Diffusion Tensor Imaging of Parkinson's Disease Patients and Their Cognitive Assessments

by

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ABSTRACT

Diffusion Tensor Imaging may be used to understand brain differences within PD. Within the last couple of decades there has been an explosion of learning and development in neuroimaging techniques. Today, it is possible to monitor and track where a brain is needing blood during a specific task without much delay such as when using functional Magnetic Resonance Imaging (fMRI). It is also possible to track and visualize where and at which orientation water molecules in the brain are moving like in Diffusion Tensor Imaging (DTI). Data on certain diseases such as Parkinson's Disease (PD) has grown considerably, and it is now known that people with PD can be assessed with cognitive tests in combination with neuroimaging to diagnose whether people with PD have cognitive decline in addition to any motor ability decline. The Montreal Cognitive Assessment (MoCA), Modified Semantic Fluency Test (MSF) and Mini-Mental State Exam (MMSE) are the primary tools and are often combined with fMRI or DTI for diagnosing if people with PD also have a mild cognitive impairment (MCI). The current thesis explored a group of cohort of PD patients and classified based on their MoCA, MSF, and Lexical Fluency (LF) scores. The results indicate specific brain differences in whether PD patients were low or high scorers on LF and MoCA scores. The current study's findings adds to the existing literature that DTI may be more sensitive in detecting differences based on clinical scores.

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CHAPTER 1

INTRODUCTION

Parkinson's Disease (PD) is a neurodegenerative disorder that affects both motor and non-motor systems that is variable in how it presents and progresses (Aleksovski et al., 2018). The symptoms associated with PD can range but the main symptoms can include tremors along the extremities, jaw and or head, stiffness of limbs and torso, slowed movements, and instability with gait and posture (NIH). Along with physical symptoms there are often psychological symptoms people with PD experience; for example, depression, dementia, mental fatigue, and affected memory recall. There is still debate on what is the direct cause of PD, but the research does not agree on one exact cause, like other disorders the general consensus is that there are typically a multitude of factors that are responsible. There is debate on causes of the different types of PD (e.g. Idiopathic Parkinson's, Vascular Parkinsonism, Drug-Induced Parkinsonism). Chen and Beate (2018) state that the cause for late-onset sporadic PD is possibly an interaction of environmental and genetic factors as well as typical aging.

PD diagnosis is not straight forward, in other words there is not a single test that can tell someone if they have PD or not, while someone may exhibit multiple of the symptoms mentioned earlier (rigidity/stiffness, slowness of movements, and tremors), blood and genetic testing as well as DaTscan and or Magnetic Resonance Imaging (MRI) can be used. DaTscan is a method for visualizing dopamine transporter in the striatum and whether it is normal or abnormal (Gayed et al. 2015). The MRI is a standard imaging technique that gives us a sense of the structure of a person's brain and allows us to see if there has been tissue damage, inflammation, abnormal size of specific brain regions and

much more. DaTscan rarely gives physicians more information than what they already assessed from patient's apparent symptoms and the symptoms patients describe having . While DTI is a unique and sensitive tool that can tell us about the direction/path of white matter bundles (also known as axons). This can give us insight on whether white matter is normal and healthy or if it is abnormal and potentially damaged. If the latter is found to be likely then it could mean that the person also has some level of cognitive impairment, about 30% of PD patients have comorbid cognitive impairments (Delgado□Alvarado et al., 2016). DTI is also capable of telling us the integrity of axons, and if/where something called demyelination is occurring. What is examined is the amount of water diffusivity, if there are higher amounts of diffusivity it means that these axons or neural fibers are not retaining water like they should be. By detecting this demyelination (or when axons lose their insulation) it is often a warning letting us know that there has been a change in a person's white matter tissue (Atkinson-Clement et al., 2017). These changes in white matter typically cause changes in both the physical and cognitive modalities. There are two key measures for DTI and observing the movement/diffusivity of water, Fractional Anisotropy (FA) and Mean Diffusivity (MD). In this study, the primary measurement that will be used will be FA to assess the link between cognition and white matter integrity (refer to Figure 1). Values of FA are usually exhibited from the range of 0 to 1, where being closer to 0 would mean the movement of water is moving in multiple or many directions and would be considered isotropic and indicate that there is likely some sort of damage to the white matter. Whereas a FA value closer to 1 would mean that water diffusion is directionally dependent/moving in one or direction and

would be considered anisotropic (water diffusion is restricted to that one axis indicating good white matter integrity) (Atkinson-Clement et al., 2017).

The primary hypothesis of this study is that there will be a difference in FA values between the participants that have low versus high scores on cognitive tests. The secondary hypothesis is that if significant FA value differences are observed between the two groups, then most of the observed difference will be located within the temporal lobes of the subjects.

