluid, and completely encased in bone, the brain is well protected from falls, attacks from predators, and the curiosity of neuroscientists. The invention of imaging technologies such as x-rays, computed tomography, and positron emission tomography offered some progress, but the reliance on ionizing radiation precluded the ethical application to studies of healthy subjects.

The advent of magnetic resonance imaging (MRI) finally broke through the formidable barrier thwarting the pursuit of James’s vision. MRI combines radio waves, strong magnetic fields, and sophisticated computer technology to provide detailed information about the anatomy and physiology of the brain without the use of ionizing radiation. The lack of ionizing radiation allows not only scanning in healthy children but also repeated scans in the same individual over the course of development.

This manuscript summarizes results of a ongoing, longitudinal, structural MRI project looking at typical and atypical brain development. Because adolescence does not have a precise biologic definition and the onset of puberty can vary by as much as 6 years in typical development, data are presented across ages 3–27 years, and readers can examine specific ages of interest in the figures accompanying the text. In addition, an Addendum after the main text provides further discussion of technical aspects of image acquisition and analysis, as well as a brief overview of some other imaging modalities used in adolescent research.

NIMH Child Psychiatry Branch Longitudinal Brain Imaging Project

Begun in 1989 under the direction of Markus Krusei, M.D., the Child Psychiatry Branch (CPB) of the National Institute of Mental Health, Bethesda, Maryland, has been dedicated to understanding the normal and abnormal development of the human brain. The CPB Longitudinal Brain Imaging Project is one of several studies of brain development currently being conducted at the CPB. The project is designed to investigate the relationship between brain development and behavior. The project uses MRI to study normal brain development and to identify brain abnormalities associated with disorders such as autism, attention-deficit/hyperactivity disorder, and schizophrenia. The project also uses MRI to study the effects of brain injury and to identify the brain regions that are most vulnerable to injury during childhood.
Institute of Mental Health has been conducting a longitudinal study of brain development in health and illness. The study design is for participants to come to the National Institutes of Health at approximately 2-year intervals for brain imaging, neuropsychologic and behavioral assessment, and collection of DNA. As of September 2007, we have acquired approximately 5000 scans from 2000 subjects.

From the outset the study has included typically developing people, both to provide a comparison from which to assess pathology and to explore mechanisms and timing of brain development as a guide to interventions. The sample of participants who have remained free of psychopathology (and constrained to only one subject per family for statistical independence), consists of 829 scans from 387 subjects aged 3–27 years. The data for the following sections regarding quantification of brain structure sizes are largely from this cohort. The emphasis on this single source is not to devalue the many excellent contributions of other investigators, but to provide an integrated account from the world’s largest collection of child and adolescent brain MRI scans with data acquired using uniform screening and assessment batteries, the same scanner, and the same methods of image analyses.

Data regarding brain physiology, such as that from functional MRI (fMRI) or other imaging modalities, are drawn from the literature reported by other investigators or from collaborative work with other neuroimaging teams. Although there is high optimism for the novel and complementary information potentially provided by the newer imaging methods currently the number of subjects for whom structural MRI (sMRI) is available dwarfs that of the other modalities. As opposed to the data set of more than 1000 for sMRI, no pediatric study using fMRI, diffusion tensor imaging (DTI), or magnetization transfer (MT) has been reported with a sample of more than 100.

**Developmental Anatomic Trajectories During Typical Childhood and Adolescence**

**Total Cerebral Volume**

In the CPB cohort, total cerebral volume peaks at 10.5 years in girls and 14.5 years in boys [1]. By age 6 years, the brain is at approximately 95% of this peak (Figure 1a). Total cerebral volume decreases during adolescence were not previously detected with postmortem data [2,3] or cross-sectional MRI studies [4,5]. Consistent with the adult neuroimaging literature [6], mean total cerebral volume is approximately 10% larger in boys. Total brain size differences should not be interpreted as imparting any sort of functional advantage or disadvantage. Gross structural measures may not reflect sexually dimorphic differences in functionally relevant factors such as neuronal connectivity and receptor density. Of note is the high variability of brain size even in this group of rigorously screened healthy children and adolescents. Healthy children at the same age may have as much as a 50% differences in total brain volume, further highlighting the need to be cautious regarding functional implications of absolute brain sizes.

