

OVERVIEW OF BIOMARKERS IN DIVERSE POPULATIONS: SEX DIFFERENCES

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LA**



**AMERICAN
PARKINSON DISEASE
ASSOCIATION**

Strength in optimism. Hope in progress.

MORE THAN A MOTOR DISORDER

While PD is most commonly associated with motor disturbances, cognitive dysfunction appears in 40% of patients

Cognitive domains include:

- Executive function
- Visuospatial function
- Processing speed



SEX DIFFERENCES IN PD

- PD is 1.5 times more common in men than in women
- Symptomatic onset is delayed in women
- Women more often present with the tremor dominant phenotype (67% compared to 48% in men) associated with less severe motor deterioration
- Hypothesis: there are sex differences in cognitive dysfunction in PD



SUBJECTS

PD group

- N = 89 (39 females)

Control group

- N = 59 (27 females)

Sex/gender was determined via self-report

Exclusion criteria:

- MMSE < 24
- WAIS-III Digit Span Total < 10
- Hx of Head Injury, Mental Illness, Drug Abuse etc.

DEMOGRAPHICS

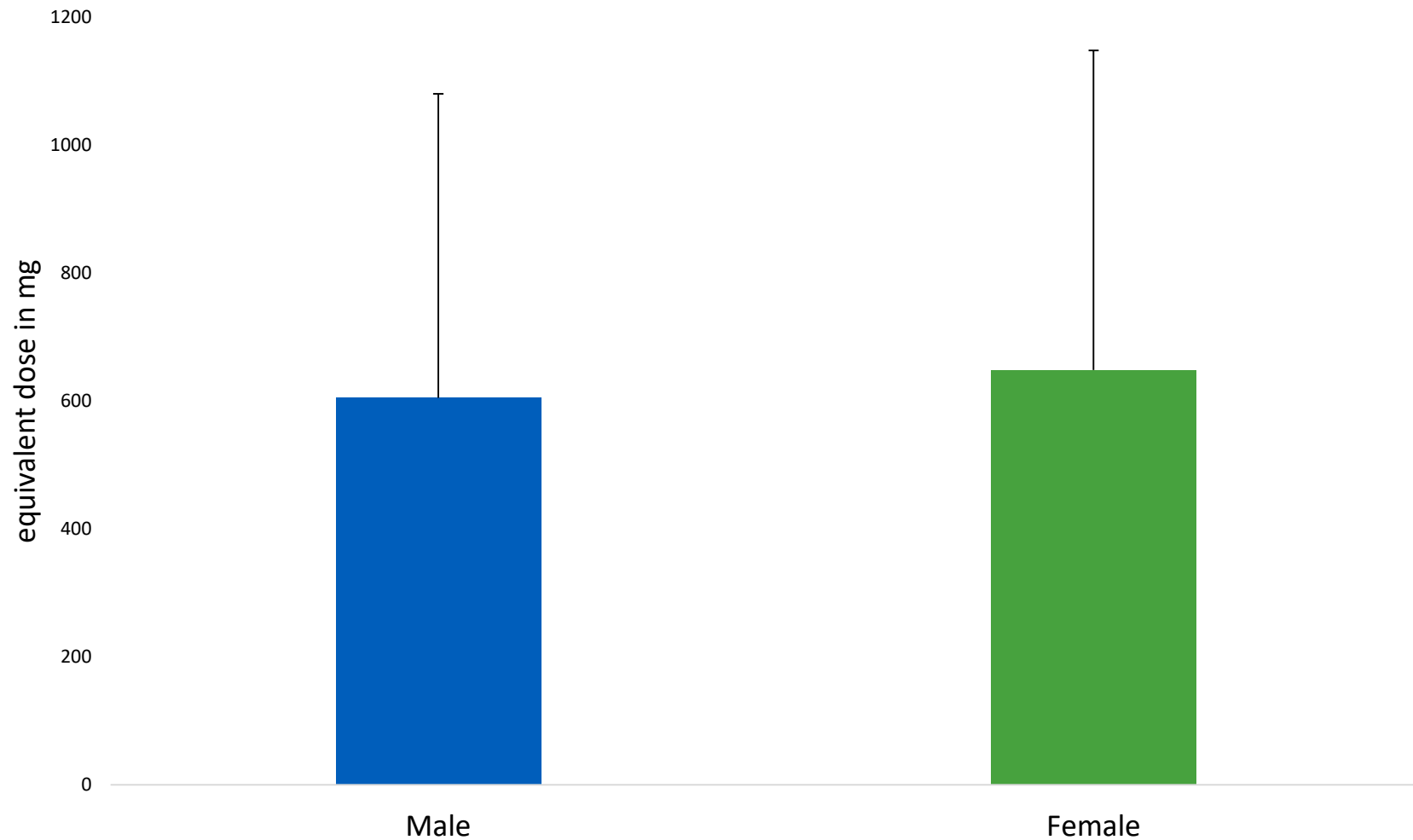
| | N | Age (years) | Education (years) | MMSE | ESS | NART-R | GDS * |
|------------------------|----------|------------------------|------------------------------|--------------|-------------|---------------|--------------|
| Control (M) | 32 | 65.63 (5.84) | 16.53 (3.29) | 28.94 (1.01) | 7.25 (3.59) | 112.03 (9.28) | 2.75 (3.07) |
| Control (F) | 27 | 65.04 (6.93) | 16.59 (3.13) | 28.59 (1.39) | 6.33 (3.37) | 113.83 (5.44) | 2.82 (3.89) |
| PD (M) | 50 | 67.9 (6.52) | 15.58 (2.9) | 28.42 (1.84) | 8.46 (4.08) | 112.82 (9.88) | 6.36 (5.61) |
| PD (F) | 39 | 66.53 (5.97) | 16.50 (2.46) | 28.84 (1.31) | 8.63 (5.07) | 115.53 (6.36) | 4.76 (3.93) |



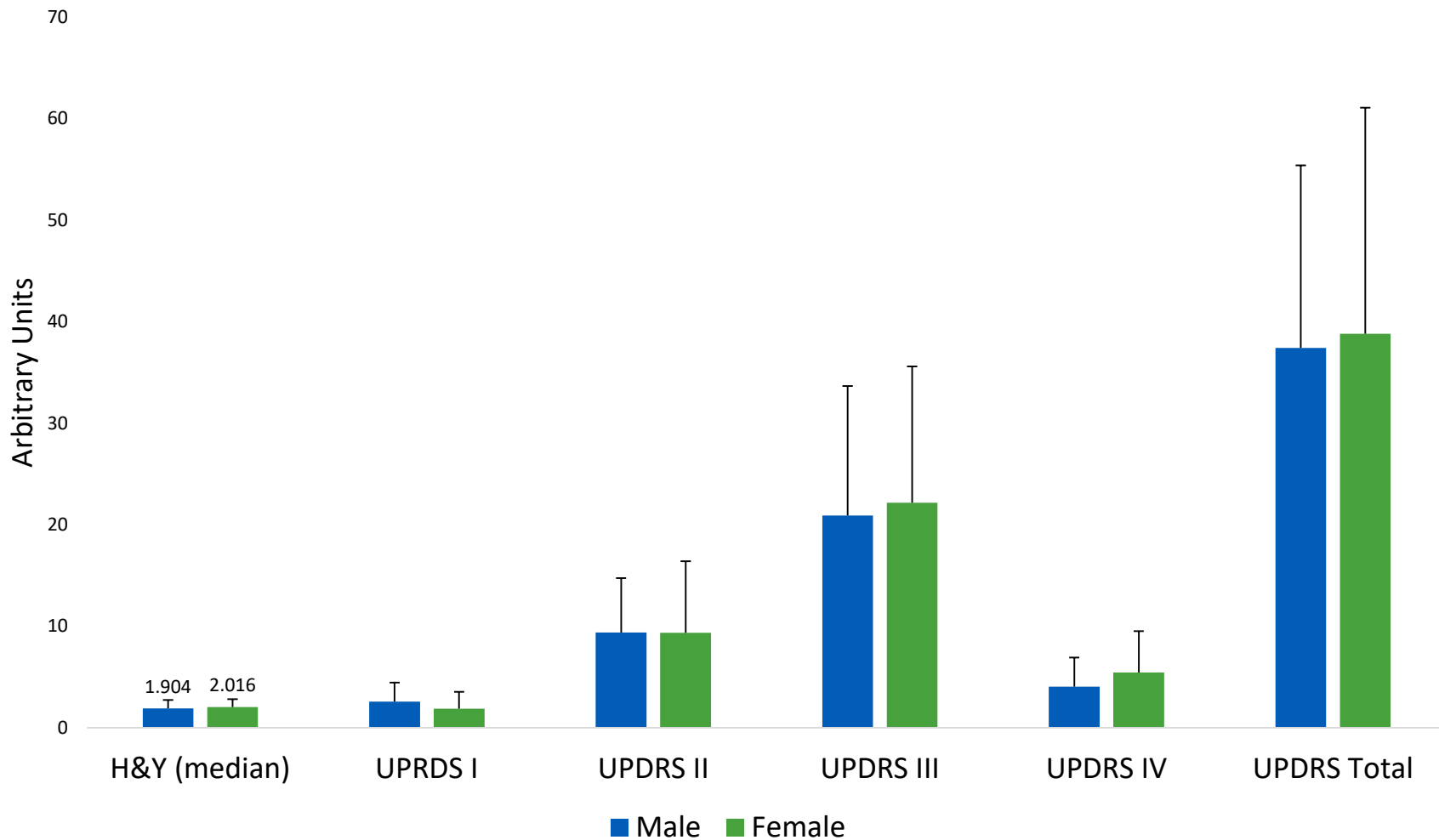
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LEVODOPA EQUIVALENTS



