

Diffusion Tensor Tractography Studies correlate with Neuropsychometric tests in patients of vitamin B12 deficiency with normal appearing brain on conventional MRI

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Introduction: Vitamin B-12 is necessary for normal red blood cell formation and its deficiency can lead to macrocytic anemia. It is also involved in tissue repair, and DNA synthesis. Besides its role in normal hematopoiesis and cellular growth, its deficiency can also lead to serious degree of neuronal damage that can cause tingling and numbness in the patient's hands and feet¹. Brain MRI studies of patients with vitamin B-12 deficiency sometimes show signs of disseminated demyelination similar to those found in multiple sclerosis². It has been reported cervical and thoracic spinal cord MRI showed increased signal intensity within the dorsal columns on T2weighted images. Diffusion tensor imaging (DTI) is known to provide a deeper understanding of the white matter microstructural changes in health and disease. The changes in DTI metrics provide information about the integrity of the axonal fibers, the coherence with which they are bundled. DTI along with cognitive measures are particularly useful in elucidating the relationships between the integrity of white matter pathways and the efficiency of cognitive and neural processing during brain development³. The popular ROI-based morphometric DTI method is limited to 2 dimensional (D) and does not reflects the whole fiber bundle in 3 D space. Diffusion tensor tractography (DTT) gives 3 D information of white matter fiber tract. The purpose of this study was to determine the change in DTI metrics in brain white matter and to find out its association with cognitive function among patients with vitamin B-12 deficiency.

Materials and Methods

Subjects: Our study included 8 patients with vitamin B-12 deficiency (age 38.3±17.5yrs) along with 9 age/sex matched healthy controls. Clinical manifestations included tingling/numbness, irritability, personality change, and mild memory impairment. The diagnosis of vitamin B-12 deficiency was based on the low levels of blood vitamin B-12.

Imaging protocol: Conventional MRI and DTI data were acquired on a 3Tesla GE MRI scanner using 8 channel head coil. DTI data were acquired by using a single-shot echo planar dual spin echo sequence with ramp sampling. The diffusion tensor encoding used was a vendor supplied DTI scheme with 30 uniformly distributed directions. DTI was performed in the axial plane. The diffusion weighting b-factor was set to 1000 s/mm² field of view (FOV) =240×240 mm², slice thickness=3mm, interslice gap=0 and number of slices=62. The algorithm and detailed methodology used in DTT are described elsewhere⁴. Cervico-dorsal imaging was also performed to look for the B12 deficiency related changes in the spinal cord.

NP Tests: NPT were performed on healthy controls and patients with vitamin B-12 deficiency. Wechsler Adult Intelligence scale (WAIS-P) was used to assess cognitive function which consists of 5 subtests, picture completion (PC), digit-symbol (DS), picture arrangement (PA), object assembly (OA) and block design (BD).Number connection tests (NCT A and B), figure connection tests (FCT A and B) were performed to measure visual motor coordination, concentration and mental speed of patients as well as controls.

Statistical analysis: Spearman correlation was performed between cognition function and DTI derived metrics. Independent t- test was used to look for difference between healthy control and patients with vitamin B-12 deficiency.

Results: The brain as well as cervico-dorsal spine of all patients with vitamin B-12 deficiency appeared normal on conventional MRI. Significantly reduced FA values were observed in the ATR & PTR fibers bundles of patient with vitamin b12 deficiency (FA values.370±.010&.407±.014) as compared to controls (FA values.390±.018&.428±.014) (fig.1). Significantly abnormal cognitive scores were observed in the PC, DS, BD & FCT-B tests of patient with vitamin b12 deficiency (NPT values 12.88±1.4,7.62±2.8,9.62±2.2&114±18.5) as compared to controls(NPT values 14.56±1.5,10.33±1.9,12.22±.97&81.78±33.3)(fig.2).A significant positive correlation was observed between FA values quantified from fornix (Fx) and PC & DS (fig.1A-B). While FA values of superior longitudinal fasciculus (SLF), inferior fronto-occipital fasciculus (IFO) fibers significantly correlated with DS (fig.1B). A significant correlation was observed between FA values of anterior thalamic radiation (ATR), cingulum (CG) and superior thalamic radiation (STR) fibers with PC, OA and FCT-A (fig.1A,C,D) respectively.