**Cerebellum**

Cerebellum volume peaks about 2 years later than cerebral volume and is the only structure we have quantified that remains significantly larger in males after covarying for total cerebral volume [7].

The cerebellum has traditionally been associated with balance and motor control. However a converging body of evidence from electroencephalography (EEG) studies [8], fMRI studies [9], studies in subjects with vascular and degenerative cerebellar disease [10,11], and histologic studies demonstrating cerebellar connections to dorsolateral prefrontal cortex, the medial frontal cortex, and the parietal and superior temporal areas [12,13] clearly establish the cerebellum’s role in many higher cognitive functions. Consistent with the extended maturation of the cerebellum, these cerebellar-subservied higher cognitive functions continue to improve during childhood and adolescence.

**Ventricles**

Lateral ventricular volume increased robustly with age in the CPB sample of healthy children and adolescents (Figure 1d). This is in agreement with previous reports of greater ventricular volume in adults versus children [4], and is noteworthy because increased ventricular volumes are associated with a broad range of neuropsychiatric conditions. That ventricular volume is highly variable [14] and increases in healthy pediatric development informs interpretation of ventricular volume changes in patient populations.

**White Matter**

Whether a voxel is classified as gray matter (GM) or white matter (WM) depends largely on the amount of myelinated axons. The MRI signal intensities of nonfluid brain matter voxels generally fall into two bell-shaped distributions; however there is overlap between the distributions, so the exact amount of myelin necessary for classification as WM is somewhat arbitrary and varies slightly depending on different algorithms. Myelination is the wrapping of oligodendrocytes around axons, which acts as an electrical insulator and increases the speed of neuronal signal transmission. An important feature of myelination that has only recently been appreciated is that it does not simply maximize speed of transmission but modulates the timing and synchrony of neuronal firing patterns that convey meaning in the brain [15].

Consistent with previous reports [1,16–21], WM volumes increased throughout childhood and adolescence in the CPB sample (Figure 1c). The rate of increase is age
dependent [18] and can increase by as much as 50\% in a 2-year period in small regions of interest [22]; but at the lobar level (frontal, temporal, and parietal lobes), developmental WM trajectories are similar.

The corpus callosum (CC) is the most prominent WM structure, and consists of approximately 200 million axons connecting homologous areas of the left and right cerebral hemispheres. The functions of the CC can generally be thought of as integrating the activities of the left and right cerebral hemispheres, including functions related to the unification of sensory fields [23,24], memory storage and retrieval [25], attention and arousal [26], and enhancement of language and auditory functions [27]. In agreement with several studies that have indicated increasing CC size during adolescence [22,28–31], total midsagittal CC area increased robustly from ages 4–20 years in the CPB sample (Figure 1e).

The growing interest in exploring neural circuitry has encouraged the development of newer MR techniques, such as DTI and MT, which allow characterization of the microstructure of WM and the direction of axons. DTI studies show decreases of overall diffusion and increases in anisotropy (a measure of the directionality or nonrandomness of the diffusion) during typical child and adolescent development [32]. High anisotropy reflects coherently bundled myelinated axons and axonal pruning, which allow greater efficiency of neuronal communication [33]. A growing body of literature has shown positive correlations between anisotropy and cognitive performance. Specifically, high anisotropy in the temporal lobe correlates with memory capacity [34], in the frontal lobe with language ability [34], in frontal and occipitoparietal association areas with IQ [35], in temporal and parietal areas with reading ability [36–38], and in frontostriatal areas with the ability to inhibit responses to a visual stimulus [39].

Studies using MT imaging have reported increasing magnetization transfer ratio (MTR) values (which increase with myelination) during childhood and adolescence [40–42], although only an adult study has linked MTR values to cognitive performance [43].
Gray Matter

Unlike WM increases during childhood and adolescence, GM trajectories follow an inverted U-shaped path (Figure 1b). This decoupling of GM and WM developmental curves belies the inseparable connection among neurons, glial cells, and myelin, which are fellow components in neural circuits and are bound by lifelong reciprocal relationships [15].

Cortical GM

The GM volumes peak in the frontal lobes at age 9.5 years in girls and 10.5 years in boys; in the temporal lobes at age 10.0 years in girls and 11.0 years in boys; and in the parietal lobes at 7.5 years in girls and 9 years in boys (Figure 2).