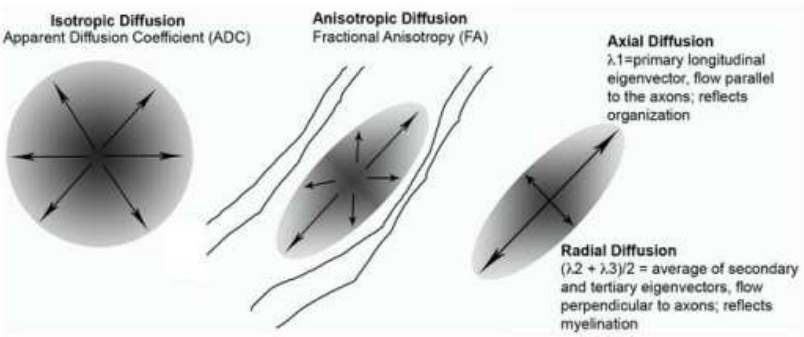

Figure 1. Illustrating Axial Diffusion, Radial Diffusion and Fractional Diffusion [8]

Figure 1. Measurements of Diffusion Tensor Imaging

Note. This image was created to depict Axial, Radial, Anisotropic and Isotropic Diffusion in Diffusion Tensor Imaging. From Salbinih, S. N. F., Taib, N. H. M., Mustapha, M., Samsudin, A. H. Z., Yusoff, M. N. S., Shuaib, I. L., & Isa, S. M. (2019, November). Analysis of genu and splenium of the corpus callosum: comparison between healthy subjects with and without Leukoaraiosis. In Journal of Physics: Conference Series (Vol. 1372, No. 1, p. 012039). IOP Publishing.

CHAPTER 2

METHODS

This study employed archival data that was recently uploaded to the Parkinson's Progression Markers Initiative (PPMI). PPMI is an extensive dataset containing bio-samples, genetic data, brain images and more from tens of thousands of subjects collected by over 100 clinical trials/research studies. Participants for this study were based on the following criteria: Subjects were 18-50 years old; subjects had both MRI and DTI images collected, and the subjects had PD. After doing the search in the Image & Data Archive (IDA) there were 65 subjects who fit the selection criteria, their MRI and DTI images were downloaded in a NIfTI format. Additionally, neuropsychological data had to be downloaded so that there were associated scores for the Montreal Cognitive Assessment (MoCA), Lexical Fluency (LF), and Modified Semantic Fluency (MSF) for the selected subjects. All imaging data was downloaded to a local hard drive, then moved onto Arizona State University's Research Computing server. Through ASU's research computing various software such as Fsl, AFNI, Mricron, and Python packages can be used remotely and be done at a much faster rate than what can normally be done a regular computer/laptop.

After downloading both the imaging data, each subject's images had to be concatenated/merged to make one NIfTI scan. This was done via a single command (flsmerge) that was done for each subjects separately. Because each subject had 33 or 65 NIfTI files these concatenated files were created individually. Next, a mask of each subject's brain had to be made (a binary mask which contains 0's for outside of the brain and 1's for inside) to be able to tell what was and was not brain.

With the masks made for each subject, then preprocessing could continue using a command from Fsl called “eddy”. This function corrected for eddy current induced distortions and any movement the subject had while in the scanner. This step in preprocessing by far was took the longest to compute. In order to run eddy for each subject, there needed to be a acquisition parameter (which indicates how the data was collected), a bvecs file (which is a text file that has the normalized vectors that define the direction of the diffusion weighting), a bvals file (another text file with b-values that describe how much you excite the water molecules in the brain during scanning), an index file that contains the indices for all volumes in the NIfTI image file, and finally the mask that was previously made in the first step of preprocessing. Within the subjects there was DTI images for, there was a small fraction of subjects that had non-gated DTI images. This meant that the files mentioned had to be different from the majority of subjects who had gated DTI images.

Once eddy was performed for each participant then the FA values could finally be generated using another command from Fsl called dtifit. To make sure that participant’s brain images could be compared, tested with and against each other image registration had to be done and “warp” each image to a standard MNI space. This image registration geometrically aligned each participant’s brain image with the MNI template to allow for comparison (Toga & Thompson, 2001).

