

Differences in White Matter FA in successfully
remitted vs relapsed older adults

Differences in White Matter FA in successfully remitted vs relapsed older adults

1. Study Design
 - a. What is the broad research question/hypothesis?
 - b. What are the specifics of the study design?
2. Analysis Methods
 - a. How do we analyze the data to answer the question?
 - b. Significance of results
3. Future Suggestions

Differences in White Matter FA in successfully remitted vs relapsed older adults

1. Study Design
 - a. What is the broad research question/hypothesis?
 - b. What are the specifics of the study design?
2. Analysis Methods
 - a. How do we analyze the data to answer the question?
 - b. Significance of results
3. Future Suggestions

1a. Broad Research Question

Background: Patients with depression typically show structural connectivity deficits in white matter integrity in certain brain regions compared to non-depressed controls

Question: Are there broad structural differences in white matter integrity between elderly patients successfully remitted from depression without relapse vs. those that relapse into depression.

Hypothesis: We are testing the hypothesis that older depressed adults who achieve remission and then relapse will have some significant microstructural deficits in fractional anisotropy compared to older depressed adults who successfully remitted without relapse

❓ Question 1: Conceptual validity

- Data on white matter FA deficits for depressed subjects is strong
- Data on FA differences on remission likelihood is weaker/conflicting
- Data on relapse broadly is also more conflicting, depression relapse is more sparse

It could be that post remission depression relapse in older adults is not best reflected in the brain by microstructural FA analysis

Differences in White Matter FA in successfully remitted vs relapsed older adults

1. **Study Design**
 - a. What is the broad research question/hypothesis?
 - b. **What are the specifics of the study design?**
2. Analysis Methods
 - a. How do we analyze the data to answer the question?
 - b. Significance of results
3. Future Suggestions

1b. Specific Study Design

Length of Study: 2 years

NBOLD Inclusion Criteria: Initial MADRS > 15 within 1 month of baseline reading

- 2 weeks of remission within 2 years from baseline reading
 - Fully remitted: MADRS <= 8
 - Partial-remission: 8 < MADRS < 13 - included as fully remitted

Relapse Criteria: Any 2 week period subsequent to remission where MADRS > 15

Additional requirements: DWI data present, necessary files for analysis present

Result: 44 patients meeting start criteria, 39 patients that successfully run through analysis (26 Relapsed, 13 Non-Relapsed)

3 Question 2: Categorization

- Including partial remitted patients increases sample size while decreasing likely differences between groups
- Criteria for remission becomes MADRS <13 when depression is >15

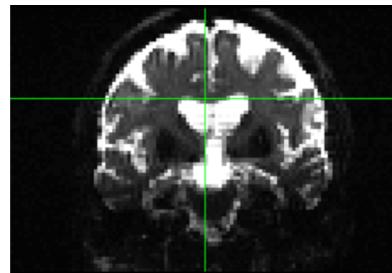
Differences in White Matter FA in successfully remitted vs relapsed older adults

1. Study Design
 - a. What is the broad research question/hypothesis?
 - b. What are the specifics of the study design?
2. Analysis Methods
 - a. **How do we analyze the data to answer the question?**
 - b. Significance of results
3. Future Suggestions

2a. Analysis of Data

128 DWI Images/Patient
(x 39 Patients)

- Distortion Correction
- DTI Calculation
- FA Calculation

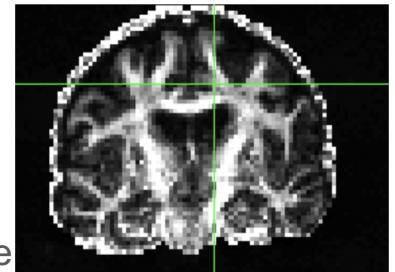


1.

A horizontal white arrow pointing from the first step to the second step.

1 FA Image/Patient
(x 39 Patients)

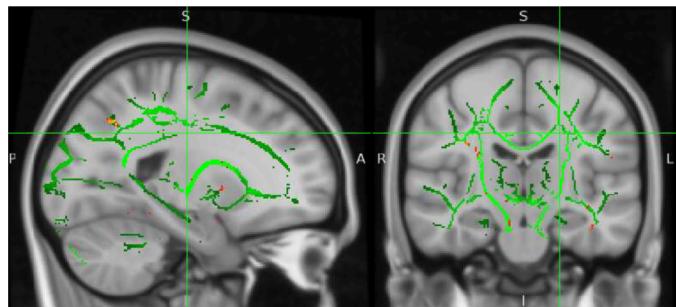
- Standardize space across patients
- Average FA values across standard space
- Apply simple thresholding to extract skeleton



2.

A vertical white arrow pointing from the second step to the third step.

Test Visualization

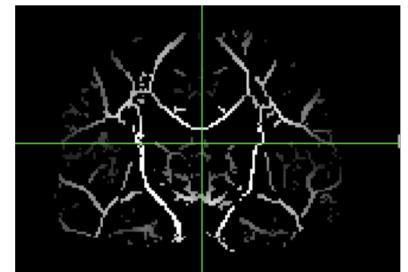


3.

A horizontal white arrow pointing from the third step back to the first step.