At the voxel level, GM densities are not uniform within a given lobe [44]. (An animation of cortical GM changes from ages 4–20 years at the voxel level derived from scans of 13 subjects who had each undergone scanning four times at approximately 2-year intervals is available at http://www.nimh.nih.gov/videos/press/prbrainmaturing.mpeg.) The age of peak GM density is earliest in primary sensorimotor areas and latest in higher order association areas that integrate those primary functions such as the dorsolateral prefrontal cortex, inferior parietal, and superior temporal gyrus.

Postmortem studies suggest that part of the GM changes may be related to synaptic proliferation and pruning [45]. The connection between GM volume reductions, EEG changes, and synaptic pruning is also supported by an MRI and quantified EEG study of 138 healthy subjects aged 10–30 years; this study that found curvilinear reductions in frontal and parietal GM were matched by similar curvilinear reductions in the EEG power of the corresponding regions [46]. Because EEG power reflects synaptic activity (as opposed to WM), the temporally linked EEG power and GM changes suggests that the GM volume reductions are accompanied by reductions in the number of synapses. Another consideration is that myelination may change classification of voxels along the interior cortical border from GM to WM, resulting in cortical thinning as assessed by MR volumetrics, but that it would not necessarily entail changes in synaptic density [20]. Knowledge of the degree to which these and other phenomena may be driving the MR changes has profound implications for interpreting the imaging results. Imaging of nonhuman primates with postmortem validation may help in this regard.

Subcortical GM

Basal Ganglia

The basal ganglia are a collection of subcortical nuclei (caudate, putamen, globus pallidus, subthalamic nucleus, and substantia nigra) that are involved in circuits mediating movement, higher cognitive functions, attention, and affective states. Basal ganglia anomalies have been reported for almost all neuropsychiatric disorders that have been investigated by neuroimaging [47]. Because of the small size and the ambiguity of MR signal contrast of the borders defining the structures, only the caudate, putamen, and globus pallidus are readily quantifiable by MRI, and reliable automated techniques have been established only for the caudate. Like cortical GM, the caudate follows an inverted U-shaped developmental trajectory, peaking at age 10.5 years in girls and 14.0 years in boys (Figure 1f). The shape of the caudate developmental trajectory is more similar to that of frontal and parietal GM than temporal, supporting the notion that brain regions that share extensive connections also share similar developmental courses.

Amygdala and Hippocampus

The temporal lobes, amygdala, and hippocampus are integral players in the arenas of emotion, language, and memory [48]. Human capacity for these functions changes markedly between the ages of 4 and 18 years [49–51], although the relationship between the development of these capacities and morphologic changes in the structures subserving these functions is poorly understood. The amygdala and hippocampus are adjacent brain structures and part of some of the same neural circuits, but they also subserve distinct functions. The amygdala is a key component of circuitry involved in assessing salience, or the importance of environmental stimuli to survival. The hippocampus is involved in memory storage and retrieval. Connections between the amygdala and hippocampus result in enhanced memory for stimuli with high salience [52,53].

Valid quantification of amygdala and hippocampus volumes still requires manual tracing by expert raters and have not been completed for the longitudinal sample. In a previous report of a cross-sectional sample subset of the CPB sample, amygdala volume increased significantly during
adolescence only in males and hippocampal volume increased significantly only in females [54]. This pattern of sex-specific maturation of volumetric changes is consistent with nonhuman primate study findings, indicating a relatively high number of androgen receptors in the amygdala [55] and a relatively higher number of estrogen receptors in the hippocampus [56].

Summary of sMRI Changes Occurring in the Second Decade

In the typically developing CPB cohort, total cerebral and GM volumes peak during the ages from 10–20 years, whereas WM and ventricular volumes increase. Age of peak size for GM volumes differs, varies by region, and is generally earlier in females than in males.

Influences on Developmental Trajectories of Brain Anatomy During Childhood and Adolescence

Genes and Environment

To discern the relative contributions of genetic and non-genetic influences on trajectories of brain development, we are conducting a longitudinal neuroimaging study of monozygotic (MZ) and dizygotic (DZ) twins. To date we have acquired approximately 600 scans from 90 MZ and 60 DZ twin pairs. Correlation differences between MZ and DZ twins are analyzed with structural equation modeling to estimate the relative contributions to phenotypic variance of additive genetic (A), shared environmental (C), or unique environmental (E) factors [57]. Structural equation modeling is also useful to assess gene–environment interactions and other epistatic phenomena that challenge conventional interpretation of twin data.