DISEASE SEVERITY



DIGIT SPAN

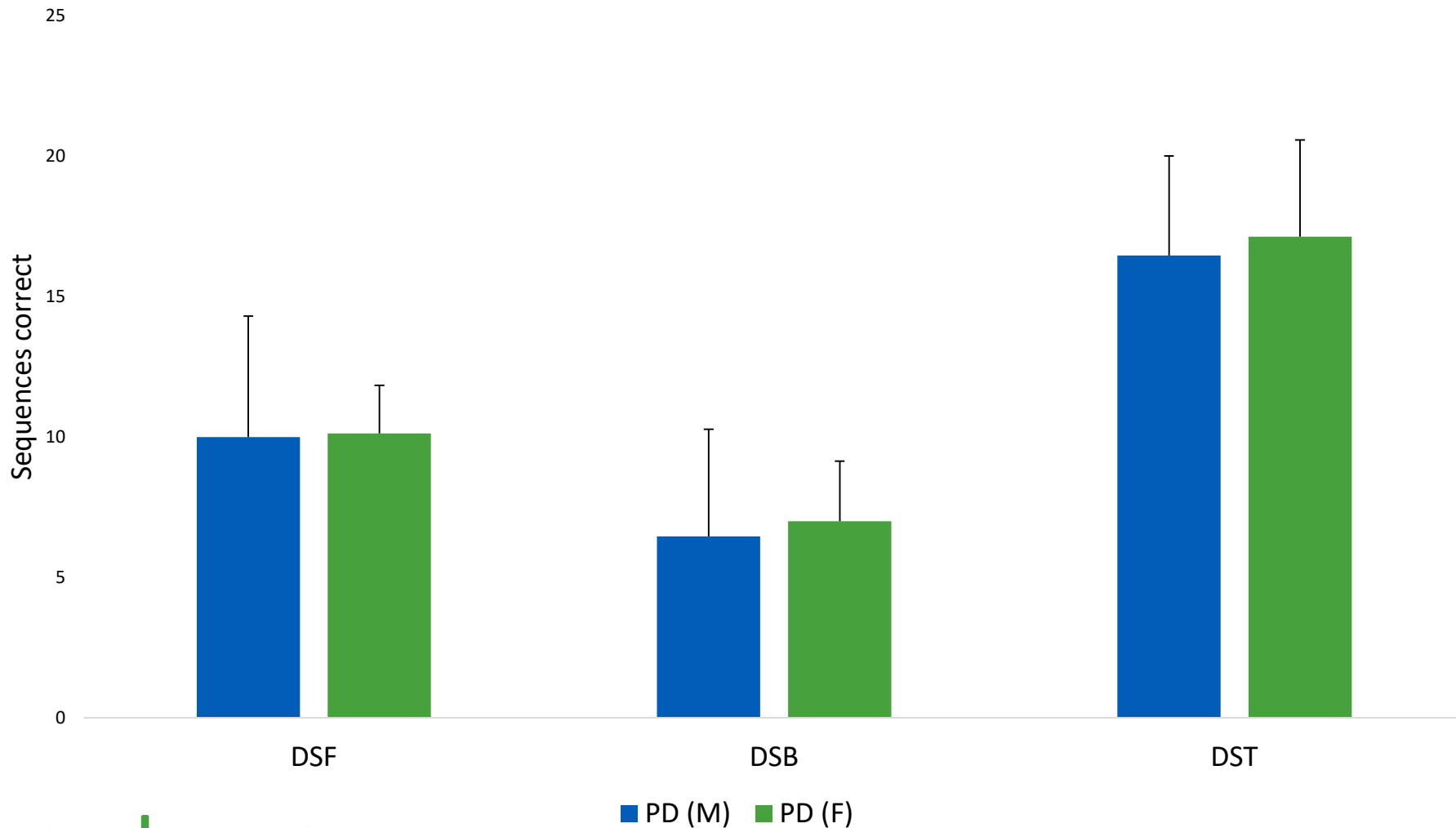
Digit Span Forward

- 9-7
- 6-3
- 5-8-2
- 6-9-4
- 7-8-2-6

Digit Span Backward

- | | |
|-----------|---------|
| • 7-1 | 1-7 |
| • 3-4 | 4-3 |
| • 6-2-9 | 9-2-6 |
| • 4-7-5 | 5-7-4 |
| • 8-2-7-9 | 9-7-2-8 |