One of the last steps executed was confirming that every participant that there was a preprocessed/processed brain image for, there were also cognitive test scores for. Unfortunately, there were some participants who had 2 out of the three tests, some who had 1 out of the three, and with this last criterion, more than half of the participants were

excluded from the study. The reason that each participant did not have scores for all three cognitive tests is not entirely clear and could be for a multitude of reasons ranging from inability to perform/complete the assessment to having the assessment not being needed for whichever study or clinical trial that specific subject was a part of. After excluding those who did not meet all the criteria 30 subjects remained. For those 30 subjects cutoffs were calculated to divide people into either scoring low or scoring high on each individual cognitive test. For the MoCA, since the range of scores was relatively small (24-30) the cutoff was if a person scores higher than 29 then they were placed in the "high" group everyone else was in the "low" group. The MSF was a test in which participants had to name as many animals in one minute as they could, as many vegetables as they could in one minute and as many fruits as they could in one minute. The totals were summed up for a total score. For this MSF test, subjects were placed in the "low" or "high" group was based on the cutoff of the median score of 57 which was almost an even split. Lastly, for the LF test the cut off for the "low" or "high" split was greater than or equal to 41.

With the participants split up into two groups based on how they scored on the cognitive test it was then possible to run t-tests comparing the groups with their associated images (refer to A1. and A2.). This statistical analysis was also done using an AFNI program via ASU's research computing, called 3dttest which allows for the comparison of 3 dimensional datasets/images. To visualize the data and view which group had high FA values, another AFNI program was utilized (using the command "afni&"). This program allowed for setting the underlay and overlay of the data comparison. With this program the criteria for significance were implemented. The

clusters that were 30 or more voxels were considered significant which were found by setting the p-value to 0.01. It was with this program that every figure was generated from which display the significant clusters found from the comparison of groups for each cognitive test. AFNI generated an interactive table of cluster results (refer to B1.,B2., and B3.) that indicate which group had high FA values, where in the brain the significant clusters were found, and what percentage of the cluster was made up by certain brain regions.

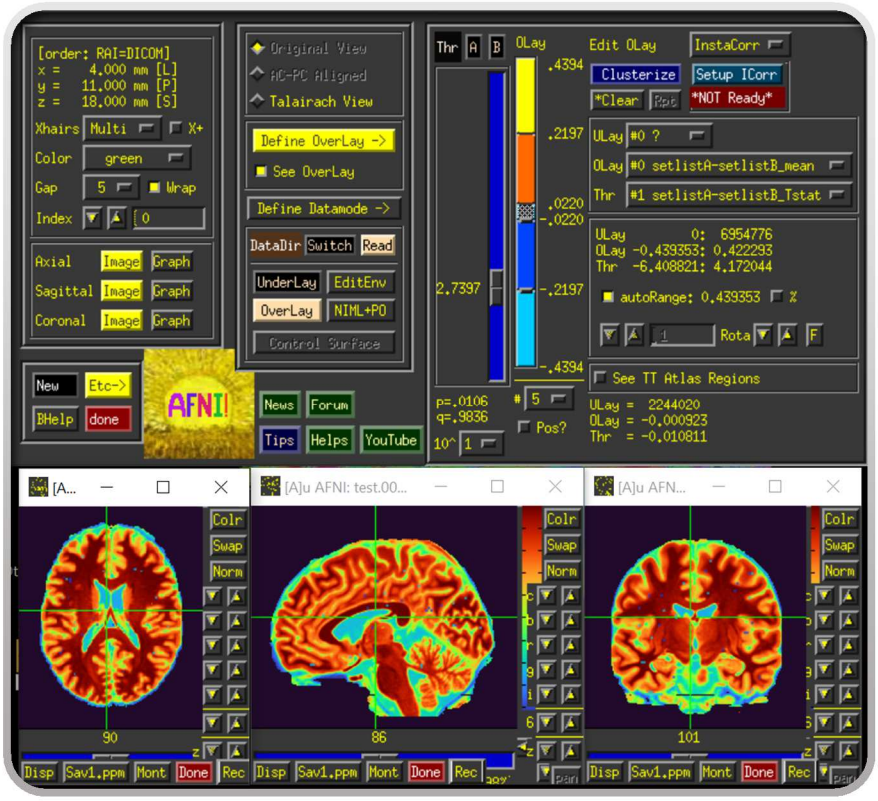

Figure 2. Graphic User Interface for AFNI

CHAPTER 3

RESULTS

It was found with the 3dttest that when comparing the FA values between PD subjects who score low or high there was a significant difference. With the p-value at 0.01 and the number of voxels set at 30 for significance, the LF-high group demonstrated increased FA in 3 significant clusters (see Table A1.). The LF-low group did not demonstrate increased FA for any clusters. For cluster number 1 (Figure 3a.) 16.8% was