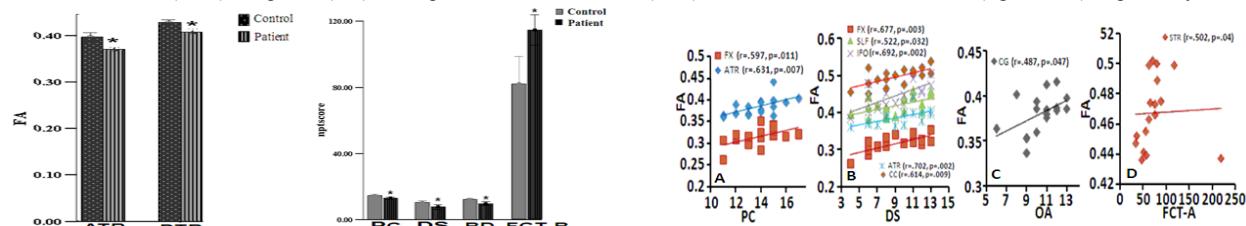


Figure 1: shows significant reduction in FA values of ATR and PTR.* denotes $p < 0.05$ in patient group compared to controls.

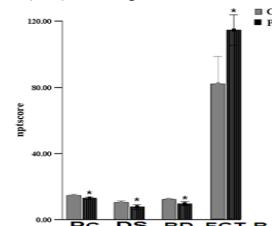


Figure 2: Bars shows significantly abnormal Neuropsychometric tests (NPT) in patients compared to controls (PC, DS and BD and FCT-B respectively).* denotes $p < 0.05$ in patient group compared to controls.

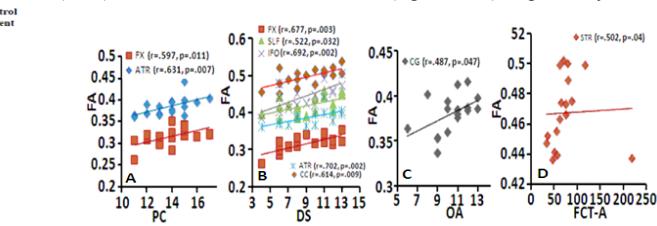


Figure 3: Scatter plot (A-D) showing positive correlation between FA values from different fiber bundles with NPT score (PC, DS, OA, FCT-A).

Discussion: In this study significantly reduced FA values were observed in ATR and PTR fibers as compared to controls. Lower score on PC, DS and BD suggests that patients with vitamin B12 deficiency have poor visual recognition, impaired long term memory, poor visual specialization, inability to organize visual material, psychomotor speed, visual motor coordination and poor sustained attention, concentration and learning². Significantly higher score of FCT-B indicates poor motor coordination and mental speed in these patients. Significant correlation between FA values of various fiber bundles with PC, DS, OA, FCT-A, indicates that vitamin B12 deficiency may be responsible for cognitive impairment in these patients. It has been reported that B-12 deficient patients have significant low neuropsychological scores¹. Abnormal visual evoked potentials have been recorded in these patients and is suggested to be due to the loss of integrity of PTR⁵. The selective changes in ATR and PTR in patients with vitamin B12 deficiency with normal appearing conventional MRI suggest these findings may be used as image biomarkers of B12 deficiency in future. A significant positive correlation between FA values of various fiber bundles with some of the neuropsychological scores suggests that the microstructural changes observed in imaging in these patients may be responsible for abnormal cognition.

References: 1) Miller. AJCN. 2006 (84), 1259-60 2) Goebels N, et al. J Neuropsych Clin Neurosci. 2000;12:389-94, 3) Munakata Y et al, Trends in Cogni. Sci. 2004;8:22-8 4) Rathore et al. Magn Reson Imaging 2011[Epublish ahead of print] 5) Pandey et al. Clinical Neurophysiology. 2004;115:914-18