White Matter Tract Development in Autistic Toddlers and Preschoolers by Diffusion Tensor Imaging and Correlation with Ongoing Therapies

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Introduction

Autism spectrum disorders (ASDs) are neurodevelopmental disorders characterized by social, communication and behavioral impairments.

ASD prevalence is 1 in 68 children in Lebanon.

Early intervention therapies have improved the outcome in toddlers.

The Verbal Behavior Milestones Assessment and Placement Program (VB-MAPP) is a battery that guides the therapy plan and assesses developmental milestones.

Growing evidence suggests impaired white matter connectivity in the brain of older ASD patients and high-risk infants.

Diffusion Tensor Imaging (DTI) is an MRI technique used to study the brain white matter tracts (orientation, integrity).

Objectives

Identify culprit white matter tracts in ASD patients through DTI indices.

Correlate these radiological findings with clinical improvement after therapies.

Materials and Methods

Recruitment: Participants were aged between 18 months to 4 years. Patients were newly diagnosed with ASD at the AUBMC Special Kids Clinics (N=15, 36± 9 mths); and normally developing controls (N=6, 36± 9 mths) were recruited at the MRI facility of AUBMC. VB-MAPP scores are tallied for 11 patients so far.

Image acquisition: All the participants underwent the same brain MRI protocol on a 3-Tesla MRI including 32 directions DTI. In addition, ASD patients underwent a repeat MRI 1 year after therapies: N=9 completed so far, so only those 9 are compared.

Materials and Methods (cont'd)

Behavioral Assessment and Therapies: The ASD group were subjected to the VB-MAPP test at diagnosis and 6 & 12 months after initiation of therapies. The treatment consisted of attending nursery school + 3 hours of "early intervention" [speech (ST), occupational (OT), psychomotor (PSM)] + 6-10 hours of ABA per week.

Data analysis: Whole brain Tract-Based Spatial Statistics was performed on the patient group before and after intervention to reveal specific **regions of interest** (ROIs) in the white matter. DTI indices including Fractional Anisotropy (FA) and radial (RD), mean (MD) and axial (AD) diffusivities will be analyzed/computed at these ROIs for all participants. Focus will be limited to FA as it yielded the most significant results.

Results

Figure 1

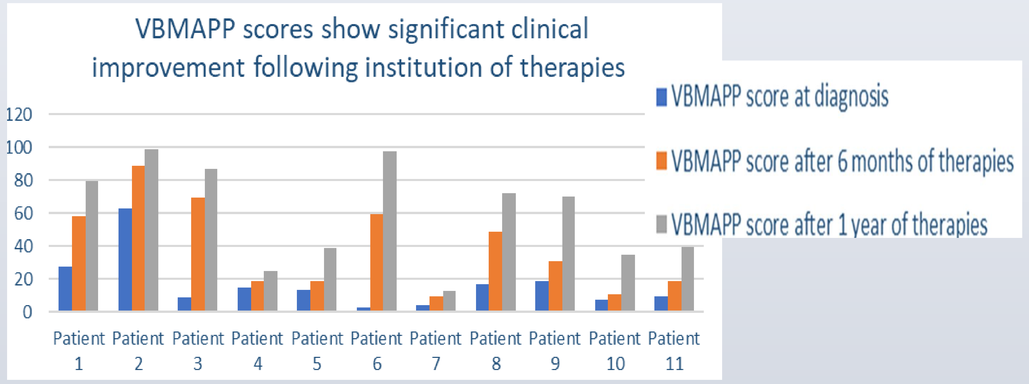
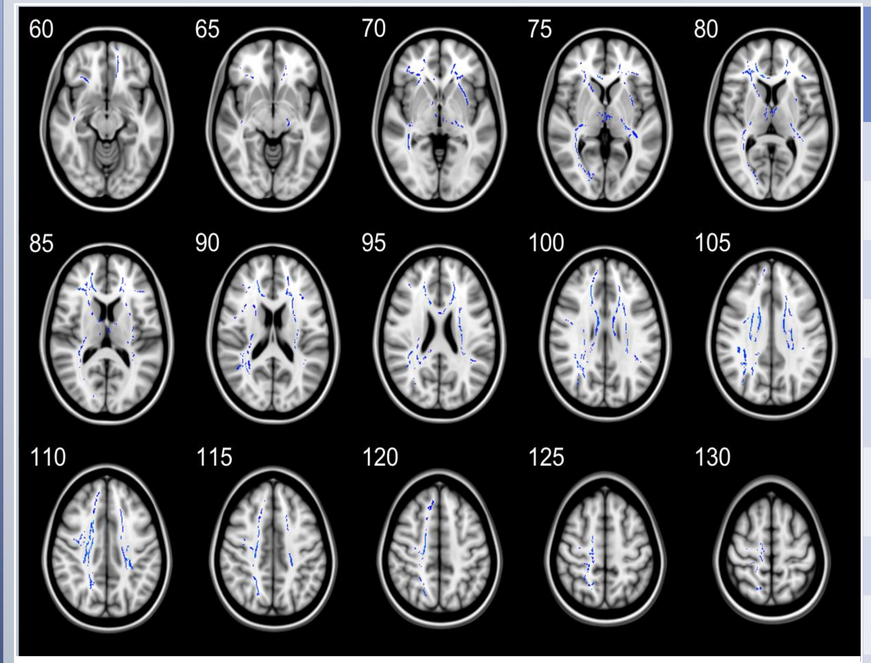