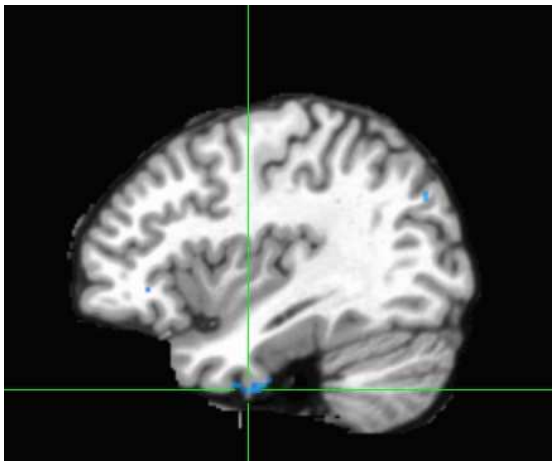

Figure 3a. Depicting a sagittal view the largest significant cluster (in blue) for the comparison of FA values between the LF low and high test score group.

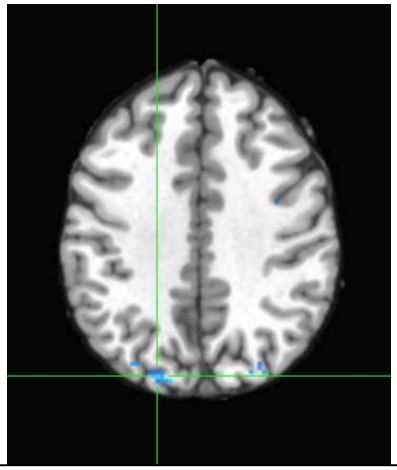

Figure 3b. Depicting an axial view the second largest significant cluster (in blue) for the comparison of FA values between the LF low and high test score group.

accounted for by the left hemisphere fusiform face area and the left hemisphere inferior temporal lobe.

With cluster number 2 (Figure 3b.) it was largely accounted for by the left hemisphere superior parietal lobule (66.6%), the left hemisphere's superior occipital lobe (49.6%), and the left hemisphere superior occipital gyrus.

Lastly, for cluster 3 (refer to Figure 3c.), 37.5% of the cluster was accounted for by the orbital frontal cortex and right hemisphere orbital gyrus accounted for 34.1% of the cluster

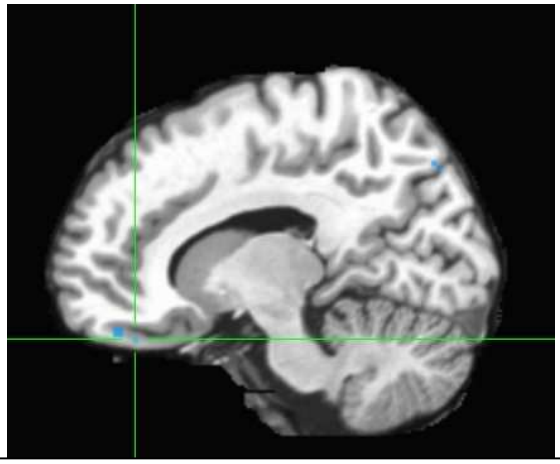

Figure 3c. Depicting an axial view the third largest significant cluster (in blue) for the comparison of FA values between the LF low and high test score group.

Employing the same significance criteria as the LF test there was a significant difference between the PD subjects who had high vs low MoCA test scores. From this 2 sample t-test, it was found that PD subjects in the MoCA-low group had on average, increased FA values when compared to the MoCA-high group.

There were two clusters with over 30 voxels that were significant, the first cluster (Figure 4a.) was found to be accounted 100% by right hemisphere cerebral white matter

(refer to Table B2.). The right hemisphere middle and inferior temporal gyrus accounted for 35.8% of the second cluster (Figure 4b.).

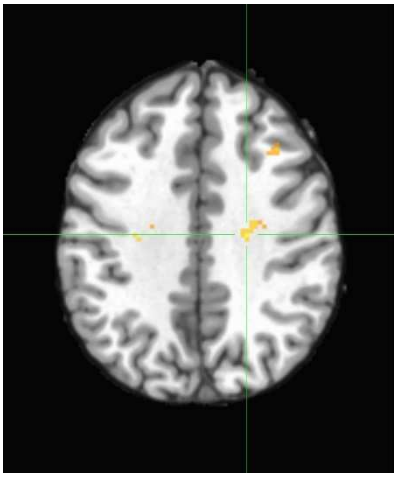

Figure 4a. Depicting an axial view the largest significant cluster (in yellow) for the comparison of FA values between the LF low and high MoCA test score group.

