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Prediction of Financial Capacity using Diffusion Compartment Imaging

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Prediction of Financial Capacity using Diffusion Compartment Imaging

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by

Lok Yi Tai

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Lok Yi Tai

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Prediction of Financial Capacity using Diffusion Compartment Imaging

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Advisor's Signature

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Date

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The Designated Project Committee Approves the Project Titled

Prediction of Financial Capacity using Diffusion Compartment Imaging

by

Lok Yi Tai

APPROVED FOR THE DEPARTMENT OF COMPUTER SCIENCE

SAN JOSÉ STATE UNIVERSITY

May 2021

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ABSTRACT

Prediction of Financial Capacity using Diffusion Compartment Imaging

by Lok Yi Tai

Financial Capacity (FC) is the ability to manage one's financial affairs, which is essential for autonomy and independence particularly for aging adults. Since dementia develops gradually, it is often difficult to detect the early signs that this cognitive dysfunction is developing This project aims to use Neurite orientation dispersion and density imaging (NODDI) to identify the white matter tracts that are associated with FC. Diffusion Tensor Images (DTI) and T1 Magnetic Resonance Images (MRI) of 18 Alzheimer's Disease (AD) subjects, 47 Mild Cognitive Impaired (MCI) subjects, and 193 healthy control (CN) are compared to neuropsychological tests. Orientation Dispersion Index (ODI) values are derived using NODDI analysis of the DTI and MRI. This study found that the ODI values in the cingulum have the highest association with FC. In conclusion, our study suggested that the degradation of white matter and episodic memory dysfunction were most strongly associated with reduced FC.

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CHAPTER 1

Introduction

Dementia develops slowly and insidiously, gradually causing older adults to lose their ability to manage their finances, leaving them susceptible to financial errors and fraud [1]. Studies have also shown that the loss of financial capacity is one of the earliest symptoms of Alzheimer's disease (AD) [2]. Patients with AD and related dementias (ADRD) suffer from loss of financial capacity years before diagnosis [3]. ADRD patients are more likely to miss bill payments as early as 6 years before their diagnosis and can develop subprime credit scores as early as 2.5 years prior to diagnosis [3]. Poor judgment and decision-making are evident in elderly adults with ADRD, especially when managing and performing essential financial matters, making them highly susceptible to scams [4]. This is the case with or without cognitive impairment. It is estimated around $30 billion is lost each year due to scams and fraud cases in adults 50 years or older [4].

Financial capacity is a complex skill that requires the ability to perform a large range of daily activities, that range from simple tasks like counting coins to more complex tasks such as making investment decisions [1]. Intact financial capacity is critical to autonomy and independence for the elderly, especially if they might lose their entire life-long savings at a time when these funds are vital to their survival as they become less independent and need care. According to Triebel et al., the warning signs of diminished financial capacity include memory lapses, disorganization, declines in checkbook management skills, arithmetic mistakes, conceptual confusion, and impaired judgment [1].

Marson et al. have developed a Financial Capacity Instrument (FCI) metric to quantify the financial capacity of adults, which has been used to study patients with dementia [5]. The FCI assesses tasks like grocery shopping, counting coins, bank statement management, and check writing to estimate the financial capacity of the older adult. The previous study has shown that FCI is sensitive to financial deficits in AD populations. Griffith et al. used FCI to show that there are mild financial deficits in patients with amnestic mild cognitive impairment (MCI), and Marson

et al. showed that there are more global deficits in patients with mild Alzheimer's Disease (AD) [5, 6].However, the FCI test takes around an hour to finish. A shorter test, Financial Capacity Instrument Short Form (FCI-SF), which only takes around 15 minutes, was later developed to quickly screen the financial capacity of an individual. The FCI-SF shows a high correlation with the FCI long-form test [7].

Brain atrophy has been related to decline in financial capacity in AD patients and patients with mild cognitive impairment (MCI) [8, 9, 2]. Stoeckel et al. found reduced medial frontal cortex volume and declines in simple attention are associated with FCI score among mild AD patients[8]. Giannouli et al. showed there is a high correlation between grey matter volume of right amygdala and left angular gyrus and FCI score, which suggested that emotion, as well as arithmetic skills are involved in financial capacity[2]. Gerstenecker et al. investigated the association between white matter connectivity and financial capacity using traditional Diffusion Tensor Imaging (DTI) metrics and found that severity gradient decline in white matter shows association with FCI scores[2]. However, the use of traditional DTI metrics has limitation because they are based on the assumption of a simple underlying Gaussian diffusion process[10].

Neurite orientation dispersion and density imaging (NODDI), which uses a non-Gaussian biophysical model, can provide higher sensitivity to the non-monoexponential diffusion in the brain, in comparison with traditional DTI measures[11]. NODDI is sensitive to white matter degradation in differentiating MCI patients and normal healthy adults [12]. NODDI parameters are also more sensitive to measures of tau pathology of Alzheimer's disease than traditional DTI measures[10].

The purpose of this study is to use NODDI analysis to study the white matter integrity of AD patients, MCI patients, and healthy older adults to predict their FCI score. If FCI scores of older adults can be predicted accurately by using imaging and standard neuropsychological tests, then potentially patients can take action to build financial protections. For example older adults could have someone monitor their financial decision or they could place limits on their ability to deplete completely their bank holdings, thus protecting them from fraud and bankruptcy.

CHAPTER 2

Background

This chapter gives a detailed description of how the Financial Capacity Instrument (FCI) measures the ability to handle finances. It also describes how neurite orientation dispersion and density imaging (NODDI) provides a more sensitive measurement than traditional Diffusion Tensor Imaging measurement. It gives a detailed explanation of how older adults are affected by Alzheimer's disease and mild cognitive impairment. The chapter concludes with a description of the technical gaps, left by previous work, that the results presented here begins to address.

2.1 Financial Capacity Instrument (FCI)

Financial Capacity Instrument measures the financial decision making in 14 tasks across 6 domains, which include Basic Money Skills, Financial Conceptual Knowledge, Cash Transaction, Checkbook Management, Bank Statement Management, and Financial Judgment. It consists of simple tasks like counting coins and 1-item grocery purchase to complex tasks like writing a check and making financial decisions. FCI has been used in Alzheimer's and mild cognitive impaired patients[5, 13]. As FCI test took around an hour to finish, which was burdensome for populations with cognitive impairment, a shorter version of FCI (FCI-SF) was created by exacting the most strongly associated items in the FCI test with progression to AD[14]. The FCI-SF test measures only 37-items compared to 105 items in the FCI test, and only takes around 15 minutes to administer. FCI-SF has 5 score components, Metal Calculation, Financial Conceptual knowledge, Single Checkbook/Register Task, Complex Checkbook/Register Task and Using Bank Statement. The total score of the FCI-SF is 74, where a higher score indicates better performance in handling finances. Besides the performance score, FCI-SF also record the time taken for each task. As shown in Table 1 and 2, the FCI-SF test does not include cash transactions and financial judgment. The basic monetary skills domain in the FCI test is also simplified into the Mental Calculation section which involves counting nickels and quarters.

Table 1: Description of Financial Capacity Instrument Domains and Tasks[5]

	Task Description	Task Difficulty
Domain 1: Basic Monetary Skills		
Task 1a: Naming coins/currency	Identify specific coins and currency	Simple
Task 1b: Coin/currency relationships	Indicate relative monetary values of coins and/or currency	Simple
Task 1c: Counting coins/currency	Accurately count groups of coins and/or currency	Simple
Domain 2: Financial Conceptual Knowledge		
Task 2a: Define financial concepts	Define a variety of simple financial concepts	Complex
Task 2b: Apply financial concepts	Practical application/computation using financial concepts	Complex
Domain 3: Cash Transactions		
Task 3a: 1-Item grocery purchase	Enter into simulated 1-item transaction; verify change	Simple
Task 3b: 3-Item grocery purchase	Enter into simulated 3-item transaction; verify change	Complex
Task 3c: Change/vending machine	Obtain exact change for vending machine use; verify change	Complex
Domain 4: Checkbook Management		
Task 4a: Understand checkbook	Identify and explain parts of check and check register	Simple
Task 4b: Use checkbook/register	Enter into simulated transaction and make payment by check	Complex
Domain 5: Bank Statement Management		
Task 5a: Understand bank statement	Identify and explain parts of a bank statement	Complex
Task 5b: Use bank statement	Identify aspects of specific transactions on bank statement	Complex
Domain 6: Financial Judgment		
Task 6a: Detect fraud risk	Detect and explain risks in mail fraud solicitation	Simple
Task 6b: Make investment decision	Understand investment situation/options; make investment decision	Complex

Table 2: Description of Financial Capacity Instrument Short Form Tasks[5]

