Abnormal Cortical and Subcortical Water Diffusivity Measured in Children with Tourette Syndrome.

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Introduction: Tourette Syndrome (TS) is a complex neuropsychiatry disorder with vocal and motor tics characterized with brief non rhythmic and involuntary symptoms. The onset of tics generally appears during the childhood period, and typically follows a waxing and waning pattern of severity and usually peak during the early second decade of life with a marked reduction of severity by the end of adolescence. However, in 20% of these children tic symptoms persist into the adulthood and they often are associated with neuropsychiatric comorbidities such as obsessive-compulsive and attention-deficit hyperactivity disorders. In this study we used voxel-based-analysis (VBA) as an objective method to measure water diffusivity (ADC) from cortical and subcortical regions within the fronto-striato-thalamo-cortical circuit thought to be involved in TS [1].

Materials and Methods: 17 right handed children (mean age: 11.6 ± 2.4 years, 14 males) diagnosed with TS and 14 right handed age-matched healthy controls (age: 12.3 ± 3.2 years, 6 males) were studied. The inclusion criteria for the TS group were history of prior diagnosis with TS according to Diagnostic and Statistical Manual of Mental Disorder IV TR [2], and absence of major illness. Neurobehavioral measures for hyperactivity, attention, externalization, internalization, and obsession and compulsion problems were also measured in TS children and on 15 of them the tic severity score for the period of 1 week prior to the MRI scan was noted. Axial DT-MRI were acquired with 6 non-collinear diffusion sensitization gradients and 1 T2W set repeated 6 times and magnitude averaged to increase SNR, and reduce imaging artifacts. For VBA, the T2W images were spatially normalized to a template using PSM2 [3]. Following this, predefined regions of various cortical [orbitofrontal (ORB_FRN), dorsofrontal (DOR_FRN), sensory motor, insular, and anterior cingaluted] and subcortical [caudate, palladium, putamen, and thalamus] structures were applied on to the transformed images to extract the ADC values. These values were analyzed using repeated measure with side (left/right), group (TS/controls) and regions (DOR_FRN, OEB_FRN, Caudate, Putamen, Palladium, Sensory-motor-Thalamus) with age as covariate. Pearson product moment coefficient was applied to correlate between neurobehavioral variables and DTI measurements with significance set to p =0.01 to correct for Type I errors for multiple comparisons.

Results: In VBA of cortical gray matter, regions showed significant 3 way interaction between regions x sides x groups (F=2.9, p=0.024). The follow up test for individual regions showed increased ADC in the left and right putamen (p=0.005, p=0.039), orbitofrontal (p=0.017, p=0.007), insular (p=0.008, p=0.021) and left globus pallidus and anterior cingualte (p=0.024, p=0.0046) (Fig 1). Other gray matter structures, right cingulum and left dorsofrontal cortex showed a trend towards increased diffusivity compared to the controls (p=0.099). The overall group difference for all regions and both sides showed a trend toward significance (p=0.052) with increased ADC value in the TS group compared to the controls. Furthermore, the ADC from right orbitofrontal cortex showed significant positive correlation with the internalization problem scores (r=0.675, p=0.006) and the left orbitofrontal cortex showed a trend towards significance with the internalization problem scores (r=0.559, p=0.03) (Fig 2).

Fig 1

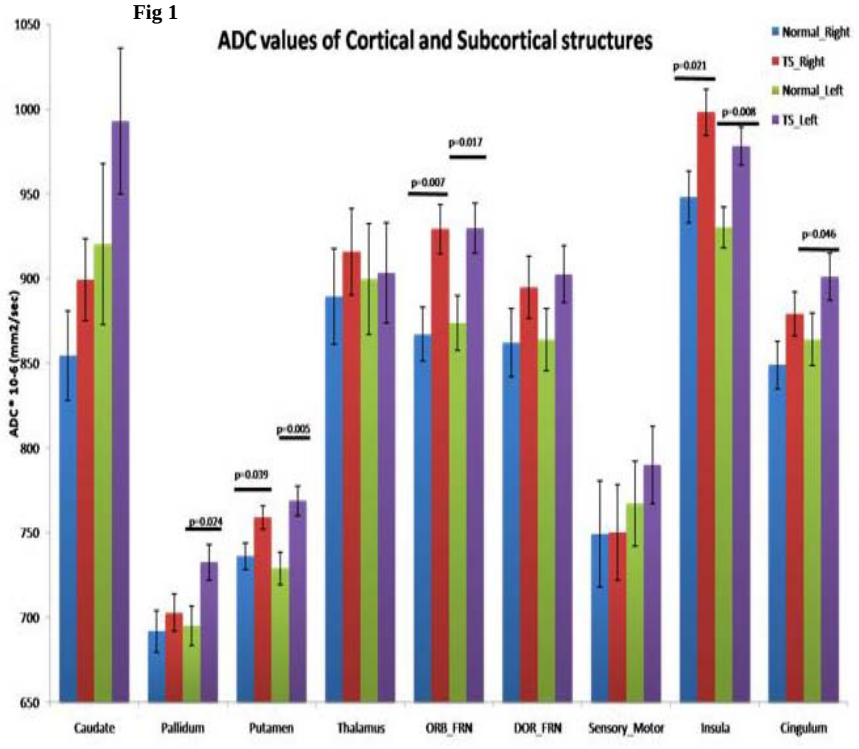
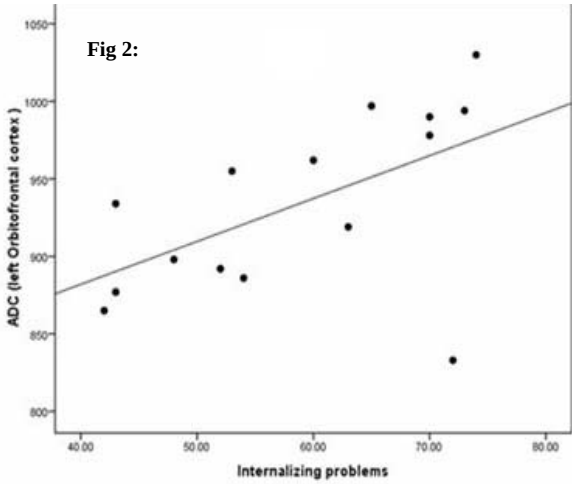


Fig 1: Differences in ADC values of the cortical (orbitofrontal = ORB_FRN, dorsofrontal = DOR_FRN, sensory motor, insular, and anterior cingulated) and subcortical (caudate, palladium, putamen, and thalamus) structures in left and right hemispheres of the TS patients as compared to healthy controls. Statistical significance was reported when p < =0.01 after Type I error correction.

Fig 2: Correlation of ADC values and internalization in the left orbitofrontal cortex (r=0.675; p=0.006) with age entered as covariate..

Fig 2:



Conclusion: Children with TS have significantly increased ADC values in the gray matter (bilateral putamen, orbitofrontal and insular cortex) as compared to healthy controls. ADC values from bilateral orbitrofrotnal cortex showed significant positive correlation with the internalizing problem score. Our findings are in agreement with glucose PET studies [4,5] showing positive correlation between putamen and orbitofrontal, inferior insular and inferior and superior temporal cortices in TS subjects in contrast to the negative correlation seen in controls.

References: Kramer H, J Neural Tasnm (2004); [2] American Psychiatric Association (2000); [3] Ashburner et al., Neuroimage (1999); [4] Behen M et al., Mov Disorder (2007); [5] Jeffries, Neuropsychopharmacology (2002).