A longitudinal structural MRI study of change in regional contrast in Autism Spectrum Disorder

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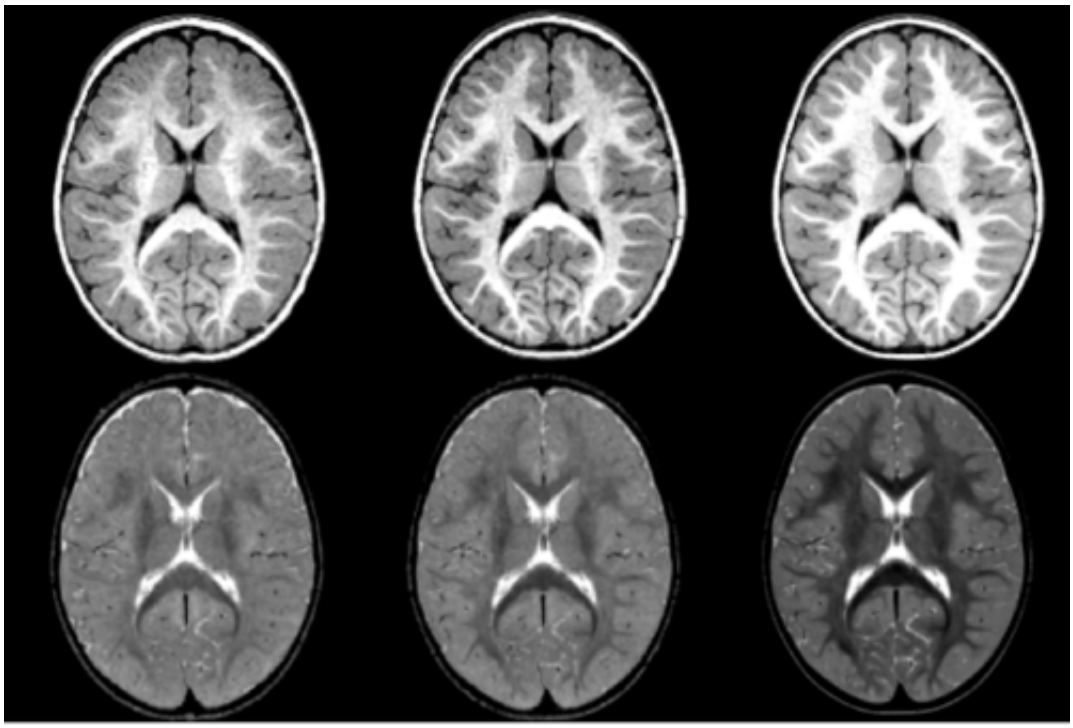
Introduction:

The brain undergoes tremendous changes in shape, size, structure, and chemical composition, between birth and 2 years of age [Rutherford, 2001]. Existing studies have focused on morphometric and volumetric changes to study the early developing brain. Although there have been some recent appearance studies based on intensity changes [Serag et al., 2011], these are highly dependent on the quality of normalization. The study we present here uses the changes in contrast between gray and white matter tissue intensities in structural MRI of the brain, as a measure of regional growth [Vardhan et al., 2011]. Kernel regression was used to generate continuous curves characterizing the changes in contrast with time. A statistical analysis was then performed on these curves, comparing two population groups : (i) HR+ : high-risk subjects who tested positive for Autism Spectrum Disorder (ASD), and (ii) HR- : high-risk subjects who tested negative for ASD.

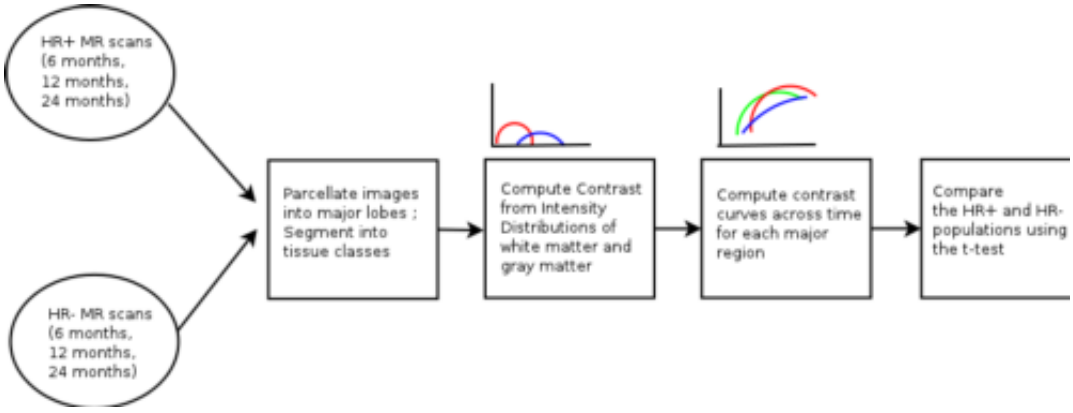


scans of a single subject taken at 6,12, and 24 months.