Task	Score Range
Mental Calculation (Items 1-2)	
1. Nickels	0 - 2
2. Quarters	0 - 2
Financial Conceptual Knowledge Score (Items 3-6)	
3. Budget	0 - 2
4. Health Care Insurance Problem	0 - 2
5. a. Tax Credit	0 - 2
5. b. Tax Credit	0 - 2
6. Payee	0 - 2
Single/Checkbook Register (Items 7-16)	
7. Payee section	0 - 2
8. $ amount section (numerical)	0 - 2
9. $ amount section (written)	0 - 2
10. Signature of payer	0 - 2
11. Date properly written	0 - 2
12. Number of check	0 - 2
13. Date properly entered	0 - 2
14. Payee section	0 - 2
15. Amount of check	0 - 2
16. New account balance	0 - 2
Complex Checkbook/Register (Items 17-30)	
17. Number of check	0 - 2
18. Date properly entered	0 - 2
19. Payee section	0 - 2
20. Amount of check	0 - 2
21. New Account Balance	0 - 2
22. Number of check	0 - 2
23. Date properly entered	0 - 2
24. Payee section	0 - 2
25. Amount of check	0 - 2
26. New Account Balance	0 - 2
27. Date properly entered	0 - 2
28. Description of Transaction	0 - 2
29. Amount of deposit	0 - 2
30. New account balance	0 - 2
Bank Statement Management Score (Items 31-37)	
31. a. Bank Statement	0 - 2
31. b. Bank Statement	0 - 1
32. Interest Rate	0 - 2
33. Time Period	0 - 2
34. Checks Cleared	0 - 2
35. Quarterly Interest	0 - 2
36. Gaps in Check Sequence	0 - 2
37. Date of the Withdrawal Payment	0 - 2

2.2 Diffusion Tensor Imaging (DTI) and NODDI

Diffusion Tensor Imaging (DTI) is a standard diffusion magnetic resonance imaging (MRI) technique that has been used to study various neurological diseases[15]. Different from T1 weighted MRI, which represents the grey matter and white matter volumes of the brain, DTI focuses on the white matter tracts, which are made up of axons and their surrounding myelin sheath[16]. DTI analysis was originally developed in 1985 and became popular over the years to the point that there were over 12000 publications related to DTI in the year 2018 [16]. DTI achieves its imaging purpose by detecting the direction over which water molecules diffuse in the brain. There are two main parameters that are used in studies - Mean Diffusivity (MD) and Fractional Anisotropy (FA). FA is a measurement of the proportion of water diffusing freely along a white matter tract, which implies the integrity of a tract[16]. Healthy white matter tracts with myelinated axons tend to have high FA values. Despite the fact that FA and MD have been shown to be sensitive in measuring microstructural tissue change in the brain during normal aging or onset and progression of neurological disease, the FA value is also affected by other tissue microstructural changes, for example, a change in neurite orientation distribution[15].

Neurite orientation dispersion and density imaging (NODDI), an algorithm that aims to provide a more sensitive measurement than FA, was developed by Zhang et al[17]. It measures the neurite density and orientation dispersion using an orientation-dispersed cylinder model[17]. NODDI gives a summary statistic value called the orientation dispersion index (ODI), which is a value ranging from 0.0 to 1.0 and it is calculated per voxel. An ODI value of 0 means there is no dispersion while 1 means maximum dispersion. ODI values in white matter are useful in measuring brain connectivity by quantifying the bending and fanning of axons[15]. It can also help to measure the number of crossing fibers [18]. Unlike FA and MD, ODI values are also useful in grey matter in that it quantifies the pattern of sprawling dendritic processes [17]. Jones has shown that NODDI provides a sensitive measurement for distinguishing MCI subjects from healthy older adults [12]. The in vivo diffusion MRI study done by Colgan et al. shows that compared to traditional DTI

measures, NODDI is more related to the level of tau protein in grey matter, which is one of the pathological hallmarks of AD.

2.3 Alzheimer's Disease and Mild Cognitive Impairment

Alzheimer's disease (AD) is a neurodegenerative disorder that is common among aging populations [19, 17]. Common symptoms of AD include gradual loss of episodic memory, difficulties in word-finding, and complex behavioral changes [19, 17]. It is diagnosed with a combination of history taken from patients and their family, neuropsychological tests that assess cognitive dysfunction, brain imaging, and medical tests, such as blood and urine tests [19, 17]. Other causes of dementia such as stroke, tumor, infection, and depression should be ruled out during the diagnosis of AD [19, 17]. There is no approved disease modifying treatment for AD and therapy consists of symptom management with medication [17]. Whereas there are clinical trials of potentially disease modifying treatments; however prevention of AD needs to be done years before the first symptom of AD appear [19]. Therefore, early diagnosis is very important and it can also help patients to participate in clinical trials, which are possible new treatments of Alzheimer's disease [17].Mild Cognitive Impairment (MCI) is often known as the preclinical stage of AD [20]. MCI patients have a higher chance of developing AD [20]. Therefore, some study has been done in finding biomarkers for MCI patients.

2.4 Neuropsychological Tests

This section covers the information of several neuropsychological tests that are used for screening for MCI or AD subjects.

2.4.1 Montreal Cognitive Assessment (MoCA)

Montreal Cognitive Assessment is a neuropsychological test that assesses different cognitive domains and is widely used for screening for MCI or AD subjects [21]. It is a one-page, 30-point test that can be administered in 10mins. MoCA scores range from 0 - 30, where a score of 26 or above is considered normal [22].

The MoCA assesses several cognitive domains:

1. The short-term memory recall task (5 points): two learning trials of five nouns and delayed recall after approximately five minutes.

2. Visuospatial abilities: a clock-drawing task (3 points) and a three-dimensional cube copy (1 point)

3. Executive functions: the trail-making B task (1 point), a phonemic fluency task (1 point), and a two-item verbal abstraction task (2 points).

4. Attention, concentration, and working memory: sustained attention task (target detection using tapping; 1 point), a serial subtraction task (3 points), and digits forward and backward (1 point each).

5. Language: naming of low-familiarity animals (e.g. lion, camel, rhinoceros; 3 points), repetition of two syntactically complex sentences (2 points), and the aforementioned fluency task.

6. orientation to time and place: asking the subject for the date and the city in which the test is occurring (6 points)

2.4.2 Rey's Auditory Verbal Learning Task (RAVLT)

Rey's Auditory Verbal Learning Test (RAVLT) is a neuropsychological test developed in the 1940s that it has widely used to assess episodic memory to study different neurological diseases such as Alzheimer's disease [23]. Studies have shown that the RAVLT test is sensitive to distinguish MCI and AD subjects from healthy controls [12, 23]. RAVLT assesses the ability to immediately recall by reading out a list of 15 words to the participant and ask the participant to recall as many words as he or she can remember. This process is repeated 5 times with the same list (Trial 1 to 5). A new list with 15 new words is then read aloud to the participant and the participant is asked to

recall all of the words(List B). Then, the participant is again asked to recall the words on the first list (Trial 6). After 30 minutes from the completion of List B recall, the participant is asked to recall the words from the first list (delayed recall).

There are 4 summary statistic measurements derived from the raw RAVLT score used in this project :

1. RAVLT immediate, the sum of the scores from trial 1 to trial 5

2. RAVLT Learning, the score of trial 5 subtract the score of trial 1

3. RAVLT Forgetting, the score of trial 5 subtract the score for delayed recall

4. RAVLT Percent Forgetting, RAVLT Forgetting divided by the score in Trial 5

2.4.3   Trail-Making Test

Trail-Making Test is a neuropsychological test that measures the visual search speed, scanning, speed of processing, mental flexibility, as well as executive functioning[24]. The test consists of two parts. In part A, the participant is asked to draw a line and connect the number in order on a piece of paper which have encircled number from 1 to 25 randomly distributed on the test sheet as shown in Figure 1. The time taken for the participant to connect all the dots is recorded as the score for part A of the Trail Making Test A. Part B is conducted similarly except for the fact that there are also letters on the test sheet as shown in bottom half of Figure 1. The participant is expected to connect the dots in order while alternating between letters and numbers. Time taken for the participant to connect all the dots is also recorded as the score for part B.
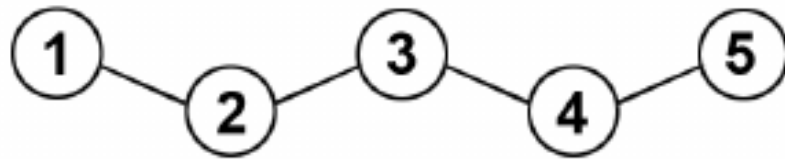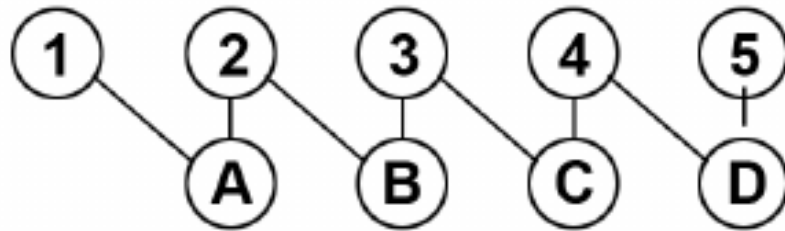
Figure 1: Trail Making Test A and B[24]

2.5 Technical Gap

It is still unclear how financial capacity is affected by the structural integrity in the brain due to inadequate research done in this field. Using traditional DTI measurements did not give a full picture of how white matter in the brain affects the FCI score. Traditional DTI model is based on the assumption of a simple Gaussian diffusion process that it is not able to provide higher sensitivity to the non-monoexponential diffusion in the brain[10]. To close this technical gap, NODDI, which is a model that uses a biophysical model based on non-Gaussian diffusion process, can be used to study how white matter degradation affects the financial capacity of older adults[17].