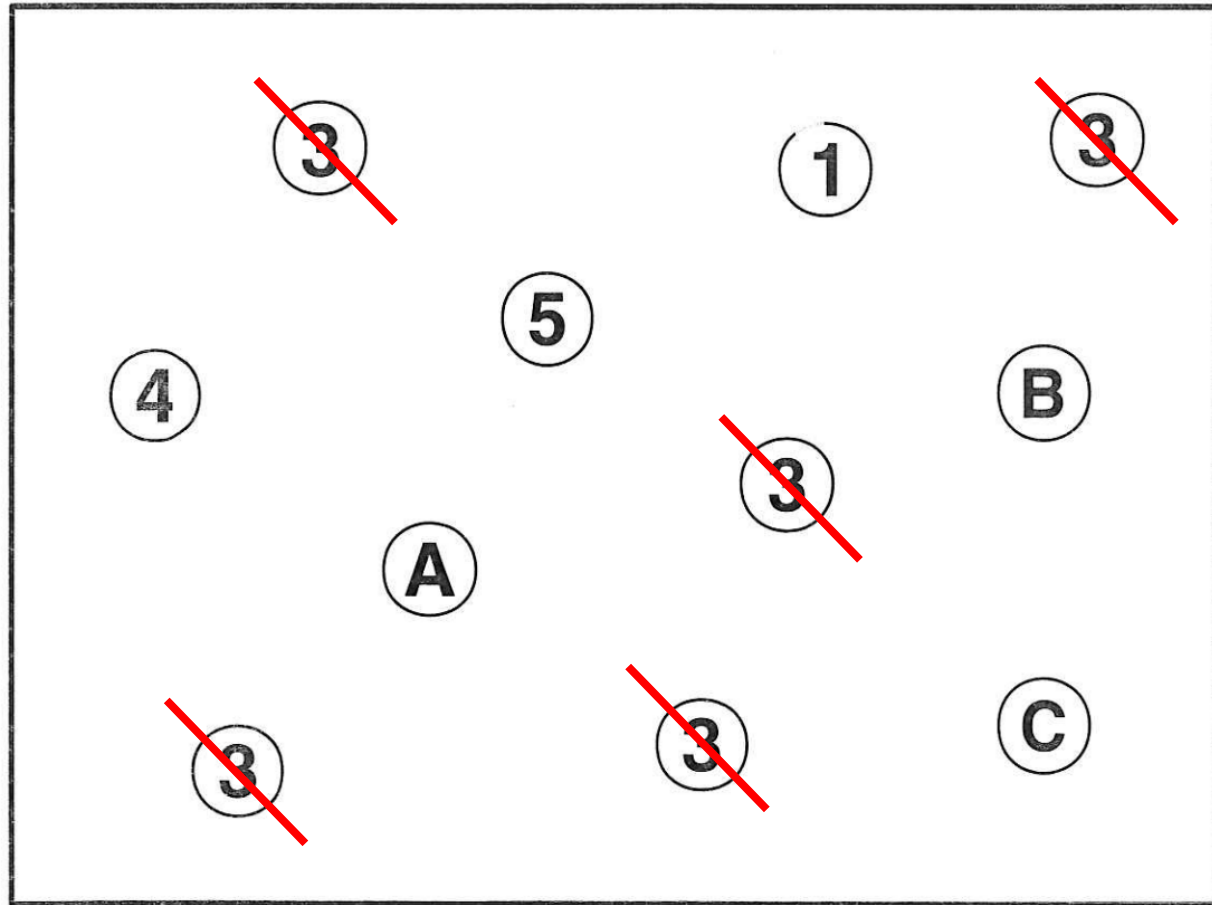
DIGIT SPAN



TRAIL MAKING TEST

Condition 1

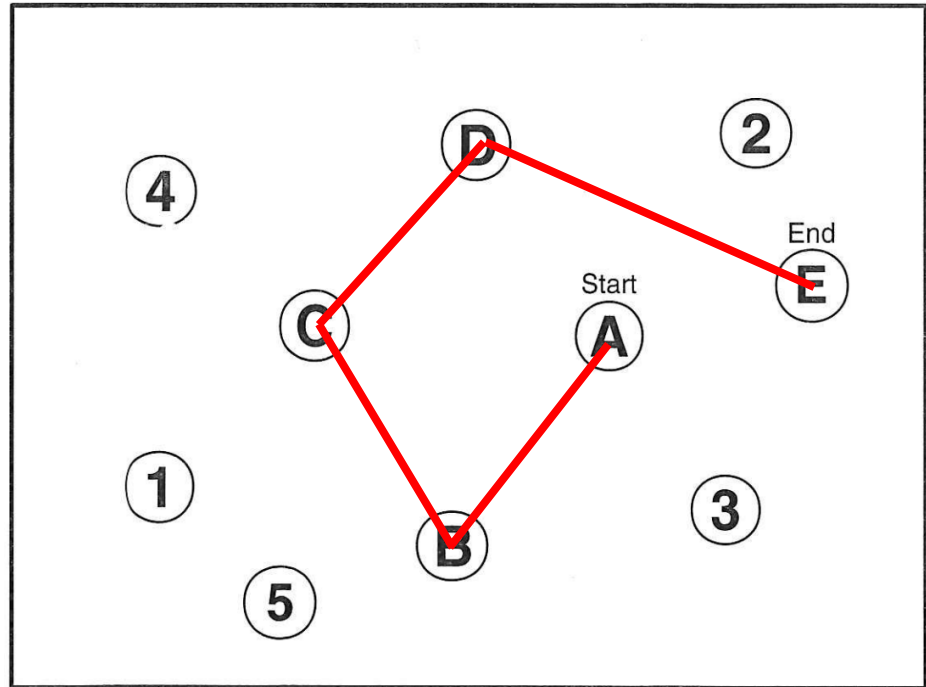
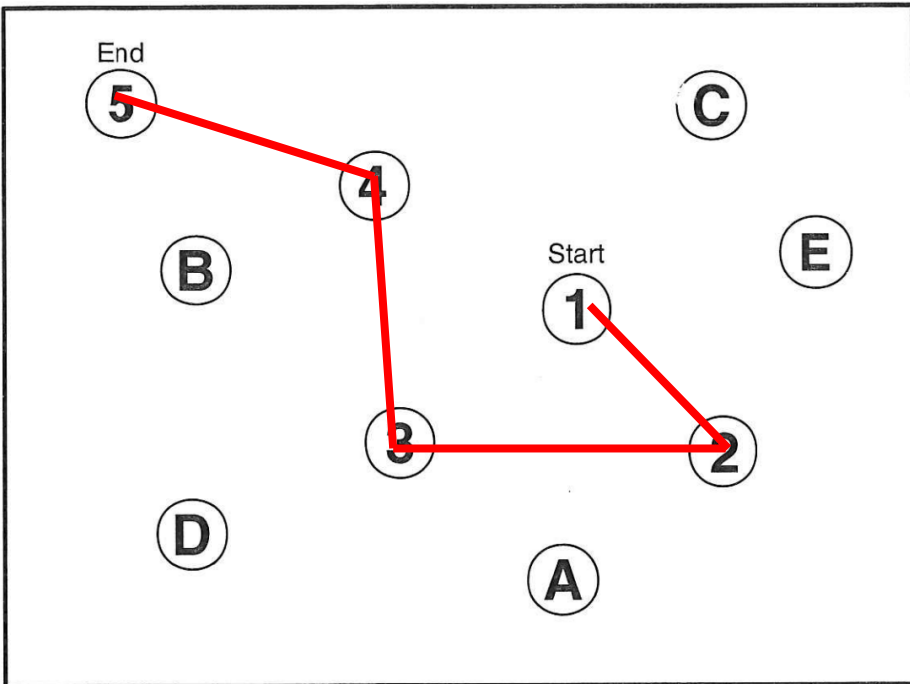
- Measure of visuospatial function