1 Mean Skeleton/Group
(+ 39 Standardized Skeletons)

- Construct t-test between group FA values
- Map average skeleton onto standardized MNI152 image
- Red clusters $p < 0.05$ Uncorrected
- Yellow clusters $p < 0.01$ uncorrected
- Blue clusters $p < 0.05$ corrected



Differences in White Matter FA in successfully remitted vs relapsed older adults

1. Study Design
 - a. What is the broad research question/hypothesis?
 - b. What are the specifics of the study design?
2. **Analysis Methods**
 - a. How do we analyze the data to answer the question?
 - b. **Significance of results**
3. Future Suggestions

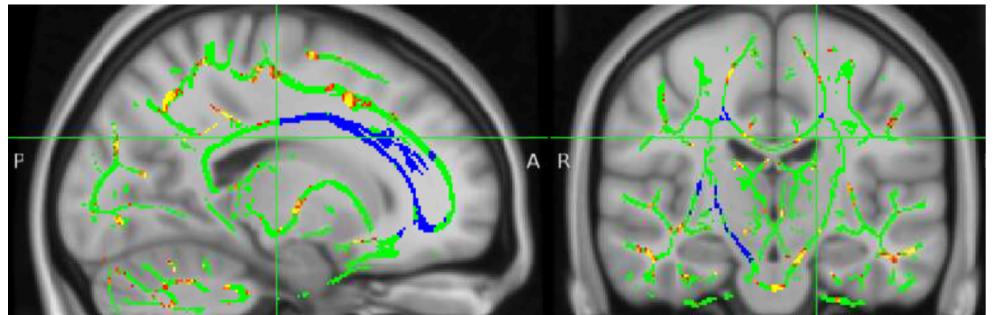
2b. Significance

- Red clusters $p < 0.05$
Uncorrected
- Yellow clusters $p < 0.01$
uncorrected
- Blue clusters $p < 0.05$
corrected

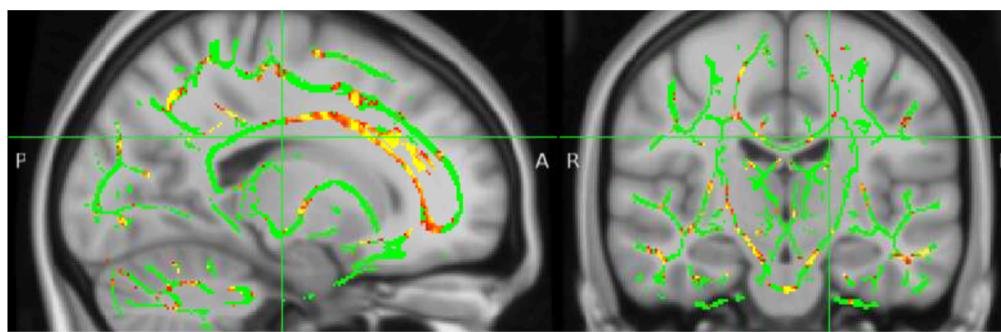
Question 3: Analysis

- ROI analysis would reduce number of comparisons to account for in data in establishing validity, but would still be unlikely to produce results if existing non-corrected data contains very few significantly different voxels

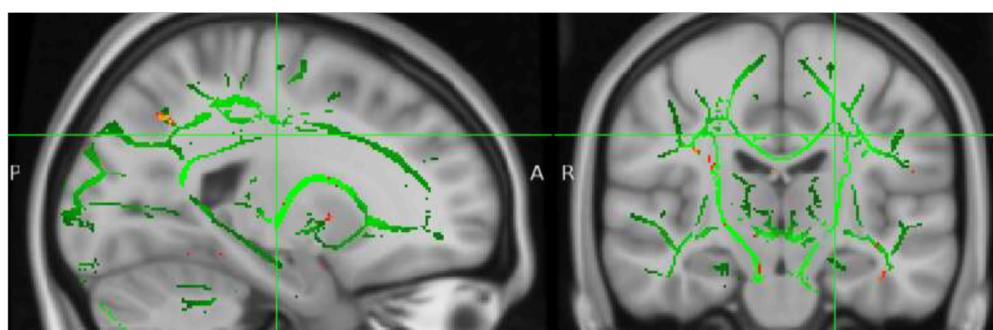
Example Data w/
corrected clusters
highlighted blue



Example Data w/o
corrected clusters
highlighted blue



NBOLD Data w/
corrected clusters
highlighted blue
(still none)



Differences in White Matter FA in successfully remitted vs relapsed older adults

1. Study Design
 - a. What is the broad research question/hypothesis?
 - b. What are the specifics of the study design?
2. Analysis Methods
 - a. How do we analyze the data to answer the question?
 - b. Significance of results
3. **Future Suggestions**

3. Future Suggestions

② Question 1: Conceptual Validity

Is there a better hypothesis to test than looking for fractional anisotropy differences between older adults who have relapsed in depression versus successfully remitted given conflicting and sparse data?

③ Question 2: Categorization

Should we change criteria for categorization between relapsed and non-relapsed patients for greater clinical differences?

④ Question 3: Analysis

Would concentrating analysis on data driven regions of interest be more likely to produce results if uncorrected skeleton comparison data already sparsely shows significant values and if so where?