CHAPTER 3

Method

In this project, we hypothesize that financial capacity is related to the integrity of the white matter in the brain, such that NODDI measures of white matter integrity will be correlated with FCI scores. Because different brain regions are known to be functionally specialized, we further expect that only some white matter (WM) tracts will show this correlation, pinpointing which area of the brain are necessary for good financial decision-making. We also hypothesize that the reduction in financial capacity might be related to cognition and memory, so we will test the relationships between FCI score, tests of cognition and memory, and ODI measures within WM tracts.

To study how white matter integrity affects the financial capacity, T1 MRI and DTI images of control (CN), MCI, and AD patients, along with their FCI scores are obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database. The NODDI pipeline, developed by a previous San Jose State University student, Matthew Jones, is used to extract ODI values from the MRI and DTI images. Regions of interest (ROI) of the different neuronal fiber tracts from the John Hopkins University (JHU) will be used to obtain the average ODI values of different neuronal white matter tracts of the brain [25, 26, 27]. The ODI values of different parts of the brain and neuropsychological tests results are used to predict the FCI score.

3.1 Data

Most of the data used in this project are obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database. It is a database that is open to the public for researching AD and related diseases. The database was founded by Principal Investigator Michael W. Weiner, MD in 2003. The database started with a five-year study (ADNI-1) then extended to ADNI-GO by a Grand Opportunity Grant, which later on extended to ADNI-2 with additional funding [28]. ADNI-3 is the latest study , which began in 2016. More than 1000 subjects with Alzheimer's dementia (AD), amnestic mild cognitive impairment (MCI), or cognitively normal (CN) are enrolled in the study and studied longitudinally for three years[28]. It provides not just a variety of MRI images such

as T1, DTI, PET and fMRI images of subjects over the 3 years, but also results of a number of neuropsychological tests [28].

In this project, T1 MRI and DTI images of 253 subjects are obtained from the ADNI-3 database, which includes 18 AD subjects, 47 MCI subjects and 193 CN subjects. Demographic informations and neurological test scores were obtained for each subject.

3.2 NODDI pipeline

The NODDI pipeline used in this project is modified from the pipeline developed by a prior student of San Jose State University, Matthew Jones [12]. It involves three steps: 1) preprocessing, 2) running NODDI Algorithm, and 3) post-processing. In the preprocessing step, T1 and DTI images obtained from the ADNI database are converted from original DCM files to NIFTI (nii) format. The MRI images of the brain are extracted, oriented, and registered into a standard space. In the next step, the nii, bval, and bvec files are used to build a NODDI model. ODI values across the brain, which range from 0 to 1 are obtained. In the post-processing step, the average ODI values within specific regions of interest (ROI) defined by John Hopkins University (JHU) atlas of white matter tracts are extracted for analysis

3.2.1 Updates

Major modification of the Jones version of pipeline completed during this project were identifying and removing bugs and the facilitation the running of multiple subjects. The time taken for running 100 subjects with 20 masks was reduced from 300 hours (3 hours per subject, running individually) to around 10 hours.

3.2.2 Environment

NODDI analysis requires such a large amount of computational resources that it is impossible to run on regular personal computers. Therefore, the NODDI analyses of this project were run on the College of Engineering (CoE) High Performance Computing (HPC) system of San Jose State University. The CoE HPC cluster is a Linux distributed cluster with a total of 36 nodes of various

configurations, where 20 of them (compute nodes) have 128 GB of RAM, and 16 of them (GPU and condo nodes) have 256 GB. Slurm workload manager is used for job deployment.

The NODDI pipeline runs on CentOs Linux 7.7.1908 (Core). Conda, which is an environment manager, is used to download and install any necessary software or package. In order to run the pipeline, python 3.7x is needed. Additional python libraries that help MRI processing like nibabel, numpy, scipy, dipy, pathos and numba are also needed. The pipeline also make use of two python packages, dmipy and diffusion_imaging. Dmipy is a software package that facilitates the reproducible estimation of diffusion MRI-based microstructure features[29], while diffusion_imaging is a python library that wraps around a variety of diffusion based imaging for magnetic resonance imaging used in the NODDI pipeline. FSL, which is a library of analysis tools for MRI and DTI images, is needed for the preprocessing and post-processing of the images.

3.2.3 JHU Tracts

The white matter tracts used in this project are obtained from the atlas package in the FSL library. It included twenty white matter tracts as listed in Table 3. They are produced by the Laboratory of Brain Anatomical MRI at the Johns Hopkins Medical Institute [25, 26, 27]. The atlas is built in MNI space which matches the requirement of the NODDI pipeline.
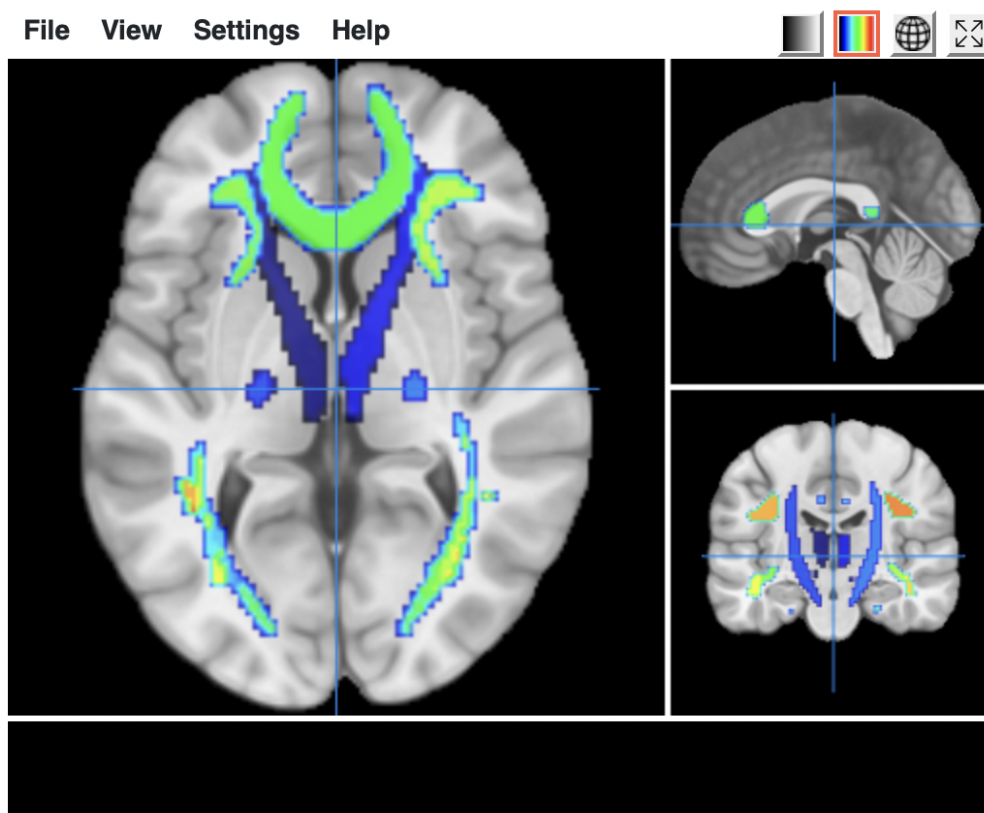
Figure 2: The Location of the JHU White Matter Tracks in the Brain.

Table 3: JHU track mask

Item no.	Name of White Matter Track
0	anterior_thalamic_radiation_l
1	anterior_thalamic_radiation_r
2	corticospinal_tract_l
3	corticospinal_tract_r
4	cingulum_1
5	cingulum_2
6	cingulum_3
7	cingulum_4
8	forceps_major
9	forceps_minor
10	inferior_fronto-occipital_fasciculus_l
11	inferior_fronto-occipital_fasciculus_r
12	inferior_longitudinal_fasciculus_l
13	inferior_longitudinal_fasciculus_r
14	superior_longitudinal_fasciculus_l
15	superior_longitudinal_fasciculus_r
16	uncinate_fasciculus_l
17	uncinate_fasciculus_r
18	superior_longitudinal_fasciculus_1
19	superior_longitudinal_fasciculus_2

3.3 Statistical Analysis

Statistical analysis were performed to study the distribution of FCI score across AD, MCI, and CN subjects. Correlation analyses were done between ODI values of different white matter tracts and FCI scores to find out which of the white matter tracts are most associated with the FCI score. We test our hypothesis that memory affects the FCI score by analyzing the relationship between several neuropsychological tests (MoCA, RAVLT, and Trail Making Test) and FCI score.