TRAIL MAKING TEST

Condition 2 and 3

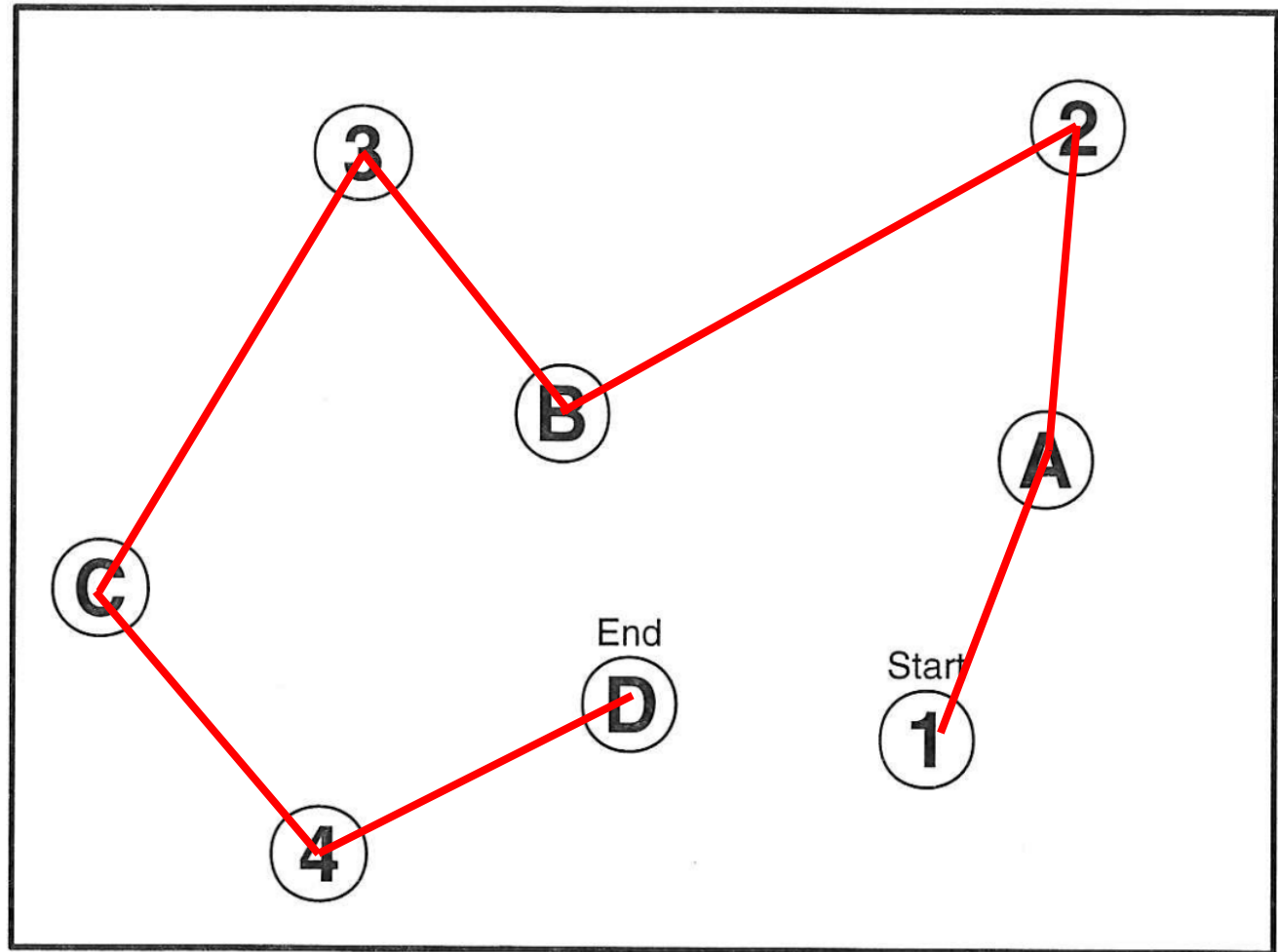
- Number and letter connection



TRAIL MAKING TEST

Condition 4

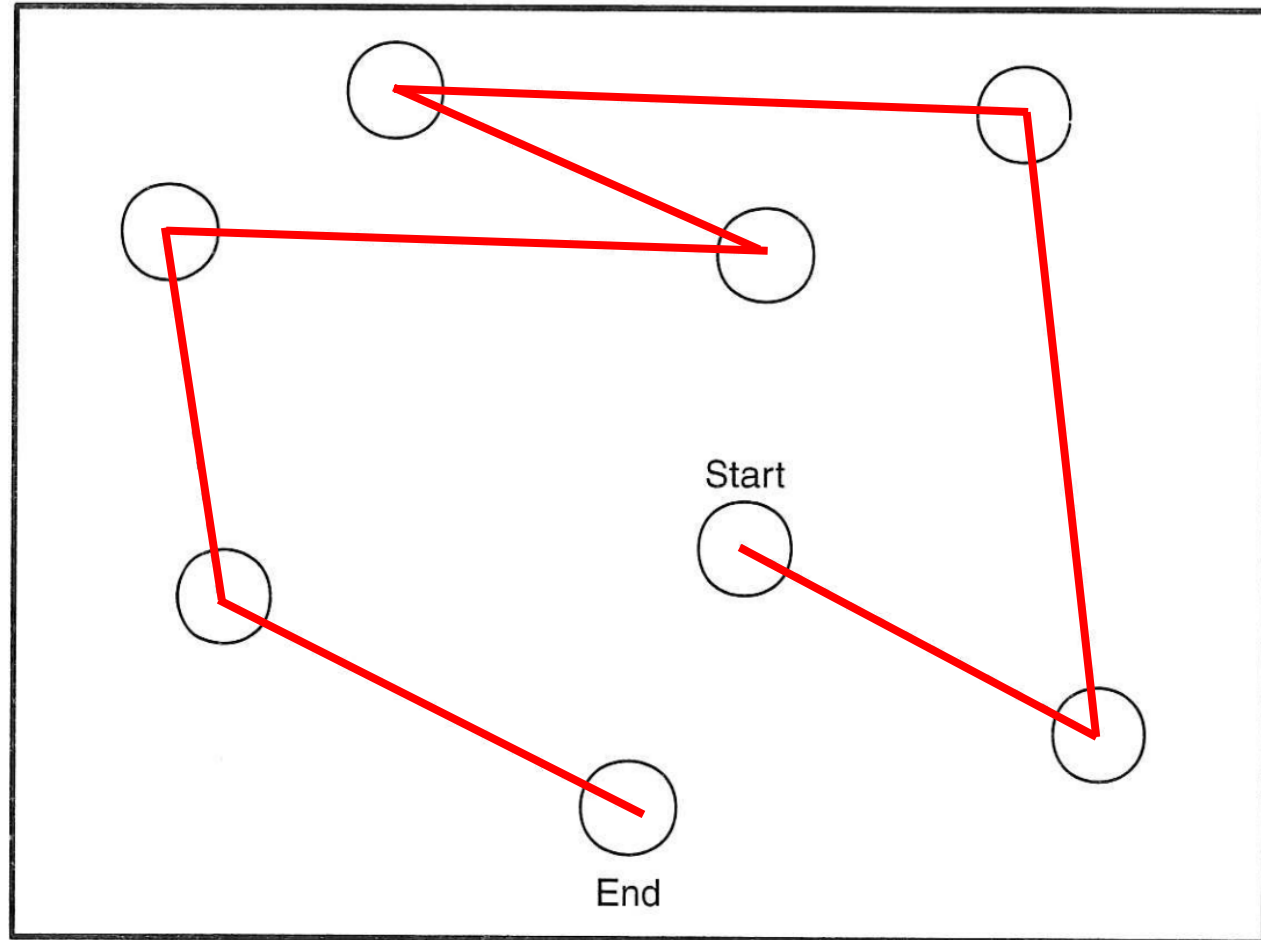
- Number/Letter Switching



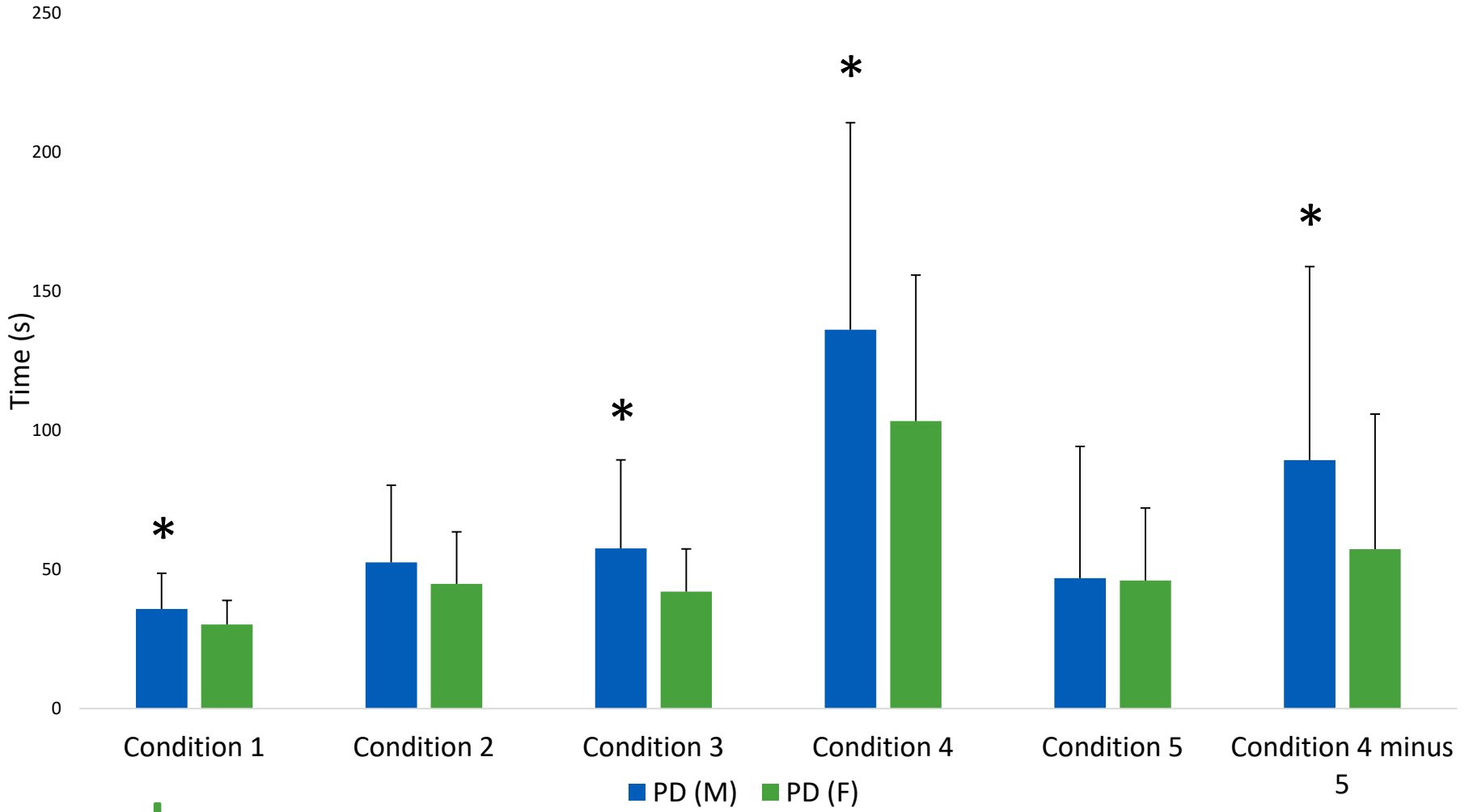
TRAIL MAKING TEST

Condition 5

- Motor Speed correction



TRAIL MAKING TEST



VERBAL FLUENCY

Condition 1

- Letter Fluency
 - F A S

Condition 2

- Category Fluency
 - Animals and Boy's Names

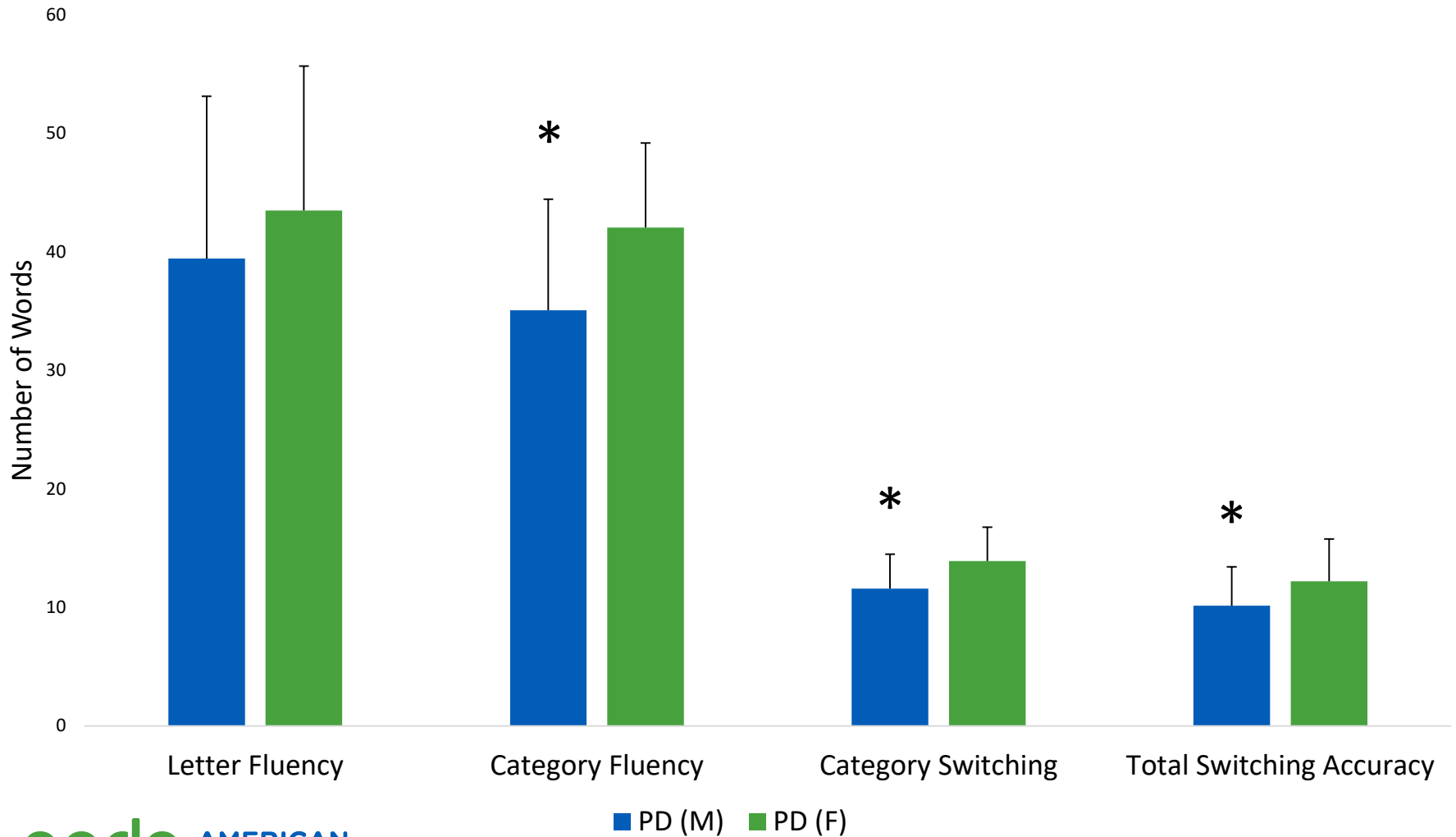
Condition 3

- Fruits/ Furniture

Total Switching Accuracy

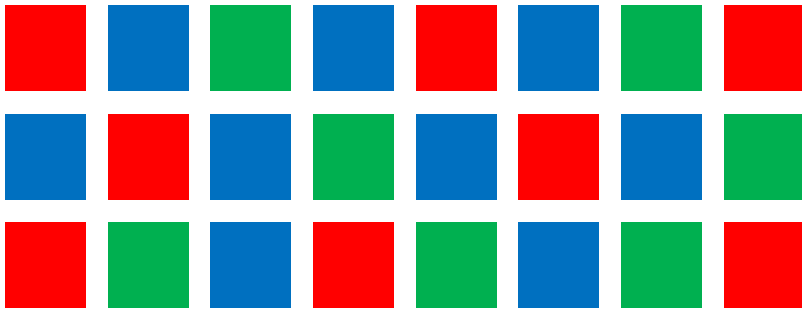