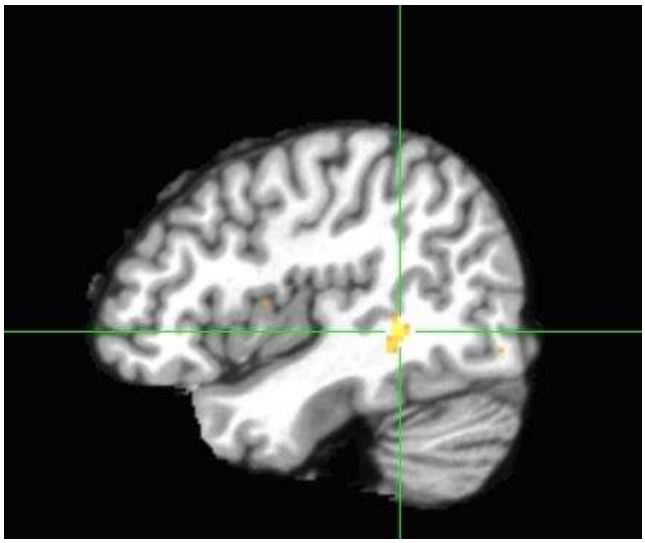

Figure 4b. Depicting a sagittal view the second largest significant cluster (in yellow) for the comparison of FA values between the LF low and high MoCA test score group.

Finally, there were no significant differences between the FA values of the PD subjects who scored low or high on the MSF test. The cluster closest to being significant was 17 voxels. For this cluster the fusiform face area accounted for 77.7% of the cluster (see Table B3.). No post-hoc analyses were performed for this data.

CHAPTER 4

CONCLUSIONS

The results from the first t-test showed that there was a significant difference in FA values between PD subjects who scored low versus high on the LF test. For this comparison, subjects who scored high on the LF test on average had higher FA values (closer to 1) than subjects who scored low. The results indicate that the LF-high group likely has increased white matter integrity in the left hemisphere's fusiform face area and inferior temporal lobe. Additionally, the results provide evidence that the subjects who score high on the LF test might also have increased white matter integrity in the superior parietal lobule.

From the second t-test, there was a significant difference in the FA values between PD subjects who scored low versus high on the MoCA, only for this comparison the clusters of high FA values were for the subjects that scored low. This could mean that for those who scored low on the MoCA that they likely had greater white matter integrity in their right hemisphere more specifically in the middle and inferior temporal gyrus. T-test results comparing the FA values of PD subjects that score high or low on the MSF did not have any significant differences between the two groups. This could provide more evidence for the theory that semantic knowledge is said to be spread out across the brain it and not localized in one "hub." Overall, aside from the MSF t-test, the results from these statistical analyses support the original hypothesis that there would be a difference between the FA values of PD subjects that score either high or low on specific cognitive tests. The results from these three ttests do not all support the second hypothesis of this study where the expected region the FA values would be different/clustered in would be

mainly in the temporal lobe. The comparison tests that used the LF test and the MoCa data did find significant clusters, but it cannot be stated that the majority of the clusters were in the temporal lobe.

The reason that observing the differences of FA values between PD subjects who score lower or higher on cognitive tests is important is because multiple studies have shown that FA and MD values have been correlated with cognition and mental faculties (Delgado□Alvarado et al., 2016). Chen et al. (2015) found that the assessment scores on the MoCA and FA values of white matter tracts in the midbrain in the left hemisphere were positively correlated.

CHAPTER 5

DISCUSSION

This is the first study to look at the differences of DTI in PD across LSF and MSF. Although these tests are representative of specific parts of executive function, they might provide clues into how to characterize or look for markers of decline in PD. We found that increased FA in specific regions involved in facial processing and word retrieval. This finding can add to the growing PD literature because while there is research that focuses on cognition and word retrieval of PD patients there are few that observe the relationship between white brain matter integrity in both cognition and facial processing.

Zhang and Burock (2020) conducted an extensive systematic review on DTI and PD subjects a section of their review discussed the findings from PPMI and stated that results of some studies found that PD has higher FA than healthy controls. This study had findings that overlapped with Zhang and Burock (2020) in that LF-high group also had increased/high FA. Li et al. (2022) conducted a study in which they used the MoCA and one other cognitive test and evaluated the white matter integrity of PD patients and found results that were dissimilar of the results found in this study . The researchers had found that for the PDMCI (PD patients who had a MCI) group had significantly lower MoCA scores than the PD group without a MCI and more damaged white matter integrity in related brain areas (e.g. right parietal and left occipital lobes). This study had found increased white matter integrity in those who scored high on the MoCA.

There are multiple regions that are associated with low FA and increased white matter degeneration in PD patients who have cognitive decline such as the inferior parietal lobe, frontal lobe and temporal lobes, these regions in particular has been shown

to have more decline in early PD (Silbert & Kaye, 2010). The results of this study found multiple clusters which involved these three lobes. Although, most of the studies in the PD literature that discuss these regions are cited heavily and have large sample sizes; and the current study did not have a large sample size, the results were still consistent. With this in mind it is interesting to see that LF tests could potentially be viable test when trying to catch early cognitive decline in PD.