CHAPTER 4

Result

4.1 ODI values

After running the NODDI algorithm, the ODI values of the brain of each of the 256 subjects were obtained. Figure 3 shows the ODI values of a slice of the brain of a subject. Each cylinder represents the ODI value of each voxel of the brain - the bigger the cylinder, the larger the magnitude ODI value which indicates it has a higher axon density. The direction of the cylinder represents the direction of the axons. In this project, whole-brain NODDI analysis is performed and masks are used to identify larger tract ROIs that contain many voxels. The average ODI value of each tract is reported in the later section of this chapter.
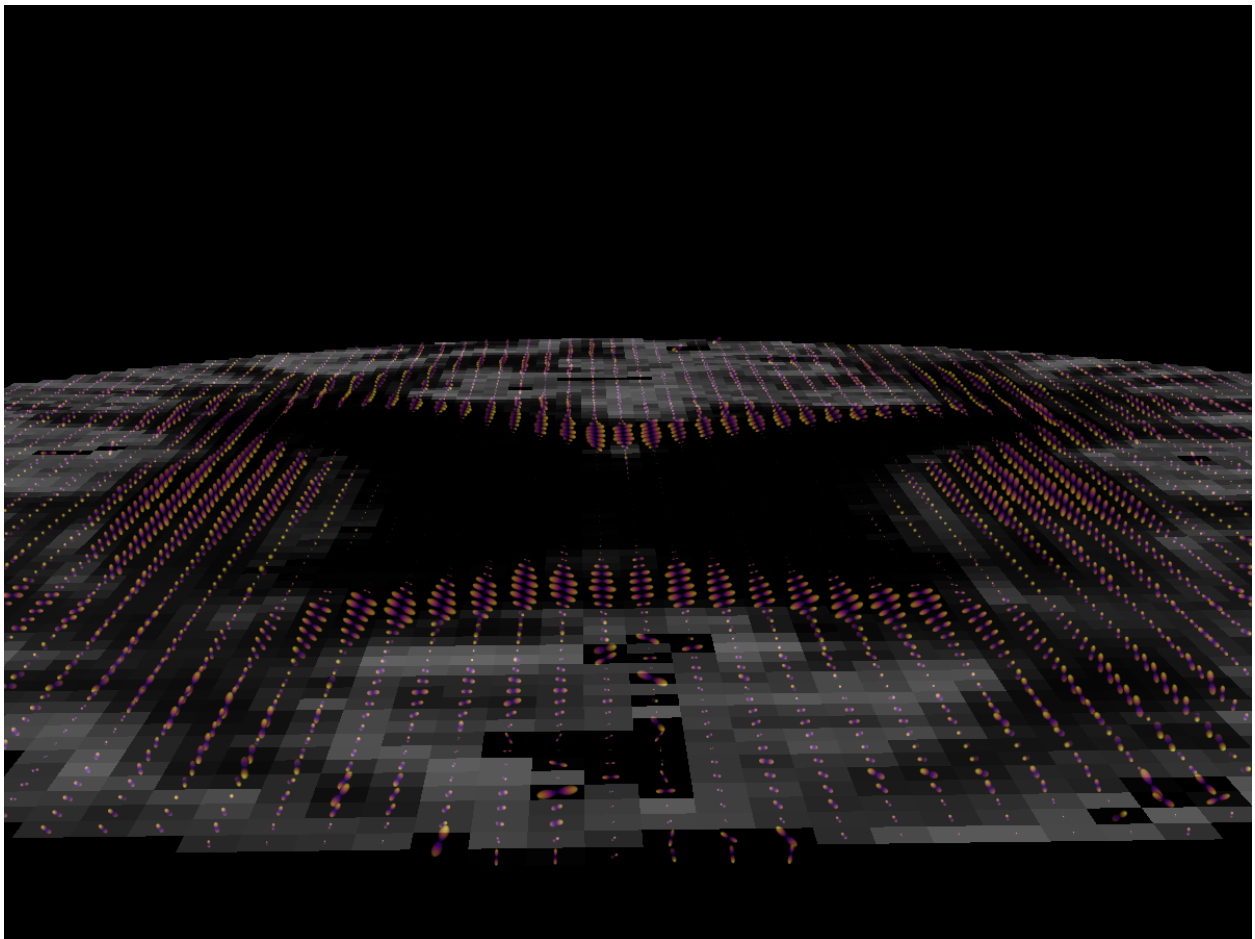
Figure 3: Visualization of ODI Values in a Slice of a Brain

4.2 Distribution of FCI score

The distribution of FCI scores in this project is left-skewed as shown in Figure 4. Most of the subjects performed very well on the FCI test. The density diagram in Figure 5 shows that the distribution of FCI score is left-skewed mainly because of the large number of CN subjects in the data set. The distribution of FCI score among MCI subjects is slightly less left-skewed than the CN group. It indicates that MCI subjects do not perform as well as the CN group. The FCI score of the AD group is spread among a large range showing that there are more subjects that did not perform as well as the other two groups.
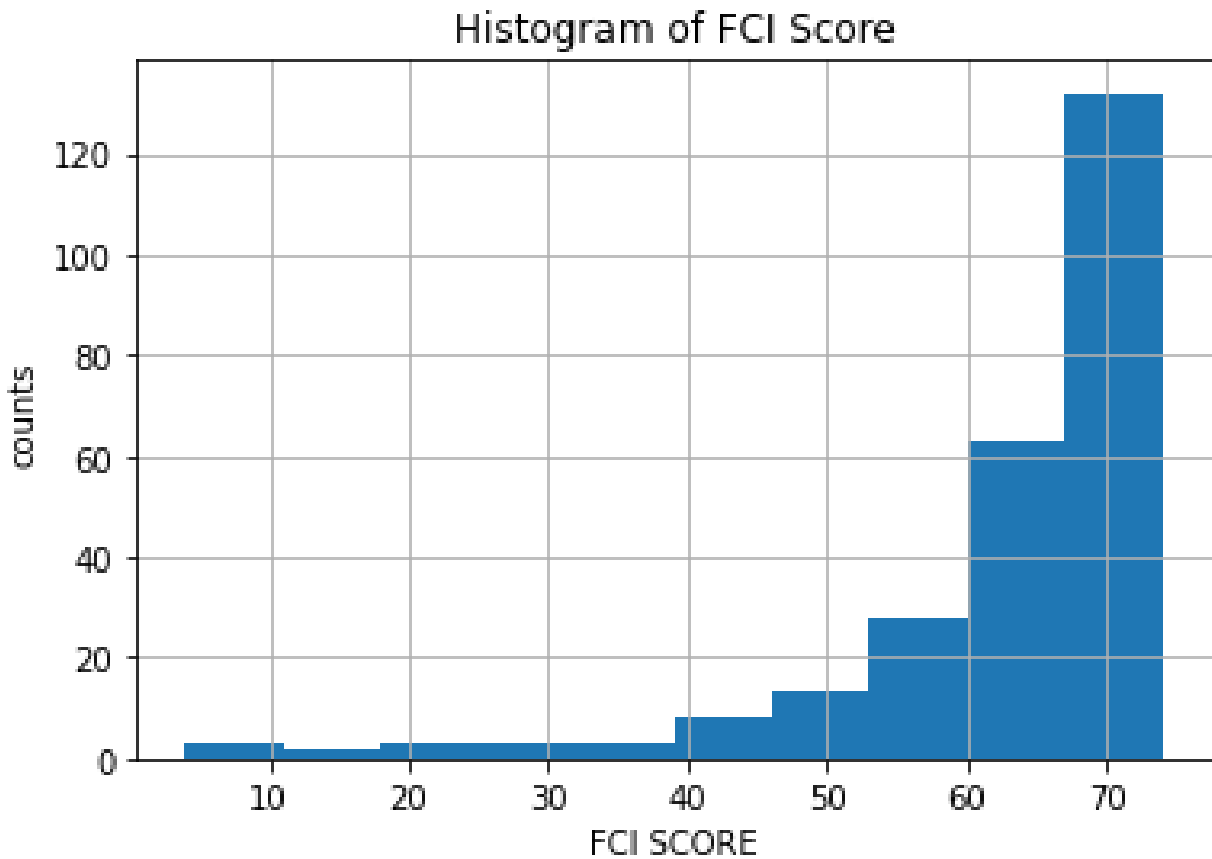
Figure 4: Distribution of FCI score
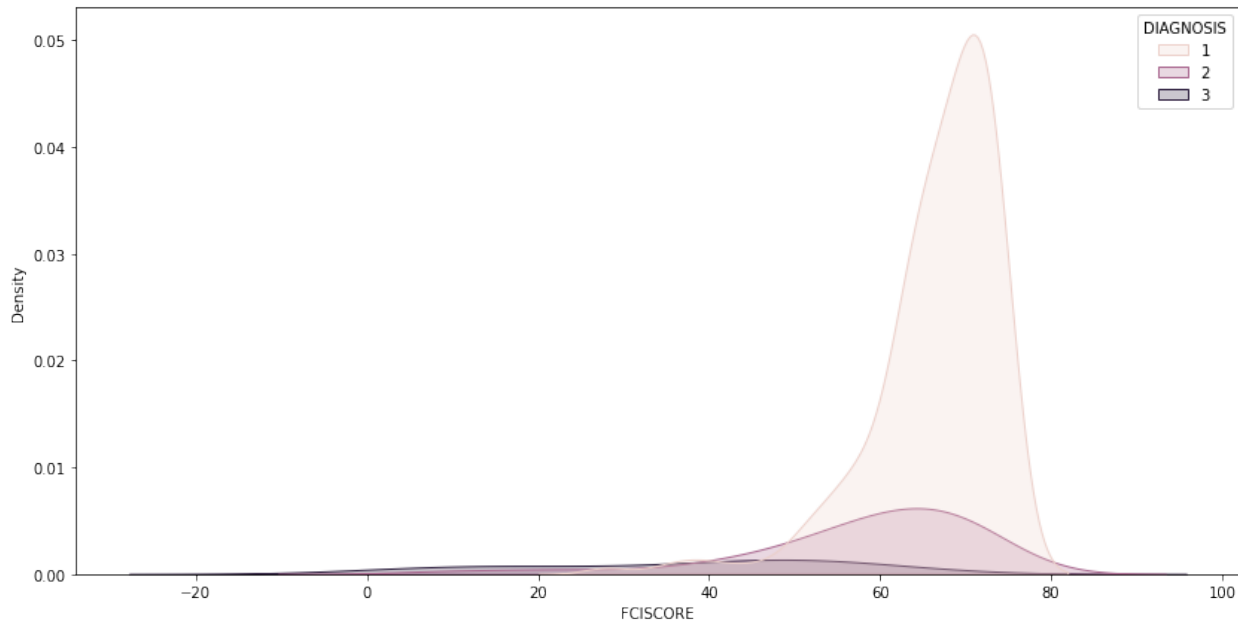
Figure 5: Density Diagram of FCI Scores by Group