For most brain morphometric measures, additive genetic effects (i.e., “heritability”) are high and shared environmental effects are low [58]. Additive genetic effects for total cerebral and lobar volumes (including GM and WM subcompartments) ranged from 0.77–0.88; for the caudate, 0.80; and for the corpus callosum, 0.85. The cerebellum has a distinctive heritability profile with an additive genetic effect of only 0.49, although wide confidence intervals merit cautious interpretation. Highly heritable brain morphometric measures provide biologic markers for inherited traits, and may serve as targets for genetic linkage and association studies [59].

Multivariate analyses allow assessment of the degree to which the same genetic or environmental factors contribute to multiple neuroanatomic structures. Like the univariate variables, these interstructure correlations can be parcelled into relationships of either genetic or environmental origin. This knowledge is vitally important for interpretation of most of the twin data, including understanding the impact of genes that may affect distributed neural networks, as well as interventions that may have global brain impacts. Shared effects account for more of the variance than structure specific effects, with a single genetic factor accounting for 60% of variability in cortical thickness [60]. Six factors account for 58% of the remaining variance, with five groups of structures strongly influenced by the same underlying genetic factors. These findings are consistent with the radial unit hypothesis of neocortical expansion proposed by Rakic [61] and with hypotheses that global, genetically mediated differences in cell division were the driving force behind interspecies differences in total brain volume [62–64]. Expanding the entire brain when only specific functions might be selected for is metabolically costly, but the number of mutations required to affect cell division would be far less than that required to completely change cerebral organization.

Age-related changes in heritability may be linked to the timing of gene expression and related to the age of onset of disorders. In general, heritability increases with age for WM and decreases for GM volumes [58], whereas heritability increases for cortical thickness in regions within the frontal cortex, parietal, and temporal lobes [65]. Knowledge of when certain brain structures are particularly sensitive to genetic or environmental influences during development could have important educational and/or therapeutic implications.

Male/Female Differences

Given that nearly all neuropsychiatric disorders have different prevalence, age of onset, and symptomatology between males and females, sex differences in typical developmental brain trajectories are highly relevant for studies of pathology. Robust sex differences in developmental trajectories were noted for nearly all structures, with GM volume peaks generally occurring 1–3 years earlier in females [1]. In our pediatric sample, brain size differences are not accounted for by differences in height or body size. To assess the relative contributions of sex chromosomes and hormones, our group is studying subjects with anomalous sex chromosome variations (e.g., Congenital Adrenal Hyperplasia, Familial Male Precocious Puberty, Cushing syndrome) [67,68].

Specific Genes

As with any quantifiable behavioral or physical parameter, individuals can be categorized into groups based on genotype. Brain images of individuals in the different genotype groups can then be averaged and compared statistically. In adult populations, one of the most frequently studied genes has been apolipoprotein E (apoE), which modulates risk for Alzheimer’s disease. Carriers of the 4 allele of apoE have increased risk, whereas carriers of the 2 allele are possibly at decreased risk. To explore whether
apoE alleles have distinct neuroanatomic signatures identifiable in childhood and adolescence, we examined 529 scans from 239 healthy subjects aged 4–20 years [69]. Although there were no significant IQ–genotype interactions, there was a stepwise effect on cortical thickness in the entorhinal and right hippocamapal regions, with the 4 group exhibiting the thinnest, the 3 homozygotes in the middle range, and the 2 group the thickest. These data suggest that pediatric assessments might one day be informative for adult-onset disorders.

Discussion

Three themes emerge from the cumulative neuroimaging research of adolescents, each buttressed by behavioral, EEG, and postmortem studies.

The first is an increase in associative cognitive activity as distributed brain modules become more and more integrated [70]. This increased connectivity is reflected by the WM changes, with fMRI studies suggesting more extensive neural networks, and by increased EEG coherence (reviewed in [71]). If we consider a literary/linguistic metaphor, maturation would not be the addition of new letters but of combining earlier formed letters into words, and then words into sentences, and then sentences into paragraphs.

The second is a general pattern of childhood peaks followed by adolescent declines. This pattern is found not only for GM volumes but for the number of synapses [72–74], glucose use [75], EEG power [76], and neurotransmitter receptor densities [77]. The powerful process of overproduction followed by selective/competitive elimination that shapes the developing nervous system in utero seems to continue to refine the brain throughout adolescent development.