Lastly, it is important to note that there was overlap between the regions Lucas-Jiménez et al. (2015) found to be associated with processing verbal memory in PD subjects and the current study's findings on where the LF-high group had significant clusters. Lucas-Jiménez et al. (2015) reported that the oribitofrontal cortex (the region the LF-high group had significant clusters in with increased FA) to be responsible in processing verbal memory in PD subjects.

This study had three main limitations, the first being that all of the subjects and their data was drawn from a database, this made it difficult to have much control on what kind of scanner participants were in to collect the brain imaging data. Using archival data also posed an issue when it came to having all of the necessary cognitive test scores for the initial group of PD subjects that were selected for this study. Another limitation of this study was that specific functions, commands, and or programs that were run via ASU's research computing were difficult to load and use because all preprocessing and processing of data was completed on a laptop with an average RAM. In any future studies that try to replicate any component of this study should be advised to use a laptop/computer that has a higher capability than a standard laptop. The third limitation is

that we did not use a control group for comparison to see whether the FA values are different from controls in these groups.

A future direction that stems from this study that would be worth research would be looking into a subset of the PD population, those who have mild cognitive impairments (MCI) and comparing them to a PD control and a neurotypical/healthy control. It could be potentially beneficial to research which cognitive test would be able to identify those who have a MCI versus those who do not, and this would still incorporate DTI and FA values and or MD values. Bledsoe et al. (2018) conducted a study similar to this proposed study only they did not incorporate a PD control who did not have MCI. From the current literature on PD and cognitive impairment it appears that around 20% of people who are diagnosed with PD already have MCI (Aarsland et al,. 2021).

REFERENCES

Aleksovski, D., Miljkovic, D., Bravi, D., & Antonini, A. (2018). Disease progression in Parkinson subtypes: the PPMI dataset. Neurological Sciences, 39(11), 1971-1976.

Aarsland, D., Batzu, L., Halliday, G. M., Geurtsen, G. J., Ballard, C., Ray Chaudhuri, K., & Weintraub, D. (2021). Parkinson disease-associated cognitive impairment. Nature Reviews Disease Primers, 7(1), 1-21.

Atkinson-Clement, Cyril, et al. "Diffusion tensor imaging in Parkinson's disease: review and meta analysis." Neuroimage: Clinical 16 (2017): 98-110.

Bledsoe, I. O., Stebbins, G. T., Merkitch, D., & Goldman, J. G. (2018). White matter abnormalities in the corpus callosum with cognitive impairment in Parkinson disease. Neurology, 91(24), e2244-e2255.

Chen, B., Fan, G. G., Liu, H., & Wang, S. (2015). Changes in anatomical and functional connectivity of Parkinson's disease patients according to cognitive status. European journal of radiology, 84(7), 1318-1324.

Chen, Honglei and Beate Ritz. "The search for environmental causes of Parkinson's disease: Movingforward." Journal of Parkinson's disease 8.s1 (2018): S9-S17.

Delgado□Alvarado, M., Gago, B., Navalpotro□Gomez, I., Jiménez□Urbieta, H., & Rodriguez□Oroz, M. C. (2016). Biomarkers for dementia and mild cognitive impairment in Parkinson's disease. Movement Disorders, 31(6), 861-881.

Gayed, Isis, et al. "The impact of DaTscan in the diagnosis of Parkinson disease." Clinical nuclearmedicine 40.5 (2015): 390-393.

Li, Q. Q., Wu, K., Xu, J. L., & Yin, L. (2022). White matter damage in patients with mild cognitive impairment in Parkinson's disease. Quantitative Imaging in Medicine and Surgery, 12(2), 1290.

Lucas-Jiménez, O., Díez-Cirarda, M., Ojeda, N., Peña, J., Cabrera-Zubizarreta, A., & Ibarretxe-Bilbao, N. (2015). Verbal memory in parkinson's disease: a combined DTI and fMRI study. Journal of Parkinson's disease, 5(4), 793-804.

NIH. "Parkinson's Disease." National Institute on Aging, U.S. Department of Health and Human Services, https://www.nia.nih.gov/health/parkinsons-disease.

Salbinih, S. N. F., Taib, N. H. M., Mustapha, M., Samsudin, A. H. Z., Yusoff, M. N. S., Shuaib, I. L., & Isa, S. M. (2019, November). Analysis of genu and splenium of the corpus callosum: comparison between healthy subjects with and without Leukoaraiosis. In Journal of Physics: Conference Series (Vol. 1372, No. 1, p. 012039). IOP Publishing.