4.3   ODI values of AD, MCI and CN

Table 4 shows ODI values within each WM tract averaged over each diagnosis, showing that each group has a similar average ODI value. By comparing the averages of the ODI values among different groups, we can see that MCI subjects has a slight decrease in ODI values compared to CN subjects, which is not statistically significant ($p=0.24$), and AD subjects a larger decrease in ODI values compare to CN ($p < 0.05$) and MCI ($p<0.05$) subjects. Table 5 also shows that all of the three groups have similar ages and education. It also shows that there is a graduate decrease in FCI score and other neuropsychological tests when patients transition from CN to MCI and from MCI to AD.

Table 4: Mean ODI values of AD, MCI and CN subjects

Mean ODI values	CN	MCI	AD
anterior thalamic radiation l	0.015444	0.015262	0.013984
anterior thalamic radiation r	0.008989	0.009051	0.007778
corticospinal tract l	0.014603	0.014700	0.014191
corticospinal tract r	0.014576	0.014621	0.014619
cingulum 1	0.026079	0.025592	0.021882
cingulum 2	0.025240	0.024914	0.023477
cingulum 3	0.019180	0.017774	0.014631
cingulum 4	0.011874	0.011098	0.009529
forceps major	0.047960	0.045434	0.041208
forceps minor	0.027131	0.027433	0.023055
inferior fronto-occipital fasciculus l	0.033141	0.032861	0.029556
inferior fronto-occipital fasciculus r	0.030997	0.030478	0.028897
inferior longitudinal fasciculus l	0.032330	0.032081	0.027590
inferior longitudinal fasciculus r	0.026689	0.026408	0.024323
superior longitudinal fasciculus l	0.031788	0.030927	0.027188
superior longitudinal fasciculus r	0.037660	0.036526	0.033878
uncinate fasciculus l	0.027487	0.027950	0.024375
uncinate fasciculus r	0.031501	0.031135	0.029257
superior longitudinal fasciculus 1	0.015390	0.015391	0.013902
superior longitudinal fasciculus 2	0.021152	0.020923	0.019228
mean	0.024961	0.024528	0.022127

Table 5: Neuropsychological test results of AD, MCI and CN subjects

	CN	MCI	AD
AGE	74.001554	73.780851	73.077778
FCI score	66.497409	57.936170	36.777778
Education	16.756477	15.723404	15.055556
MoCA	25.031746	21.217391	15.777778
RAVLT forgetting	3.904255	4.106383	5.000000
RAVLT immediate	46.680851	35.723404	23.187500
RAVLT learning	5.882979	4.191489	1.875000
RAVLT percent forgetting	37.609084	49.171573	94.305555
Trail Making Test A	31.712766	41.276596	49.600000
Trail Making Test B	81.058511	122.311111	169.615385

4.4 Correlation of diagnosis and education with FCI Score

ANOVA showed an effect of diagnosis, education and age on FCI score ($p \ll 0.001$). Education, which is represented by the number of years of education received, has a positive correlation with FCI score. Age shows some correlation with FCI score but not as strong as diagnosis and education. Race shows some effect on FCI score ($p < 0.05$) but not as strong as diagnosis, age and education. Ethnicity shows little effect on FCI score ($p = 0.487$).

Table 6: Correlation of diagnosis, age and education with FCI score

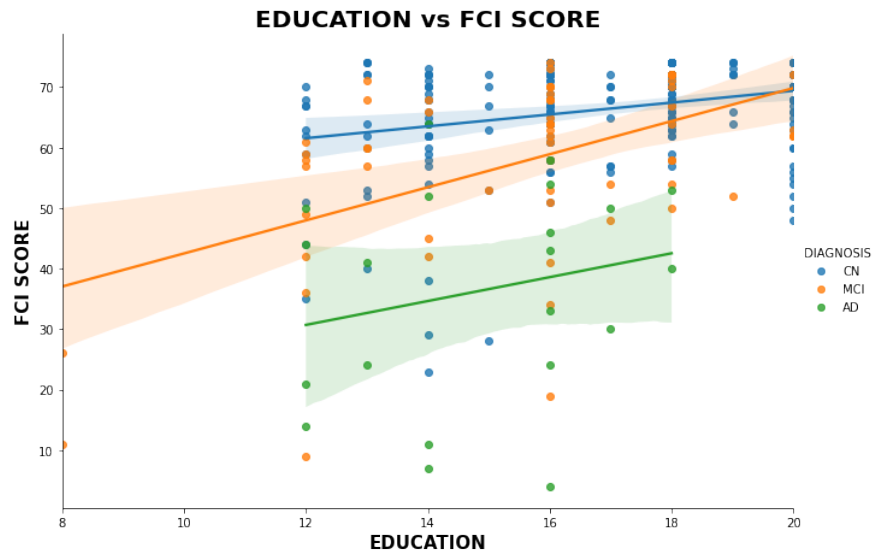| Feature	Correlation	p-value
DIAGNOSIS	Not Applicable	<<0.001
AGE	-0.180290	<<0.001
EDUCATION	0.357644	<<0.001
ETHNICITY	Not Applicable	0.487
RACE	Not Applicable	<0.05

Figure 6: Scatter Plot of Education against FCI Score

4.5 Correlation of ODI values and FCI score

Overall, there is a small positive correlation between FCI scores and the average ODI values of the white matter tracts. Out of all the white matter tracts, cingulum 3 and 4 have the strongest

correlation with the FCI score (0.29 and 0.29 respectively). The location of cingulum 3 and 4 are shown in Figure 9 and 10. Both the left and right corticalspinal tract have a very low correlation with FCI score (0.06 and -0.01). However, there are several subjects with a low ODI values in cingulum 3 and 4 but high FCI score, which is shown in the scatter plots in Figure 7 and 8.