- Number of total correct category switches between fruit and furniture

VERBAL FLUENCY



COLOR WORD INTERFERENCE

Condition One



Condition Two

green red blue green blue red blue green
blue green red green red blue green red
green blue red green blue red green blue

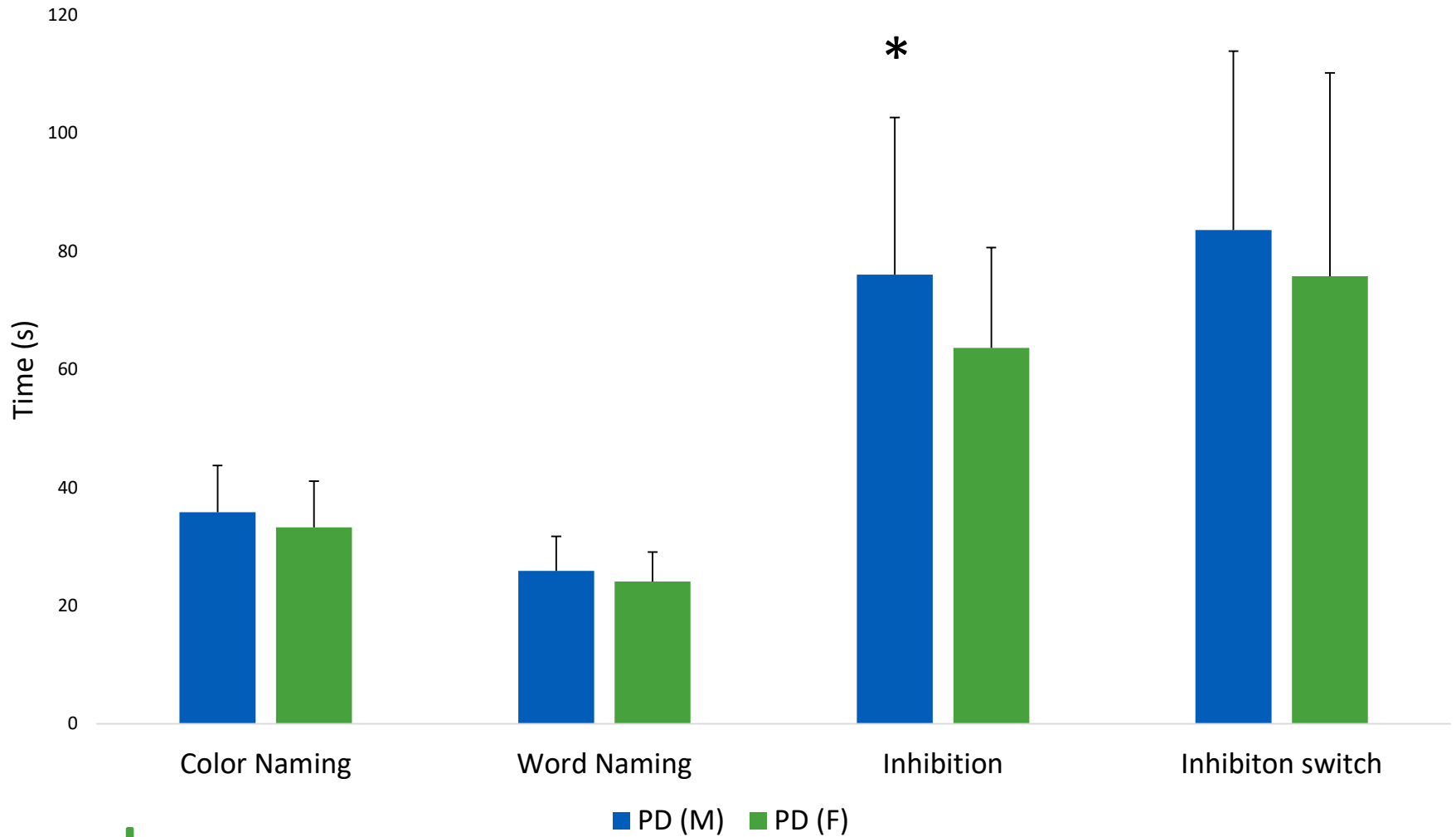
Condition Three

green red blue green blue red blue green
blue green red blue green red green red
red blue green blue red green green blue

Condition Four

green red blue green blue red blue green
blue green red green red blue green red
green blue red green blue red green blue

COLOR WORD INTERFERENCE



SYMBOL DIGIT MODALITIES TEST (SDMT)