The third theme is a changing balance between competing neuronal networks as different cognitive and emotional systems mature at different rates. Many of the cognitive and behavioral changes taking place during adolescence may be understood from the perspective of increased “executive functioning,” a term encompassing a broad array of abilities, including attention, response inhibition, regulation of emotion, organization, and long-range planning. These abilities are thought to rely heavily on frontal lobe circuitry that, as indicated above, is relatively late maturing. In addition to the sMRI studies, fMRI consistently shows an increasing proportion of frontal versus striatal or limbic activity from childhood to adulthood for a variety of cognitive tasks [78]. Some changes in limbic reward and motivational systems seem to be associated with the onset puberty, whereas other changes occur earlier or well after the advent of puberty. For example, in an fMRI study of 37 subjects aged 7–29 years that assessed response to rewards, adolescent nucleus accumbens response was equivalent to that in adults, but adolescent orbitofrontal activity was similar to that in children [79].

Elucidating the relationship between neuroimaging findings and behavior is an area of active investigation. Because behaviors emanate from the integrated activity of distributed networks, demonstrating straight-forward relationships between the size of a given brain structure and a particular behavior or ability has been elusive. An important consideration in linking form and function in the brain is that differences in the trajectories of development may in some cases be more informative than the final adult differences. For instance, in our longitudinal study looking at the relationship between cortical thickness and IQ differences in age by cortical thickness, developmental curves were more predictive of IQ than differences in cortical thickness at age 20 years [80].

A target for future investigations is puberty-specific versus puberty-independent changes in brain development. In the CPB sample, we assessed Tanner stage by self-report but did not quantify hormone levels. Studies specifically designed to address this issue, including more precise measures of puberty and comparison of performance in pre- and postpubertal individuals of the same age may help to address this question.

The diagnostic utility of neuroimaging in psychiatry has been the subject of much debate. Although group neuroimaging differences have been reported for nearly all neuropsychiatric disorders, the large overlap of values between clinical and control populations precludes routine application for individuals, except to rule out possible central nervous system insults such as tumors, intracranial bleeds, or congenital anomalies as etiologies for the symptoms. There is no identified “lesion” common to all, or even most, children with the most frequently studied disorders of autism, attention-deficit/hyperactivity disorder, childhood-onset schizophrenia, dyslexia, fragile X, juvenile onset bipolar disorder, post-traumatic stress disorder, Sydenham’s chorea, or Tourette’s syndrome. The more immediate utility of neuroimaging may be to provide endophenotypes, biologic markers that are intermediate between genes and behavior. Neuroimaging endophenotypes have the potential to define biologically meaningful subtypes of disorders that may respond to different interventions.

Future neuroimaging studies are likely to increasingly combine multiple imaging modalities in the same individuals, such as structural MRI, fMRI, diffusion tensor imaging, magnetization transfer imaging, EEG, and MEG, which will synergistically enhance our ability to interpret the signals for each of the modalities. Being able to simultaneously examine interindividual variation from cellular to macroscopic levels will be instrumental in bridging gaps among genes, the brain, and behavior. A related future direction may be an increase in postmortem studies of animals that have undergone neuroimaging. This would help to clarify the nature of changes driving the MRI findings, such as discerning the degree to which cortical GM changes, as detected with MRI, are related to arborization or pruning of neurons, or to encroachment of WM on the inner cortical border. Another important direction for
future neuroimaging studies will be increased integration with social and educational science, which have remained relatively separate despite the shared goal of guiding individuals through the adolescent years safely and optimally prepared for the adult world.

Adolescence is a time of substantial neurobiologic and behavioral change, but the teen brain is not a broken or defective adult brain. The adaptive potential of the overproduction/selective elimination process, increased connectivity and integration of disparate brain functions, changing reward systems and frontal/limbic balance, and the accompanying behaviors of separation from family of origin, increased risk taking, and increased sensation seeking have been highly adaptive in our past and may be so in our future. These changes and the enormous plasticity of the teen brain make adolescence a time of great risk and great opportunity.

Addendum: Technical Aspects, Analysis, and Modalities of Imaging

The term magnetic resonance imaging (MRI), if not specifically qualified as a different type, usually refers to the technique that yields different signal intensities for different tissue types (i.e., white matter [WM], gray matter [GM], or cerebrospinal fluid [CSF]). It is sometimes referred to as structural MRI (sMRI) or anatomic MRI to distinguish it from the more recent variants, such as diffusion tensor imaging (DTI), magnetization transfer (MT), or functional MRI (fMRI).

