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# MRI of Childhood and Adolescent Brain Development: What have we learned and where are we going?

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## Methodologic Considerations

### Image acquisition

Magnetic resonance imaging (MRI) combines a powerful magnet with radio waves and sophisticated computer technology to provide exquisitely accurate pictures of brain structure and physiology. It does so without the use of ionizing radiation allowing not only safe use in children but of repeated scans in the same individual throughout the course of development. This capacity to safely acquire longitudinal brain maturation data has launched a new era of child and adolescent neuroscience.

The smallest size of tissue that the MRI can measure is termed a voxel. The word voxel is a contraction of "volume element" and each voxel is assigned a single MRI signal value. For most studies the cube shaped voxel is around 1 milliliter, although with more powerful magnets and longer time in the scanner smaller voxel sizes are possible.

MRI has the flexibility to measure several different characteristics of tissue, broadly categorized into those involving brain physiology and those involving brain anatomy. One type of physiologic MRI is functional MRI (fMRI) which capitalizes on differing magnetic properties of oxygenated versus deoxygenated hemoglobin to assess resting state or task related changes in local blood flow, presumed to be an indirect reflection of neuronal activity in that region.

Structural MRI (sMRI) includes Diffusion Tensor Imaging (DTI), which measures water diffusion properties to infer anatomical microstructure, Magnetization Transfer Ratio Imaging (MTR) which assesses the transfer of magnetization from hydrogen nuclei of freely moving water to hydrogen nuclei of water bound to macromolecules, and anatomic MRI (aMRI) which provides tissue contrast based on the local environment of hydrogen nuclei. AMRI acquisitions can be further sub divided into types such as T1, T2, T2*, or Proton Density weighted depending on the tissue features emphasized. For this review the focus is on T2-weighted aMRI data which provides images most similar to what post mortem tissue looks like and is the most common type of MRI reported in the literature.

**Image analysis**

One of the first steps in measuring brain morphometric characteristics in aMRI is to classify individual voxels as corresponding to cerebrospinal fluid (CSF), white matter (WM), or gray matter (GM). Whether a voxel is classified as WM is largely determined by the amount of myelin, the high lipid content electrically insulating material from oligodendroglia extensions that wrap around axons to increase the speed of signal propagation. GM voxels consists mostly of cell bodies, dendrites, and dendritic processes but also of axons, glia, blood vessels, and extracellular space {Braitenberg, 2001 #12407}. Voxels with a mixture of gray and white matter components can be difficult to classify. Probabilistic atlases are used in a Bayesian manner to inform the likelihood of a voxel being gray or white based on the voxel's location as well as its signal intensity.

Once categorized by tissue type, various parcellations can be performed to derive volumes at the level of lobes (e.g. frontal, temporal, parietal, or occipital); regions defined by gyral, sulcal, or GM, WM, CSF boundaries (e.g. caudate nucleus); or individual voxels. Certain structures that share boundaries with adjacent gray matter regions (such as the hippocampus, amygdala, putamen, and globus pallidus) remain problematic for automated analysis and are usually quantified by manual tracing.

A fundamental objective of image analysis is to obtain a one-to-one correspondence between a given voxel in one brain to a corresponding voxel in the brain from different people or from the same person at a different point of development. If this one-to-one correspondence is reasonably well achieved it opens the door to more powerful statistical approaches of comparing brains such as creating "average" brains of groups.