Table 7: Correlation of ODI with FCI score

| White Matter Tract	Correlation
anterior thalamic radiation l	0.152617
anterior thalamic radiation r	0.161339
corticospinal tract l	0.061312
corticospinal tract r	-0.013052
cingulum 1	0.162190
cingulum 2	0.149732
cingulum 3	0.288977
cingulum 4	0.293869
forceps major	0.165599
forceps minor	0.070836
inferior fronto-occipital fasciculus l	0.161119
inferior fronto-occipital fasciculus r	0.127359
inferior longitudinal fasciculus l	0.158166
inferior longitudinal fasciculus r	0.172081
superior longitudinal fasciculus l	0.101596
superior longitudinal fasciculus r	0.222018
uncinate fasciculus l	0.145269
uncinate fasciculus r	0.125000
superior longitudinal fasciculus 1	0.057661
superior longitudinal fasciculus 2	0.174092
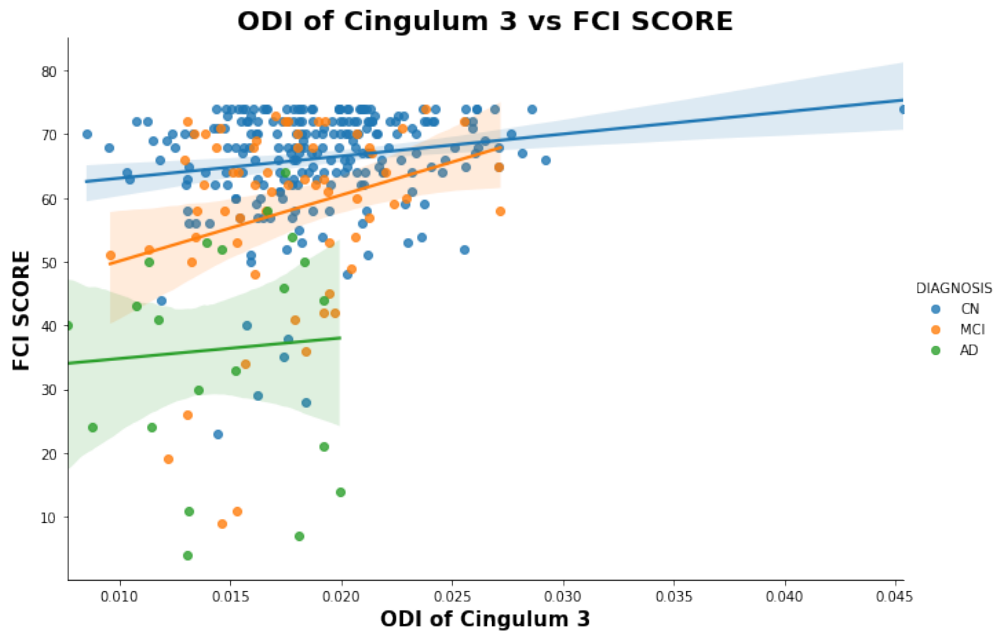
Figure 7: Scatter Plot of ODI value of cingulum 3 against FCI Score
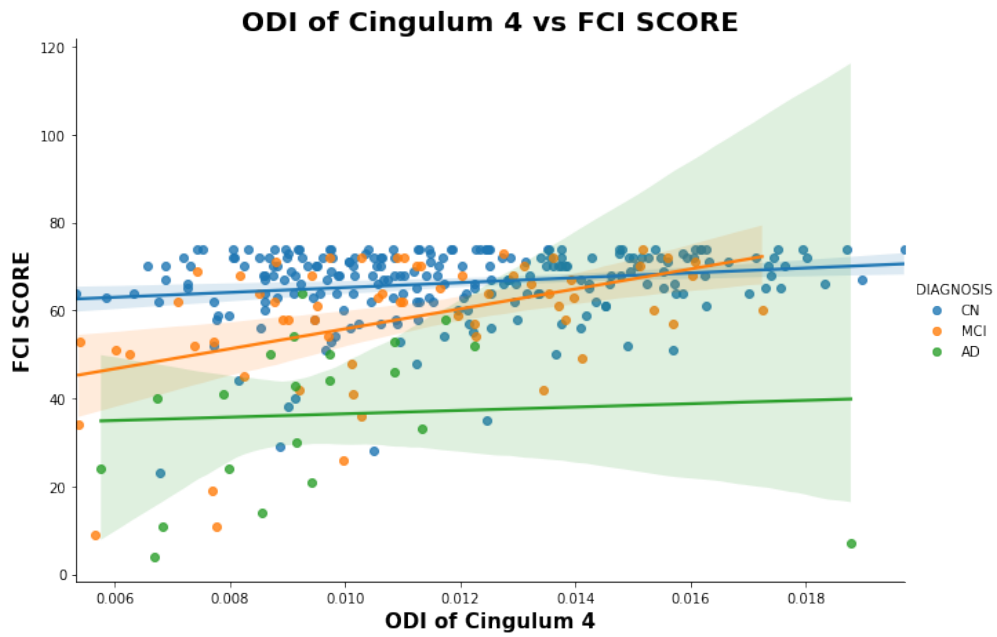

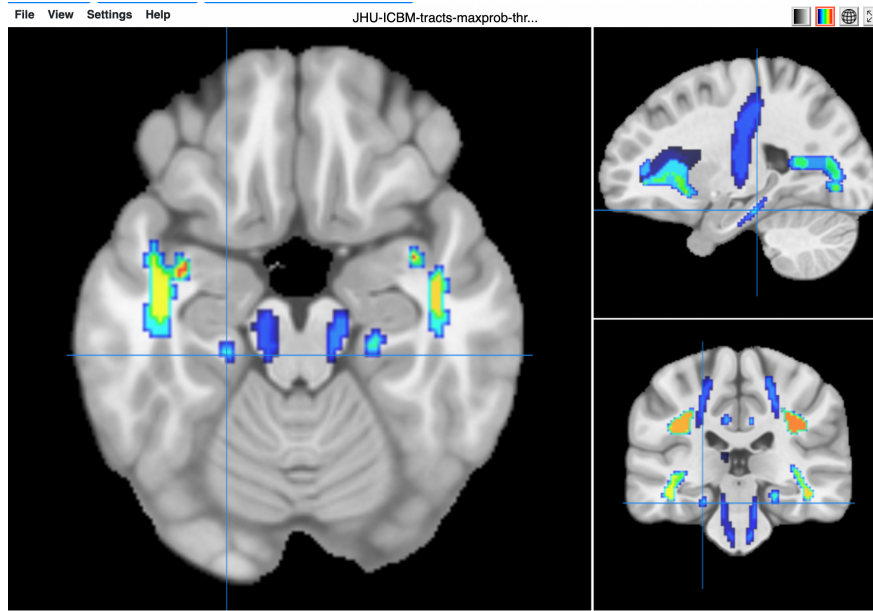Figure 8: Scatter Plot of ODI value of cingulum 4 against FCI Score

Figure 9: Location of Cingulum 3
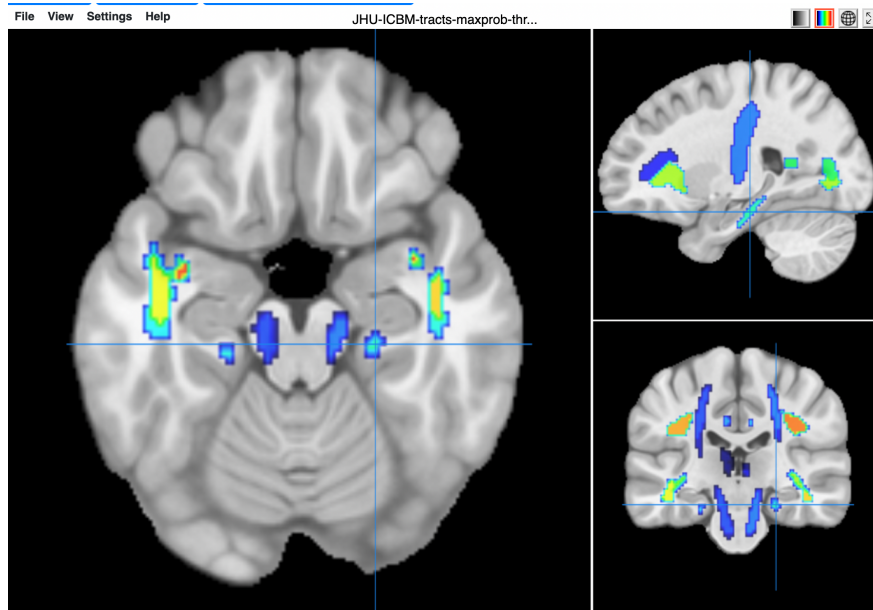Cingulum 3 is located at the blue dot indicated by the blue cross.

Figure 10: Location of Cingulum 4
Cingulum 4 is located at the blue dot indicated by the blue cross.

4.6 Correlation of Neuropsychological Tests and FCI Score

Table 8 neuropsychological tests that were significantly correlated with the FCI scores with $p<0.05$. MoCA, which measures cognitive function, has the strongest correlation with the FCI test (0.79). It is also shown in Figure 11 that there is a linear relationship between MoCA and FCI score and the diagnosis also affects both the scores. RAVLT, which is a memory test, is also correlated with the FCI scores, especially RAVLT immediate, RAVLT learning, and RAVLT percent forgetting. The Trail Making Tests are even more strongly correlated with the FCI score than the RAVLT test, where the Trail Making Test A has a correlation of -0.56 and the Trail Making test B has a correlation of -0.71 with the FCI scores.