Silbert, L. C., & Kaye, J. (2010). Neuroimaging and cognition in Parkinson's disease dementia. Brain pathology (Zurich, Switzerland), 20(3), 646–653. https://doi.org/10.1111/j.1750-3639.2009.00368.x

Toga, A. W., & Thompson, P. M. (2001). The role of image registration in brain mapping. Image and vision computing, 19(1-2), 3–24. https://doi.org/10.1016/S0262-8856(00)00055-X

Zhang, Y., & Burock, M. A. (2020). Diffusion Tensor Imaging in Parkinson's Disease and Parkinsonian Syndrome: A Systematic Review. Frontiers in neurology, 11, 531993. https://doi.org/10.3389/fneur.2020.531993

APPENDIX A

STEPS FOR STATISTICAL ANALYSIS

Steps In Statistical Analysis

- Determine what the median test score value for each test
- Divide participants into two groups depending on whether they score high or low based on the median value
- Open 3dttest with command “uber_ttest.py” which is an AFNI program
- Input which test was going to be used for the FA comparison
- Select the mask that was going to be used (a MNI standard space)
- Select the participants who scored low on the specific test
- Select the participants who scored high on the specific test
- Set the data index/labels to 0 for both subsets
- Click on the “generate processing script” and then execute the processing script

Figure A1. List of steps taken to run statistical analysis

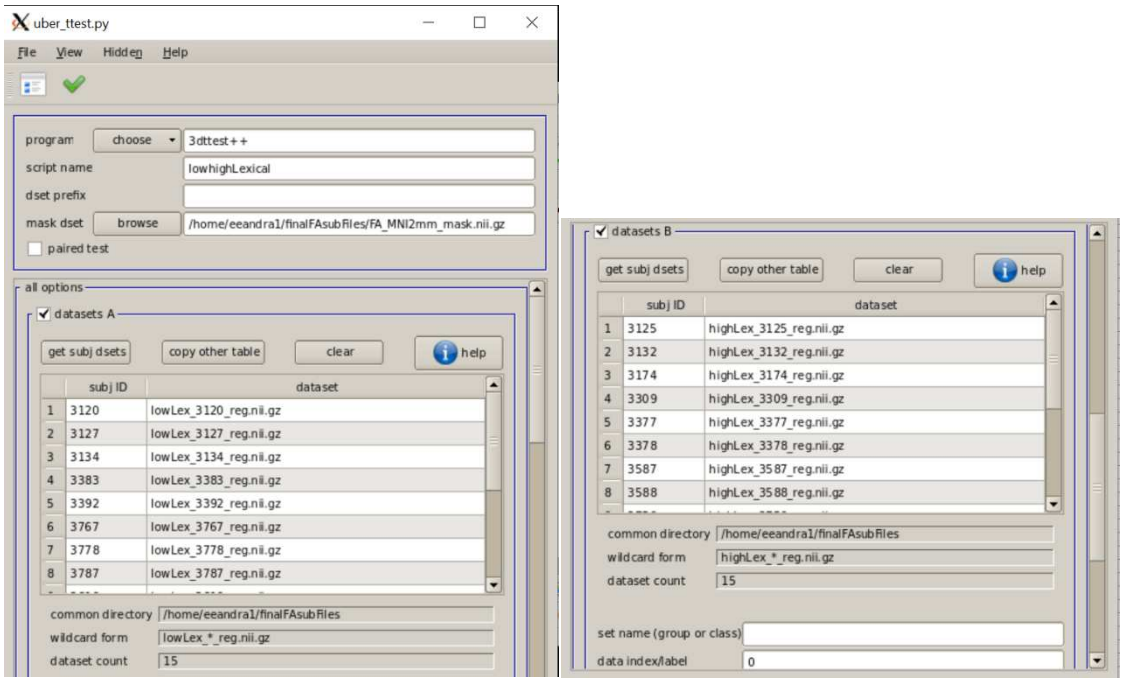

Figure A2. Graphical user interface for selecting participants for 3d-ttest

APPENDIX B

CLUSTER TABLES FOR PD SUBJECTS/EACH COGNITIVE TEST

```
AFNI interactive cluster table
 3dClusterize -nosum -1Dformat -inset
/home/eeandra1/finalFAsubFiles/Lexical_Fluency_group_results/test.00
1.3dttest++/test.results/lowvshighLexical+tlrc.HEAD -idat 0 -ithr 1
-NN 3 -clust_nvox 10 -bisided -2.7397 2.7397
Coordinate order = RAI
```