Figure 2



Regions of significantly ($p<0.05$) greater fractional anisotropy (blue) in patients following therapies compared to scan at diagnosis (N=9) and were corrected for age.

Table 1

ROIs with at least 30% change after therapies	% Difference before/after
Superior corona radiata left	48.8
Uncinate fasciculus right	47.1
Superior corona radiata right	47.0
Body of the corpus callosum	46.5
Retro-lenticular part of the internal capsule left	43.2
Retro-lenticular part of the internal capsule right	42.2
Posterior corona radiata right	39.8
ANTERIOR CORONA RADIATA left	38.4
Posterior thalamic radiation right	36.9
ANTERIOR CORONA RADIATA left	34.1
GENU OF THE CORPUS CALLOSSUM	30.7

Results (cont'd)

The 3 regions underlined and bolded in the table were among 13 regions showing significantly greater FA in controls compared to treatment-naïve ASD patients.

Changes in Fractional Anisotropy of the Right Superior Longitudinal Fasciculus in Treatment-Naïve ASD Patients VS Controls

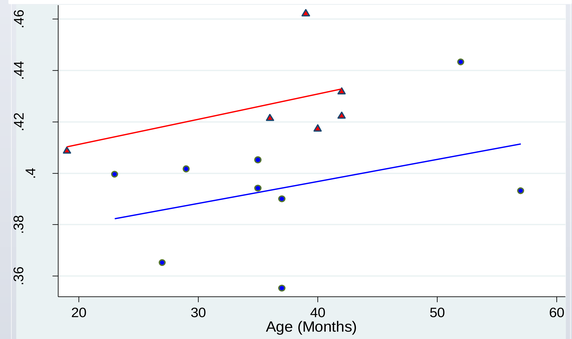


Figure 3

Conclusions

- **VB-MAPP scores were higher at 6 mths & 1 yr for patients in nursery/receiving ST, OT, PSM & 6-10 hours of ABA per week.**
- **In the treated vs. non-treated ASD group (Fig. 2& Table 1) FA was higher endorsing better white matter connectivity.**
- **In normo-typic controls vs. non-treated ASD patients (Fig 3) FA was higher.**

Note: ROIs showing increase in FA in ASD patients after therapies are implicated in ASD symptoms (table 1): language, planning, motor coordination, repetitive behavior (**corpus callosum**); Fine motor control, reasoning, decoding performance (**corona radiata**); Visual learning, socio-emotional, cognitive processing (**uncinate fasciculus**); Visual processes (**retro-lenticular internal capsule**).

- **The radiological white matter improvement correlates with clinical improvement with therapies documented by higher VBMAPP scores.**
- **Remaining DTI scalars (RD/ MD/AD are under analysis. We hypothesize they will be lower in controls indicating better white matter integrity.**

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