Table 8: Correlation of Neuropsychological Tests with FCI score

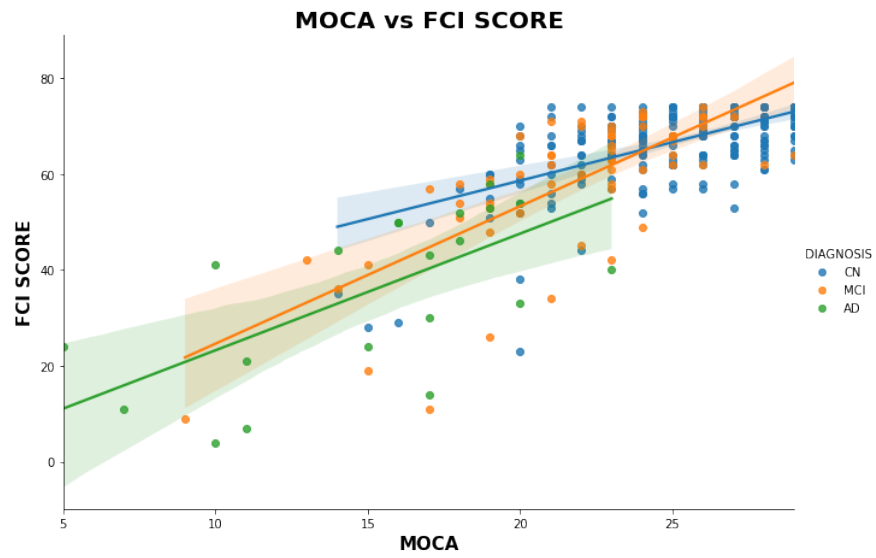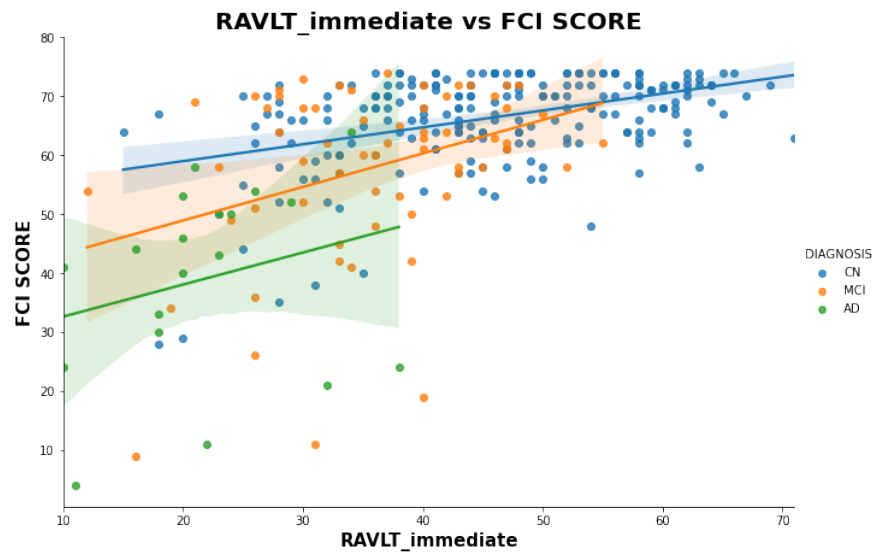| Feature	Correlation
MOCA	0.792520
RAVLT forgetting	-0.147035
RAVLT immediate	0.533968
RAVLT learning	0.399864
RAVLT percent forgetting	-0.392420
Trail Making Test A	-0.564745
Trail Making Test B	-0.714100

Figure 11: Scatter Plot of MoCA against FCI Score

Figure 12: Scatter Plot of RAVLT immediate against FCI Score
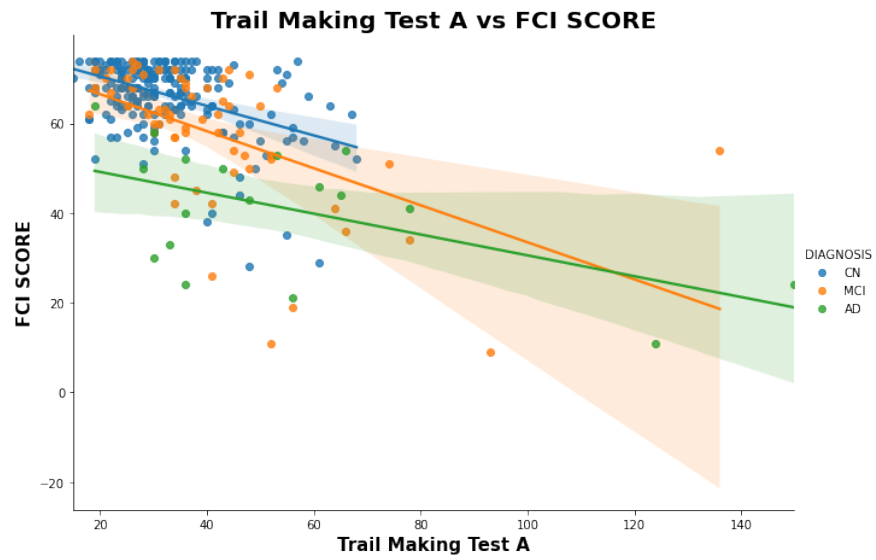
Figure 13: Scatter Plot of RAVLT Trail A Test against FCI Score
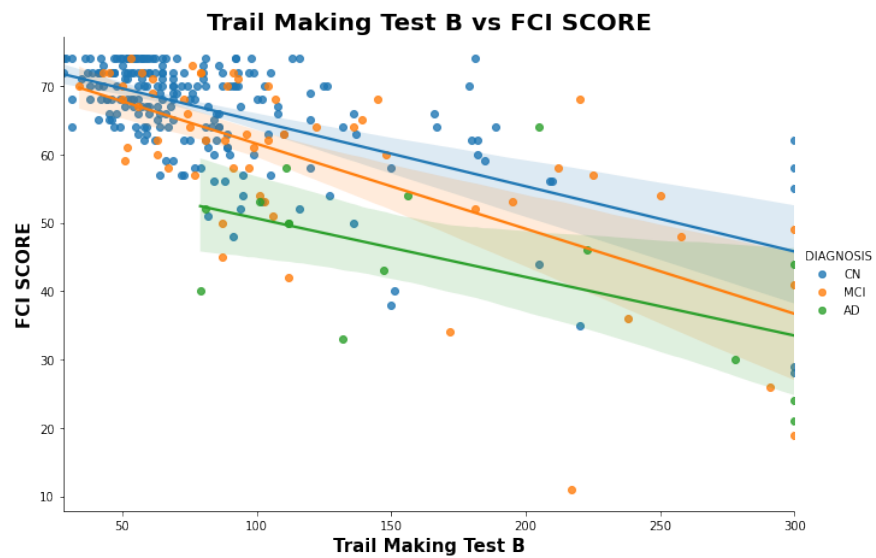

Figure 14: Scatter Plot of RAVLT Trail B Test against FCI Score

CHAPTER 5

Discussion

5.1   FCI score and Diagnosis

In general, the financial capacity of patients decreases with the progression of the disease that is shown in both distribution of lower FCI scores in Figure 5 and the decreased average FCI score in Table 5 in people with more progressed disease states. Most of the CN subjects get a high score in the FCI test so that the histogram in Figure 4 is left-skewed. This ceiling effect CN is consistent with the role of the test in identifying decline rather than individual differences in ability. There are fewer MCI subjects who obtained a high score. The distribution of FCI score in AD subjects spread across a much larger range than some subjects did very well in the FCI test while some did very poorly in the FCI test. However, there is still an overall decrease in FCI in the progression of the disease. AD patients suffer from memory and other cognitive impairment, and functional declines so that it is expected that they would not perform as well in the FCI test. This aligns with previous studies where preclinical AD patients show symptoms of financial capacity loss, resulted in missed payment and subprime credit scores [3]. However, MCI subjects or AD patients with high FCI scores, and CN subjects with low FCI scores are also found that FCI score is not fully accounted for by diagnosis alone that which will be discussed in the later section of the chapter.