Methods:

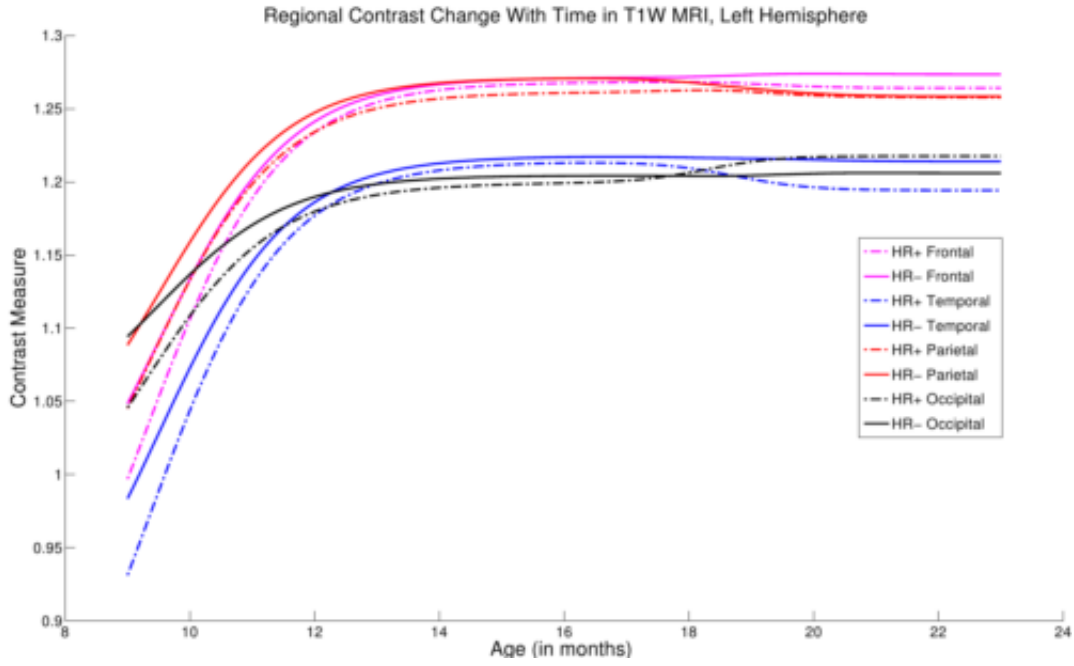
Our dataset consists of a total of 71 subjects at a high risk for ASD, of which 14 subjects tested positive, and 57 subjects tested negative. Each subject was scanned repeatedly at 3 different time points, approximately at 6 months, 1 year, and 2 years of age. The resulting T1W and T2W structural MR images were then transformed into a common 3D space and their intensity ranges

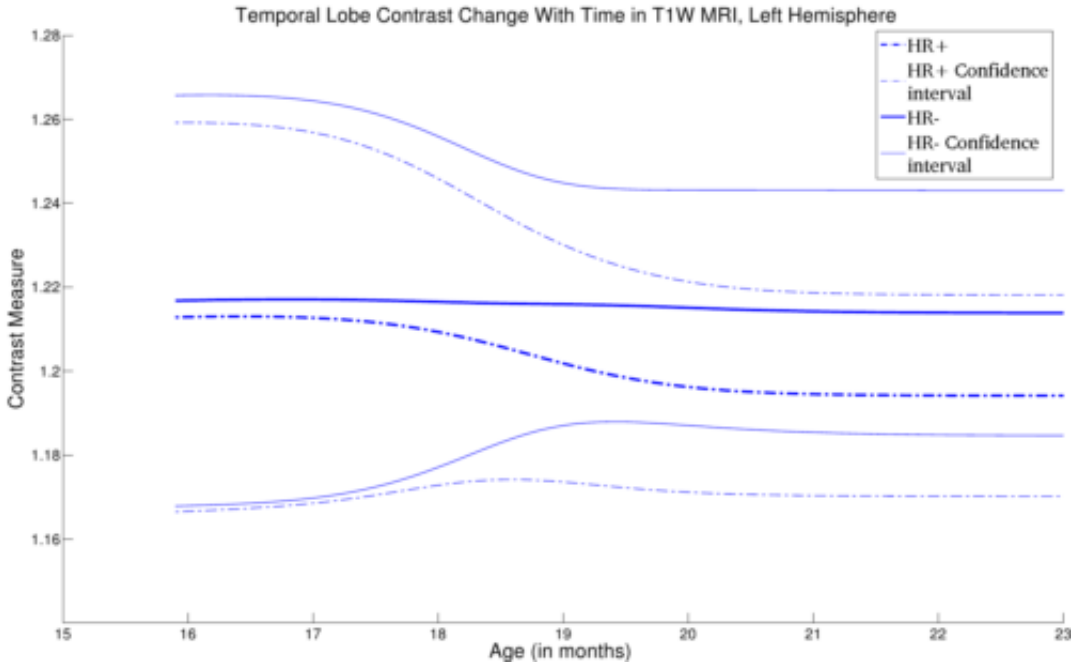
were normalized using a scaling factor. The tissue intensities were modeled as continuous distributions using a kernel-based density estimation method. The contrast for the major cortical lobes was then quantified by measuring the divergence in the intensities of the gray and white matter regions. A two-sample student t-test was then performed to find the statistical differences between the HR+ and HR- populations at time points spaced 2 months apart. Since our analysis was performed across several lobes, corrections were performed for multiple comparisons using the False Discovery Rate algorithm [Genovese et al., 2002].



Results:

We found that the contrast of T1W scans of the left hemispheric temporal lobe shows significant differences ($p = 0.0148$, significance level = 10%) between the two groups at 22 months of age. The other major cortical lobes (frontal, occipital, and parietal) do not show any significance when T1W scans of HR+ and HR- populations were compared. The T2W scans do not show any significant differences at all. On studying the average contrast trajectories in the T1W modality for the HR+ group, the contrast in the temporal lobe tends to increase up to 12 months but then decreases after 16-18 months.





Conclusions:

The study indicates that the time period between 18 and 24 months is the beginning of a crucial stage in the developmental trajectory that seems to distinguish those who develop ASD and healthy subjects, as validated in other microstructural and volumetric studies [Wolff et al., 2012]. It has also emerged from the study that the novel use of contrast change over time could be a useful indicator of alterations from expected early brain growth. Finally, the current analysis has potential to include a larger population and a richer set of brain regions, thereby making it a more extensive study.

Disorders of the Nervous System:

Autism

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