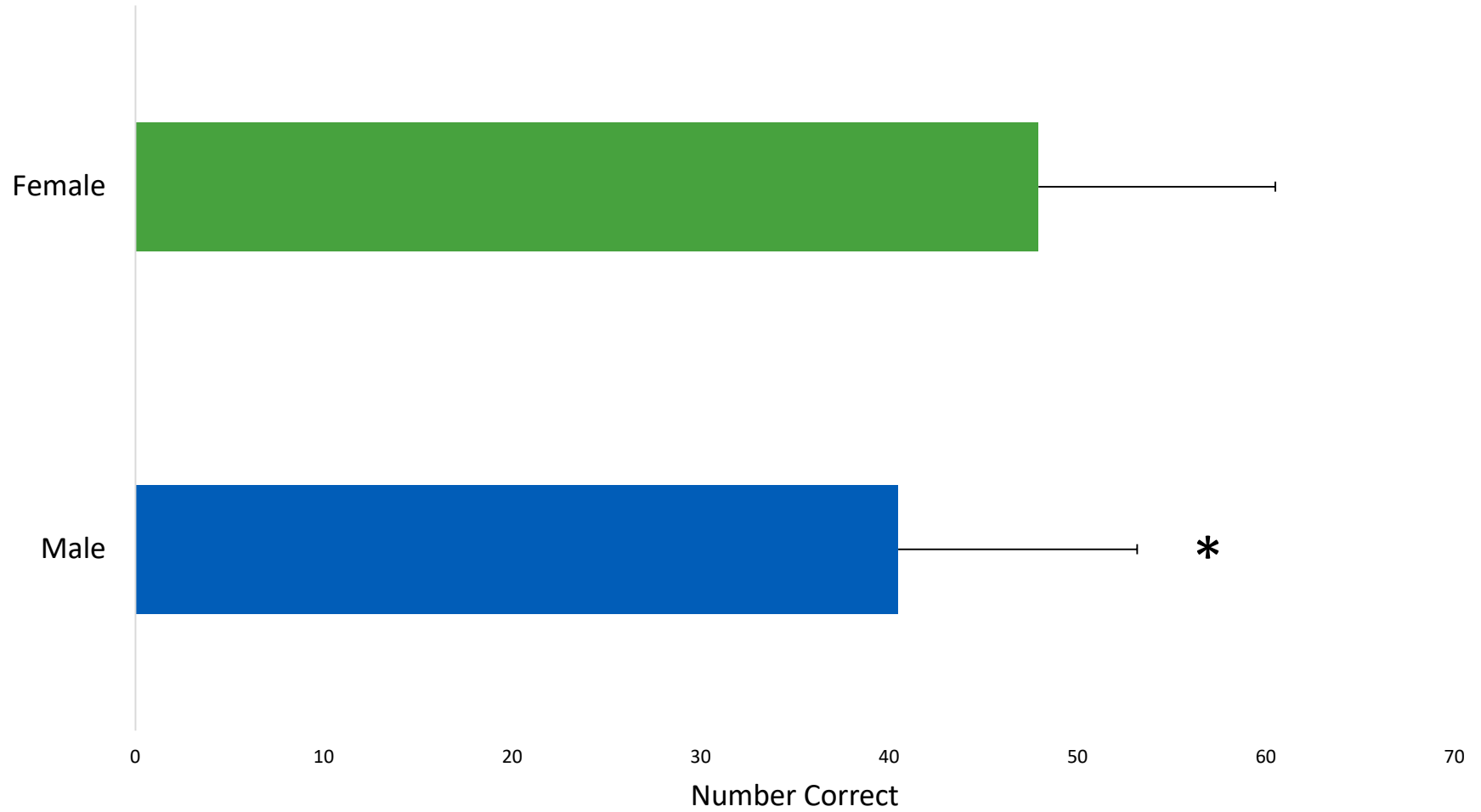
| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| C | ÷ | ┌ | ┐ | └ | > | + | ∩ | ÷ |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| C | └ | ÷ | C | ┌ | > | ÷ | ┐ | C | > | ÷ | C | > | C | ÷ |
| | | | | | | | | | | | | | | |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ┐ | > | C | ÷ | └ | > | ┌ | ┐ | C | ÷ | > | ÷ | ┐ | ┌ | ∩ |
| | | | | | | | | | | | | | | |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ┐ | └ | + | ∩ | C | ┌ | + | ┐ | ∩ | └ | ÷ | ÷ | ┌ | ┐ | + |
| | | | | | | | | | | | | | | |

SYMBOL DIGIT MODALITIES TEST (SDMT)



REAL WORLD IMPLICATIONS

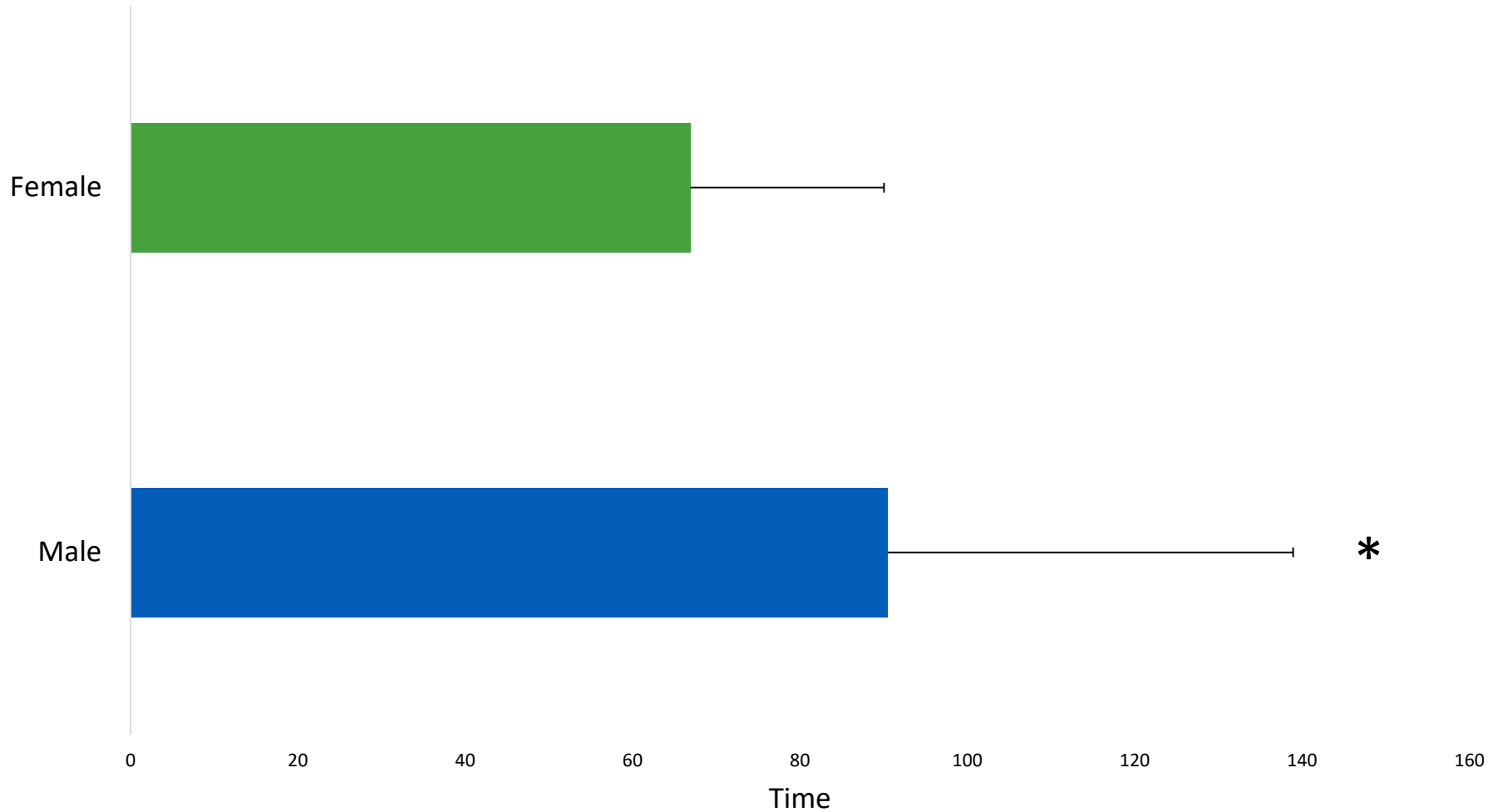
How do cognitive deficits impact activities of daily living?