5.2   White Matter Degradation and FCI Score

The overall lower ODI values in AD and MCI subjects compared to CN subjects suggested that white matter degradation has occurred all over the white matter tracts of the brain, which is consistent with previous research using FA rather than ODI [2]. The white matter degradation and decline in financial skill and knowledge are also consistent with beginning of the AD process[2]. This project also found the left and right cingulum hippocampal tract (cingulum 3 and 4 in the JHU DTI atlas) has the highest correlation with the FCI score out of all of the 20 white matter tracts. The cingulum is a C-shaped structure that encircles the entire brain as shown in Figure 15. It is consist of two parts of the cingulate cortex: the posterior cingulate cortex, which responsible for cognitive

function, including attention, visual and spatial skills, working memory, and general memory. The cingulum hippocampus tracts on the left and right include the left and right posterior cingulum that is closer to the hippocampus, as shown in Figure 9 and 10. Previous research using FA values has shown that the cingulum is found to be the first region where white matter degradation begins for both AD and MCI, and predominantly in the left posterior cingulate[30]. However, our result shows that both the left and right cingulum have similar association with the FCI score. The degradation is specific and consistent with the known pathology of AD since other regions like the corticospinal tract, which has nothing to do with episodic memory and which is relatively presered in AD has a very low correlation with the FCI score. The association between FCI and memory suggests that financial capacity depends on episodic memory to some degree.

Figure 15: Location of the Cingulum [31]
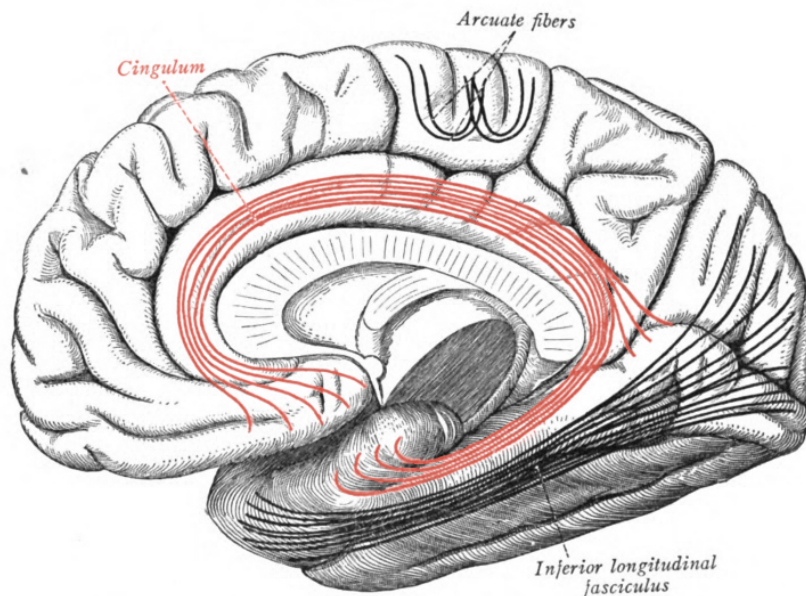
The scatter plots in Figure 7 and 8 show a clearer relationship between the FCI score and the ODI values. Both of the scatter plots show that most of the correlation present in people with degenerative disease (AD and MCI) but not as much in CN. This might be due to the ceiling effect of the FCI test in the CN group where a large proportion of the CN subjects obtains a score that is

close to the highest score of FCI and it failed to distinguish the financial capacity within the group. It is also because the FCI test is designed to detect financial capacity loss in MCI and AD and the functioning of the CN group is intact.

Moreover, previous studies have found that the angular gyrus, which is a grey matter tract that has functionality in arithmetic calculations, has a high association with the FCI score [9]. Another study has also pointed out that white matter tracts connect to the angular gyrus have an association with the FCI score [2]. However, those tracts are not included in the JHU white matter tract package and they are not analyzed in this project.

5.3 Cognition and FCI score

The strong correlation of the MoCA test (0.79) has suggested that financial capacity is vulnerable to decline when there are declines in overall level of cognition on this screening measure. The MoCA test is a ttest that briefly screens short-term memory, executive function, high-level language abilities, and complex visuospatial processing [21]. These mental processes likely contribute to performing well in the FCI test. For example, writing checks, which is a huge part of the FCI test, requires language skills to fill in the date, payee section and amount of the check correctly. Previous research has shown that the MMSE, which is another cognitive screening tool, has a strong correlation with the FCI score [9]. MoCA test is also known to be a more sensitive test in screening for AD and MCI patients compared to the MMSE [21]. One contributor to this increased sensitivity is that the MoCA test contains a measure of executive control, a shortened version of the Trail Making Test [21]. The RAVLT test, which is a memory test, and the Trail Making Test B, also have correlations with the FCI score. The effects of memory and executive function on FCI score will be discussed in the later sections of this chapter. These results suggest that the MoCA test, with its high correlation with FCI score, may be an important warning sign of financial capacity decline.

Unlike the correlation between ODI values in cingulum hippocampal tracts and FCI score, the relationship between MoCA score and FCI forms a strong relationship that is not affected by

the ceiling effect of FCI score in CN group. MoCA test can identify CN subjects who did not do well in the FCI test as shown in Figure 11. It is interesting how well the MoCA test correlates with the FCI score despite the differences in the nature of the two tests. The FCI test measures the financial capacity of a subject by giving them tasks related to writing a check or understanding bank statements, which requires knowledge in finance to perform well. However, the MoCA test does not require any prior financial knowledge to perform well and yet there is an association. This results suggests that even in apparently healthy participants FCI may be detecting dysfunction but there may be educational and cultural contributors to this association that need to be explored more fully.

5.4   Memory and FCI score

Memory has affected the FCI score in many ways, which it is shown by the correlation of RAVLT scores and FCI score. Four different summary statistics, RAVLT immediate, RAVLT forgetting, RAVLT learning, and RAVLT percent forgetting of the RAVLT test were used in this study. RAVLT immediate recall measures the learning memory ability of a subject and it has the highest correlation (0.53) with the FCI test among all three scores. RAVLT immediate which measures the ability of immediate recall has a stronger correlation than the other measurement that measures delay recall. From the scatter plot in Figure 12, it shows that there is a stronger correlation between the RAVLT immediate score and the FCI score in MCI and AD than in CN which might be due to the ceiling effect of the FCI score. This also correlates with the previous section that how the ODI values in the cingulum affects the FCI score.

5.5   Sequence of events

The Trailing Making Test B has a higher correlation with the FCI score than the Trail Making Test A because the Trail Making Test B has a higher complexity than Trailing Making Test A. Trail Making Test A only involves connecting points from 1-25 while Trailing Making Test B involves dividing attention between two lists, alternating numbers and alphabet. The complexity of

the Trailing Making Test B accounts for the complexity in performing sequence of events. Writing a check involves multiple items, filling out the name, date, amount of money.

5.6   Education, Age and FCI score

According to Gerstenecker et al., age and education affect FCI score in normal older adults [7]. However, our study shows that the effect might not be as strong. There is a 0.35 correlation between education and FCI score, and a -0.18 between age and FCI score. The scatterplot graph in Figure 6 also shows that the effect of education is subtle. From logical thinking, the FCI test requires knowledge in finance to perform well, especially in sections that examine financial conceptual knowledge, checkbook register, and bank statement management, which means that long term memory and prior experiences are important to perform well. However, the correlation tells us that other factors might be more important to perform in the FCI test. The high correlation between the MoCA test, which requires little knowledge to do well, and FCI score mentioned in the previous section also suggested the same.

5.7   Limitations

There are some limitations of this project. First of all, not all white matter tracts are examined in this project. This project is limited to the 20 white matter tracts provided by the JHU atlas. Moreover, the individual DTI and T1 images from participants were transformed into standard MNI space to match the template maps from the JHU atlas that mapping between individuals and templates may have subtle errors. Using tracts generated from each individual should increase the accuracy of the average ODI values obtained. There are also limitations in the FCI test where it does not cover modern online banking methods that are more typical now. E-banking became more and more popular and writing a check is not as necessary as before. However, these out-dated banking methods are the ones that used by older adults in the past. Such subtle functional abilities like financial capacity must thus be revalidated in order to be sensitive as society changes.

CHAPTER 6

Conclusion

In conclusion, this project extends the previous research in studying the association between white matter integrity and FCI using the NODDI algorithm, which is a more sensitive measurement compare to traditional DTI measures. We found that the cingulum 3 and 4, which are left and right cingulum hippocampal tracts have the highest correlation with FCI score among all the 20 white matter tracts we explored. Cingulum is crucial for memory functions. The correlation of neuropsychological test results and FCI also supports our hypothesis where memory and executive control are critical for financial capacity.

CHAPTER 7

Future Research

Future studies can be done by building machine learning models using the factors identified in this project to predict the FCI score. The NODDI pipeline can be also improved by using individualized tractography to locate the tracts. Using a more accurate tracts according to each patient can increase the accuracy of the result. A longitudinal study of how FCI and ODI values changed over the years can be done to study how white matter tract changes over the progress of AD. The analyses in this project only examined the magnitude of the ODI-vectors and neglected the effect of orientation. Future research should evaluate whether adding ODI-orientation information improves the prediction of financial capacity. The format of the FCI test can be also updated to include newer technology to handle finances, for example, the use of online banking over a cell phone app or on a computer.

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