The DTI technique assesses how free water is to diffuse in any direction and provides information about the directionality of WM tracts [32]. The MT imaging technique assesses the ratio of the number of protons bound to macromolecules to the number of unbound protons [81]. This ratio provides a characterization of the microstructure of brain tissue that is different from that provided by sMRI or DTI. Functional MRI (fMRI) capitalizes on the different magnetic properties of oxygenated versus deoxygenated hemoglobin to localize areas of the brain that have increased blood flow during a given task, presumably as a result of neuronal activity triggering greater metabolic need. All of these types of MRI can be performed on the same machine using different software.

An overarching goal of image analysis is to characterize the tissue properties of discrete brain units and to discern a one-to-one correspondence between the unit in one brain image to the unit in another brain image, either from a different person or from the same person at a different time. Discerning one-to-one correspondence between brains is challenging because of the high variation in structural and functional localization. Striving to optimize valid correspondence remains one of the most active areas of image analysis research. The smallest units of MRI pictures are called pixels (or picture elements) and their three-dimensional counterparts voxels (volume elements). Each voxel is assigned a single value based on the average magnetic properties of the tissue in that box. Computer algorithms that combine information about the intensity of the voxel with atlases that inform the probability of tissue type based on the voxel’s location in the brain to classify tissue as GM, WM, or CSF are commonly used in sMRI analyses [82].

The size of the voxel can vary depending on magnet strength, and reductions in voxel size can usually be purchased with the currency of time. Most of the literature is from scans producing voxels of 1–3 ml. It is worth noting that even a 1-ml voxel may contain millions of neurons and trillions of synaptic connections, which confers substantial—but often unheeded—implications for interpretation. Also, the single value for a given voxel arises from the average of its more microscopic constituents, and two voxels with the same value may not have identical constituents. In general, voxels classified as WM are thought to consist mostly of myelinated axons, and voxels of solid brain tissue without enough myelin are classified as GM. An electron microscope analysis of a single GM voxel from an adult mouse comprised 29.3% axons, 30.2% dendrites, 12.06% dendritic spines, 9.5% glia, 13.8% cell bodies and blood vessels, and 5.2% extracellular space [83]. However the specific composition may be slightly different in human beings and may vary by age and region. In some voxels, a modest increase in myelin may switch the voxel designation from GM to WM.

Despite these interpretation challenges, MRI’s combination of safety, diversity of output parameters (e.g., anatomy, physiology, tissue composition, directionality of WM), and widespread accessibility has unleashed unprecedented insight into the living, growing brain.

A limitation of fMRI is that it relies on changes in blood flow that take place on the scale of several seconds. Modalities such as electroencephalography (EEG) and magnetoencephalography (MEG) have less spatial resolution but provide better temporal resolution by capturing electrical changes at a scale of milliseconds, and provide important complementary information to our understanding of brain development.

The EEG technique measures brain electrical activity thought to be generated largely by ion flow during synaptic activity. A large body of EEG literature has documented stepwise changes in electrical activity throughout the lifespan, including adolescence. Correlations between changes in the coherence of EEG signals from different parts of the brain and the Piagetian capacity for formal operations have been reported [84]. EEG changes in response to various stimuli (i.e., event-related potentials [ERP]) have demonstrated child–adolescent–adult differences that correspond to behavioral changes in capacities [85]. One recent study reports early versus late adolescent ERP differences in the anterior cingulate during detection of error-related conflict [86].

The MEG technique is related to EEG by Maxwell’s equations, which eloquently reveal that an electrical current will produce an orthogonally oriented magnetic field. Although both EEG and MEG presumably capture the same phenomena of electromagnetic changes stemming from ions flowing during neural activity, magnetic fields tend to be
less distorted by the skull, affording MEG potentially better spatial resolution [87]. Thus far, MEG studies in adolescents have primarily addressed epilepsy; however a growing number of projects are underway to assess language, impulse control, and other cognitive phenomena.

The drawback to these high temporal resolution techniques is that they have poorer spatial resolution than MRI. Currently no single technique offers excellent spatial and temporal resolution of physiologic activity, and comprehensive characterization therefore relies on the integration of information from multiple modalities.

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