Voxels	CM x	CM y	CM z	Peak x	Peak y	Peak z
73	+34.0	+5.9	-43.5	+38.0	+6.0	-44.0
50	+17.7	+83.9	+38.6	+20.0	+84.0	+38.0
37	-9.7	-44.2	-21.9	-12.0	-40.0	-24.0
26	-29.9	+80.3	+36.7	-26.0	+82.0	+40.0
22	-35.3	+15.4	+61.1	-38.0	+16.0	+60.0
20	+30.0	+74.7	+42.7	+32.0	+78.0	+38.0
18	-22.6	-38.1	+44.1	-22.0	-36.0	+46.0
17	+35.7	+77.7	+32.7	+42.0	+74.0	+32.0
17	-15.7	+77.6	+45.2	-10.0	+80.0	+46.0
16	-64.8	+23.9	+0.2	-66.0	+22.0	+2.0
14	+1.6	+42.0	+68.7	+2.0	+36.0	+70.0
14	+32.4	-31.5	-0.2	+32.0	-32.0	+0.0
11	-37.4	+3.9	+33.3	-36.0	+4.0	+34.0
10	+52.3	+42.1	-25.2	+54.0	+42.0	-22.0
10	-37.0	+87.5	+9.3	-36.0	+88.0	+12.0
10	-5.1	+31.5	+12.8	-2.0	+34.0	+10.0

Table B1. Cluster table for Lexical Test (low vs high group) included 16 clusters with at least 10 voxels.

```
 AFNI interactive cluster table
 3dClusterize -nosum -1Dformat -inset
/home/eeandra1/finalFAsubFiles/MoCA_group_results2/test.001.3dttest+
+/test.results/lowvshighMoca+tlrc.HEAD -idat 0 -ithr 1 -NN 3 -
clust_nvox 10 -bisided -2.7397 2.7397
Coordinate order = RAI
```

Voxels	CM x	CM y	CM z	Peak x	Peak y	Peak z
48	-24.0	+17.6	+34.2	-22.0	+16.0	+38.0
45	-43.7	+42.9	-2.6	-44.0	+44.0	-2.0
27	-25.2	+6.0	-8.7	-24.0	+6.0	-10.0
26	-18.5	+69.1	-12.5	-26.0	+68.0	-14.0
26	+27.3	+35.2	+15.5	+26.0	+36.0	+16.0
23	+4.9	-1.0	-12.1	+0.0	+6.0	-12.0
22	-14.3	-22.4	+15.3	-16.0	-24.0	+16.0
18	-20.0	+40.9	-42.7	-20.0	+38.0	-44.0
16	+5.7	-29.0	+24.8	+6.0	-28.0	+28.0
16	-34.8	-21.5	+35.9	-36.0	-20.0	+36.0
15	-37.9	-29.6	+20.1	-38.0	-28.0	+20.0
14	-9.1	+48.9	-43.8	-8.0	+48.0	-44.0
14	-19.3	+77.9	-44.5	-20.0	+74.0	-46.0
14	-21.2	+10.9	-24.8	-24.0	+14.0	-30.0
14	+25.4	-22.0	-8.4	+24.0	-22.0	-8.0
14	-13.9	+90.5	-2.0	-14.0	+92.0	-2.0

Table B2. Cluster table for the MoCA (low vs high group) included top 16 clusters with at least 10 voxels

```
 AFNI interactive cluster table
 3dClusterize -nosum -1Dformat -inset
/home/eeandra1/finalFAsubFiles/Modified_Semantic_VLT_group_results/t
est.001.3dttest++/test.results/lowvshighVLT+tlrc.HEAD -idat 0 -ithr
1 -NN 3 -clust_nvox 10 -bisided -2.7397 2.7397
Coordinate order = RAI
Voxels  CM x   CM y   CM z  Peak x Peak y Peak z
------ ------ ------ ------ ------ ------ ------
     17  -33.6  +10.2  -35.3  -36.0  +12.0  -36.0
     15  +15.0  +21.2   +1.2  +16.0  +24.0   +0.0
     14  +27.9  -45.1  -12.2  +30.0  -44.0  -10.0
     13  -36.6  +36.9  -33.7  -38.0  +36.0  -38.0
     12  +35.7  +38.2  -34.6  +36.0  +36.0  -36.0
     11  +19.5  -60.9   +9.4  +22.0  -60.0  +10.0
     11  -15.1  +36.8  +29.8  -16.0  +34.0  +30.0
     10  -12.1  +60.4  -43.0  -12.0  +60.0  -42.0
     10  -15.5  +85.5  -16.1  -14.0  +82.0  -14.0
     10  +35.6  +29.6  +62.6  +36.0  +36.0  +62.0
```

Table B3. Cluster table for the MoCA (low vs high group) included 10 clusters with at least 10 voxels