

Reliable Analysis of Tract-specific Multiparametric MR Data via Automated Isolation of Nigro-Striatal Tract

Ryan Hutten¹, Nisa Desai¹, Demetrius Maraganore^{2,3}, Robert R. Edelman^{1,4}, and Ying Wu^{1,5}

¹Radiology, Northshore University Health System, Evanston, IL, United States, ²Neurology, Northshore University Health System, IL, United States, ³Neurology, University of Chicago, IL, United States, ⁴Radiology, Northwestern University Feinberg School of Medicine, Chicago, IL, United States, ⁵Radiology, University of Chicago, Chicago, IL, United States

Introduction: The nigrostriatal tract (NST) connects the substantia nigra (SN) with the striatum and is a major dopamine pathway that has important involvement both in Parkinson's Disease (PD) pathogenesis and treatment modulation [1]. Diffusion Tensor Imaging (DTI) and Magnetization Transfer Ratio (MTR) are two sensitive and promising quantitative multiparametric MR techniques that have shown clinical utility in PD and are suitable for assessing neural integrity in vivo [2, 3]. Previously, MR research on PD has focused mainly on subcortical nuclei with very few studies on tract based DTI [4], and tract based MTR has not been studied. Furthermore, methods for automatically isolating the NST are not yet available. Commonly used tractography methods require manually outlined seed regions that potentially introduce measurement inconsistency. We report an automated post-processing algorithm that successfully isolates the NST and derives tract-specific DTI and MTR measurements without any manual intervention.

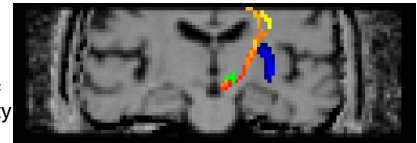


Fig 1: The NST in Red-Yellow overlaid on a MTR map with automated ROIs of SN in green and the Putamen in blue

Methods: Twenty subjects (Age: 65.4 ± 6.8 yrs Gender: 12M, 8F) were included. All subjects signed an IRB approved consent document. **IMAGING:** A Siemens 3T scanner (MAGNETOM Verio, Siemens, Erlangen, Germany) with a 12 channel phased array head coil was used to collect the following images: 1) *MPRAGE* (TE/TR/TI/FA = 2.94ms/2300ms/900ms/9°, resolution=1x1x1mm³); 2) *DTI* 2D SE-EPI (TR=5000ms, bvalue=1000sec/mm², resolution= 2x2x2 mm³); 3) *MT* 3D GRE sequence with and without an MT saturation pulse (TE/TR/FA= 3.92ms/30ms/5°, resolution = 1x1x1.2 mm³); 4) *QSM* 3D-GRE multi-echo sequence(TE/TR/FA=3.6-45ms/55ms/15°; resolution = 0.9x0.9x1.5 mm³). **POST PROCESSING:** Diffusion maps including fractional anisotropy (FA) and mean diffusivity (MD) maps were generated with FDT [5]. MTR maps were calculated as the normalized difference between signal intensities with and without MT saturation pulse. **QUANTITATIVE ANALYSIS:** We integrate a probabilistic fiber tractography algorithm with a novel automated segmentation of SN and basal ganglia to extract tract-specific FA, MD and MTR measurements without manual intervention. T1-weighted images were used to segment the putamen using Freesurfer [6]. The SN was isolated using an in-house developed automated segmentation algorithm that makes use of high regional contrast in quantitative susceptibility maps. Diffusion tensor images were used to produce probability maps of the location of fibers within the brain using FDT's bedpostx and probtrackx algorithms [5]. For comparison, conventional tractography was also conducted with manual seed ROIs outlined by two different trained operators. The NST was isolated using the SN as seed and the putamen as target for both automated and manual methods. Mean values of FA, MD and MTR were computed for NST. **STATISTICAL ANALYSIS:** A Bland-Altman analysis was conducted to test the agreement between manual and automated method. Inter- and intra-rater reliability were calculated using intraclass correlation coefficients (ICC).

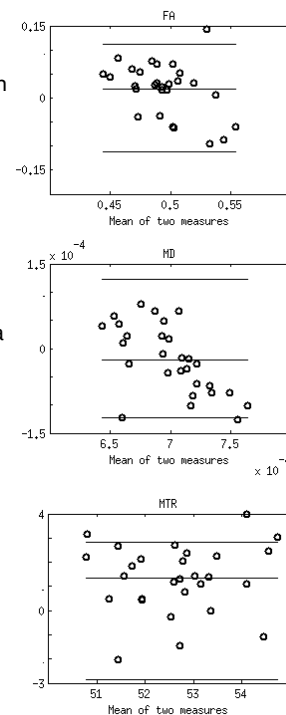


Fig 2: Bland-Altman tests indicate good agreement between automated and manual measurements of FA, MD and MTR. Horizontal lines are the mean and 2 standard deviations from the mean

Results and Discussion: Fig. 1 illustrates the automated NST and the results of the automated segmentation of SN and putamen. Fig. 2 shows quantitative FA, MD and MTR of the automated NST had excellent agreement with the conventional manual method, suggesting that the two methods are interchangeable. Results of the inter and intra-rater reliability of the manual and automated methods are summarized in Table 1. ICCs = 1.0 were yielded for the automated NST analysis of FA, MD and MTR without any intra and inter-rater bias. The manually derived NST resulted in ICC values ranging from 0.71 to 0.98. Among the manual measurements, the MTR exhibits high inter and intra-rater reliability with ICC between 0.80 and 0.98. DTI FA and MD measurements showed lower reliability with ICC between 0.71 and 0.87. Our results suggest that both the conventional manual and the new automated method are reliable and feasible for quantitative NST DTI and MTR measurements. However, the automated method outperformed the manual method by eliminating the requirement of manual seeding process free of operator bias.

Conclusion: Our automated algorithm for extracting multi-modal measurements from the NST improves reliability for both DTI and MTR measurements. Sensitive and objective methods for assessing tissue integrity in NST may allow for earlier detection and monitoring of disease progression potentially valuable for both diagnosis and treatment of PD.

Manual: Inter-rater	MTR	ICC	FA	ICC	MD	ICC
Left NST Rater 1	51.280	0.803	0.473	0.773	0.00073	0.874
Left NST Rater 2	51.673		0.474		0.00073	
Right NST Rater 1	51.167	0.985	0.486	0.707	0.00071	0.792
Right NST Rater 2	51.157		0.483		0.00071	

Manual: Intra-rater	MTR	ICC	FA	ICC	MD	ICC
Left NST Time 1	51.280	0.8996	0.473	0.8091	0.00073	0.7977
Left NST Time 2	50.890		0.463		0.00074	
Right NST Time 1	51.167	0.9752	0.486	0.7541	0.00071	0.8246
Right NST Time 2	51.095		0.476		0.00072	

Automated	MTR	ICC	FA	ICC	MD	ICC
Left NST	52.964	1.00	0.511	1.00	0.00069	1.00
Right NST	52.488	1.00	0.491	1.00	0.00071	1.00

References: [1] Grahn 2009 *Behavioural Brain Research*; [2] Dousset 1992 *Radiology*; [3] Bassler 1996 *Journal of Magnetic Resonance Imaging*; [4] Zheng 2013 *Human Brain Mapping*; [5] Behrens 2007 *Neuroimage*; [6] Fischl 2012 *Neuroimage*