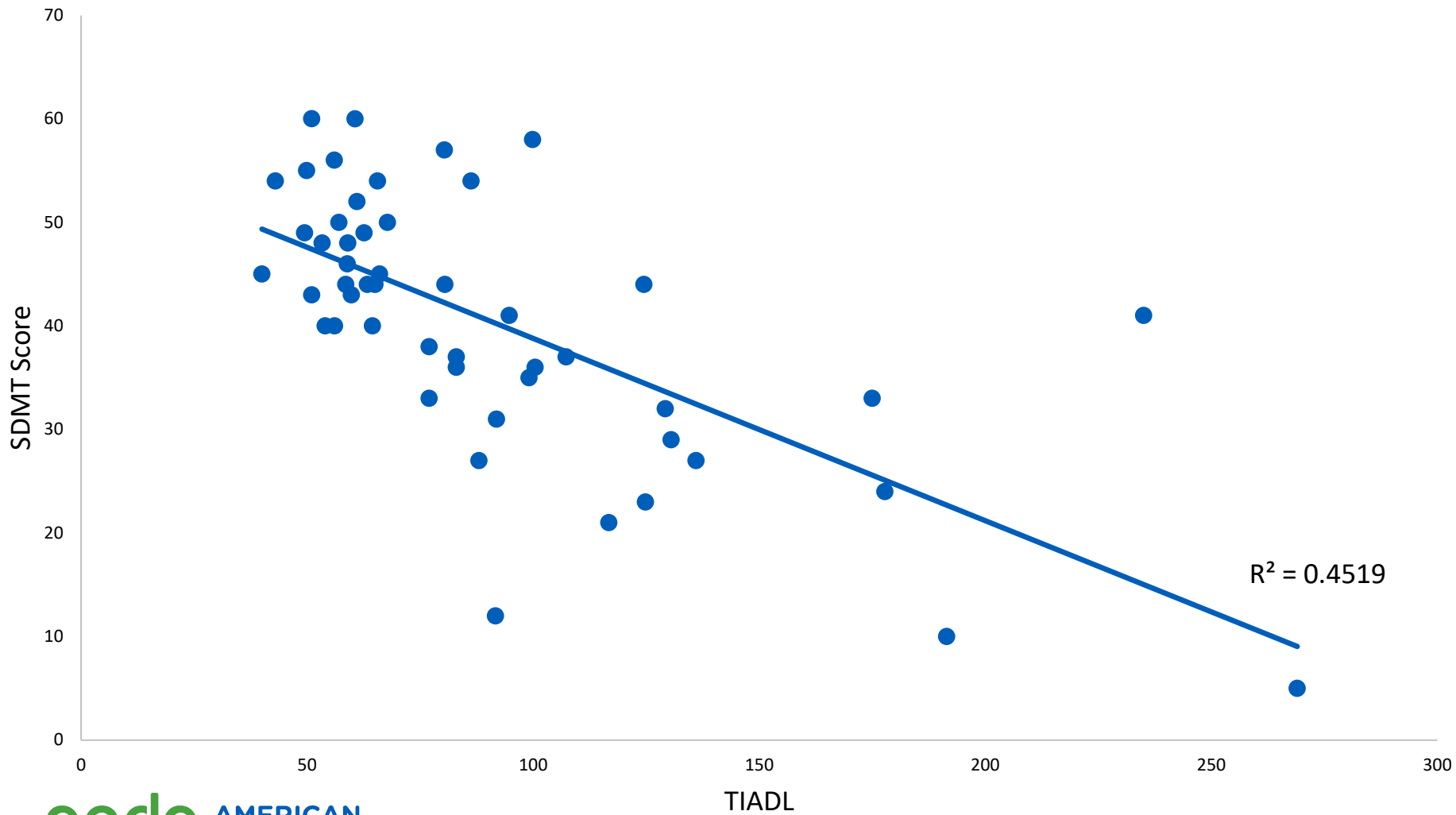
TIMED INSTRUMENTAL ACTIVITIES OF DAILY LIVING (TIADL)

| Domain | Task |
|---------------|--------------------------------------------------|
| Communication | Finding a telephone number |
| Finances | Making Change |
| Food | Reading the first 3 ingredients on a can of food |
| Shopping | Finding 2 items on a shelf |
| Medicine | Reading the direction on a medicine bottle |

TIMED INSTRUMENTAL ACTIVITIES OF DAILY LIVING (TIADL)



REGRESSION



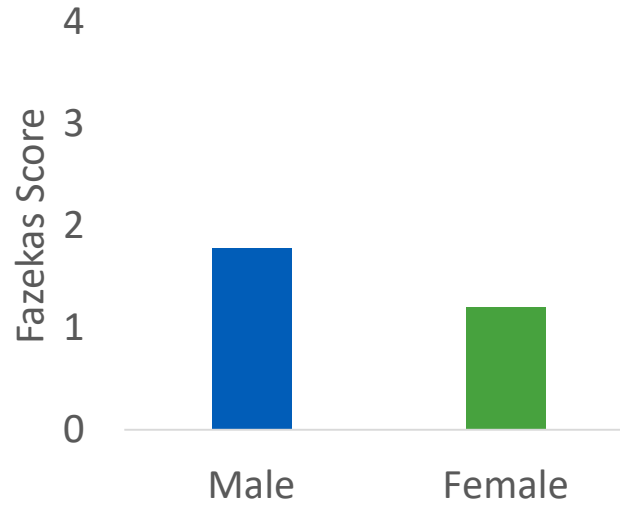
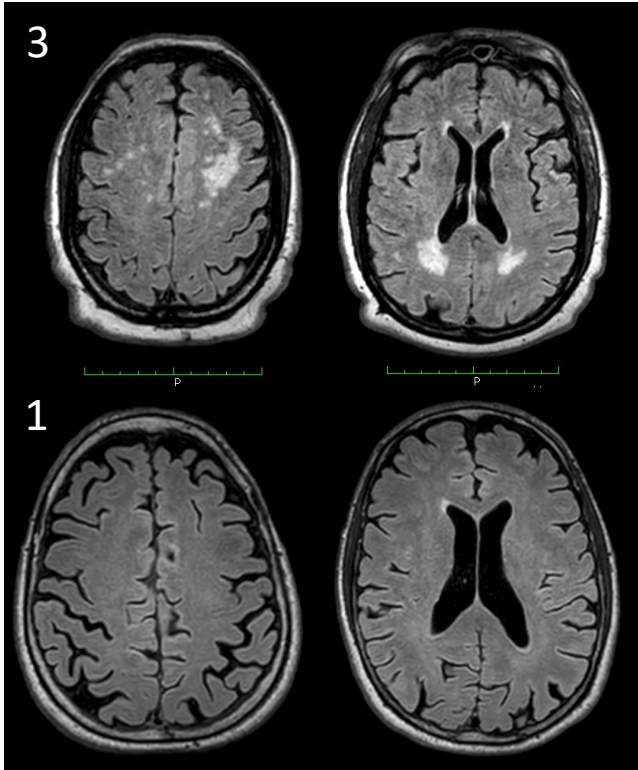
- Processing speed deficits have been hypothesized to account for the majority of age-related variance for a variety of cognitive tasks. A necessary assumption of this theory is that **processing speed is a fundamental part of the cognitive architecture that is common across cognitive domains.**
- Limited Time Mechanism: Cognitive performance may decline with decreased speed of processing because relevant operations cannot be successfully completed in a timely manner. If early operations are not completed, then later processes will be less effective.
- Simultaneity Mechanism: Decreased processing speed results in reduced performance on complex tasks because the products of early processing are no longer available when later processing occurs, thus reducing the amount of simultaneously available information.

Salthouse et al., 1996; Nguyen et al. 2017

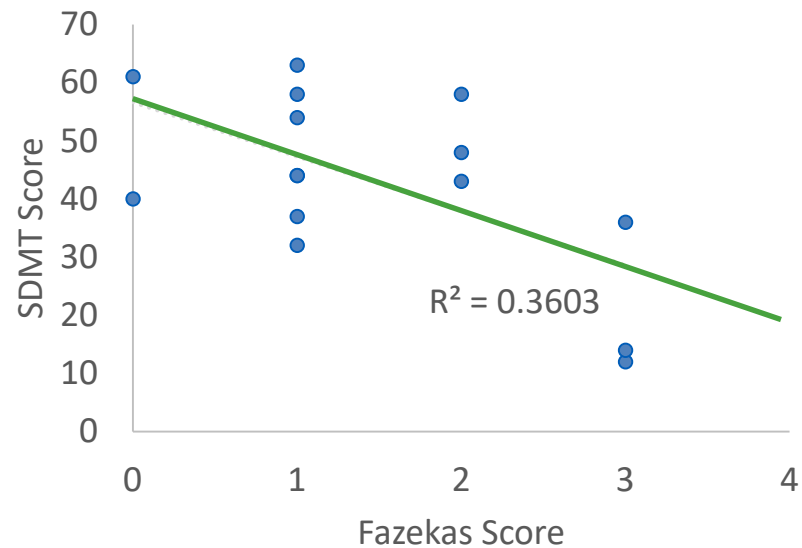
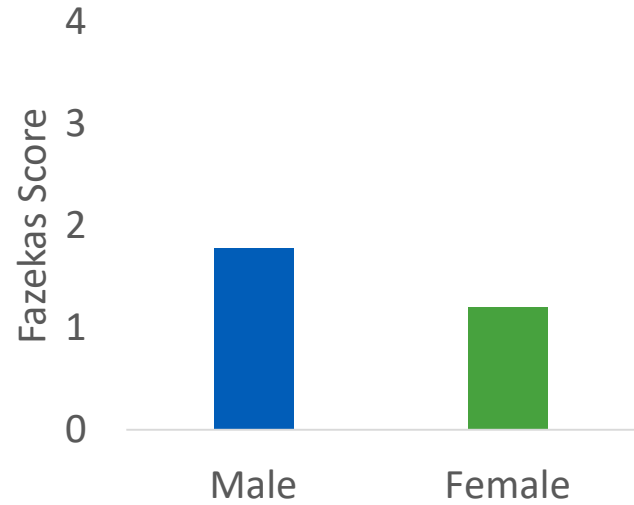
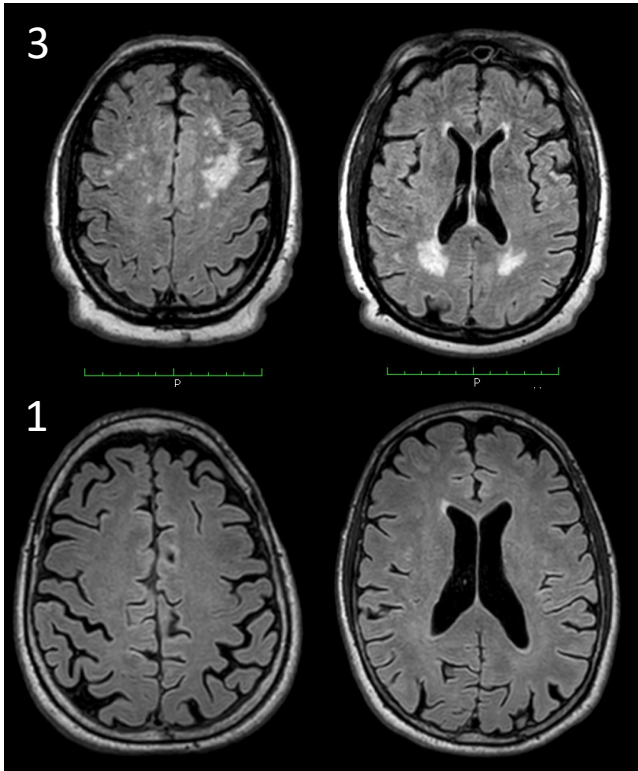
MRI BASED BIOMARKERS OF COGNITIVE FUNCTION

- Fluid-attenuated inversion recovery (FLAIR)
- Spectroscopy
- Functional Connectivity

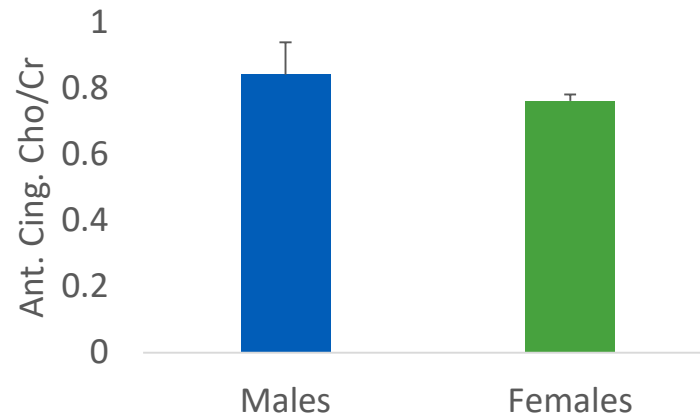
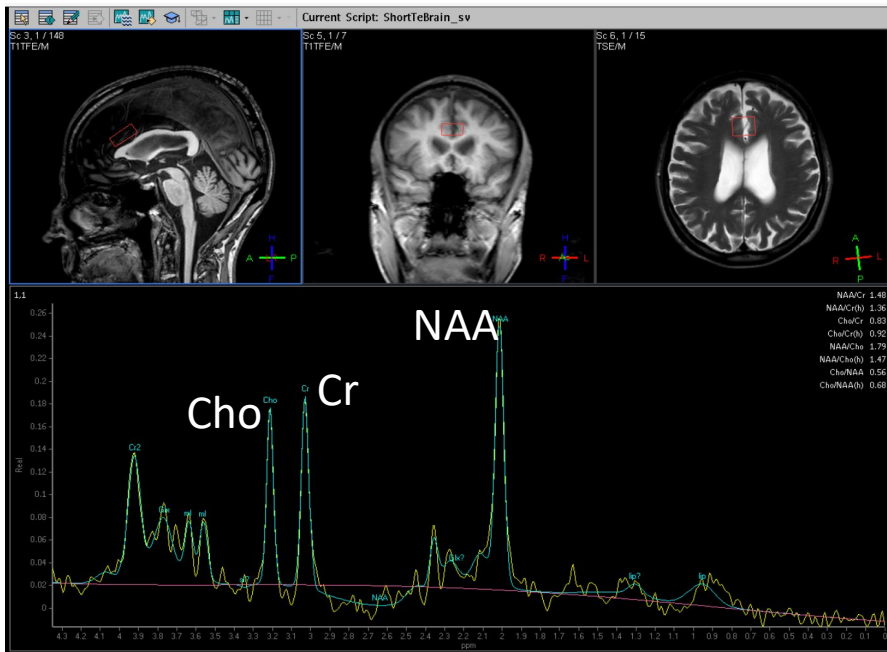
FLAIR: WM Disease



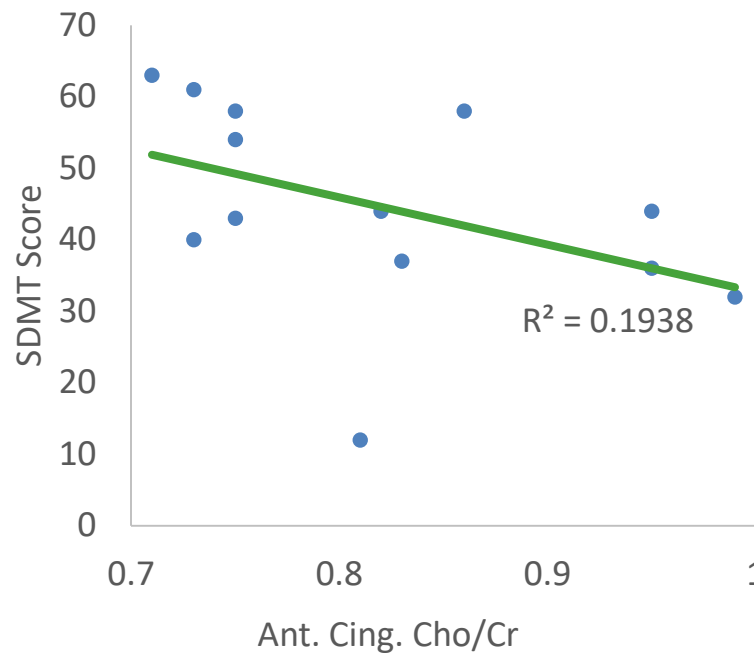
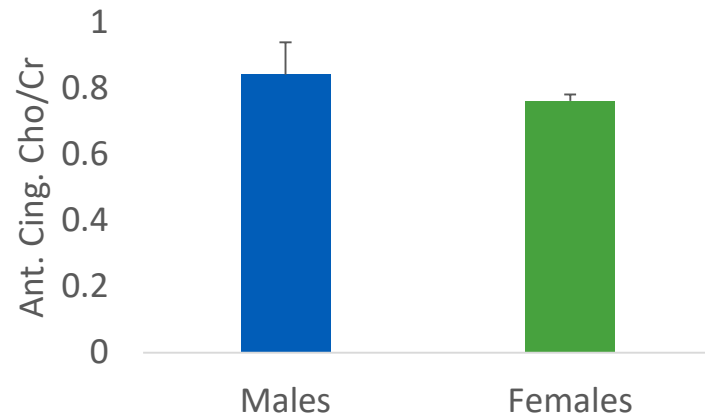
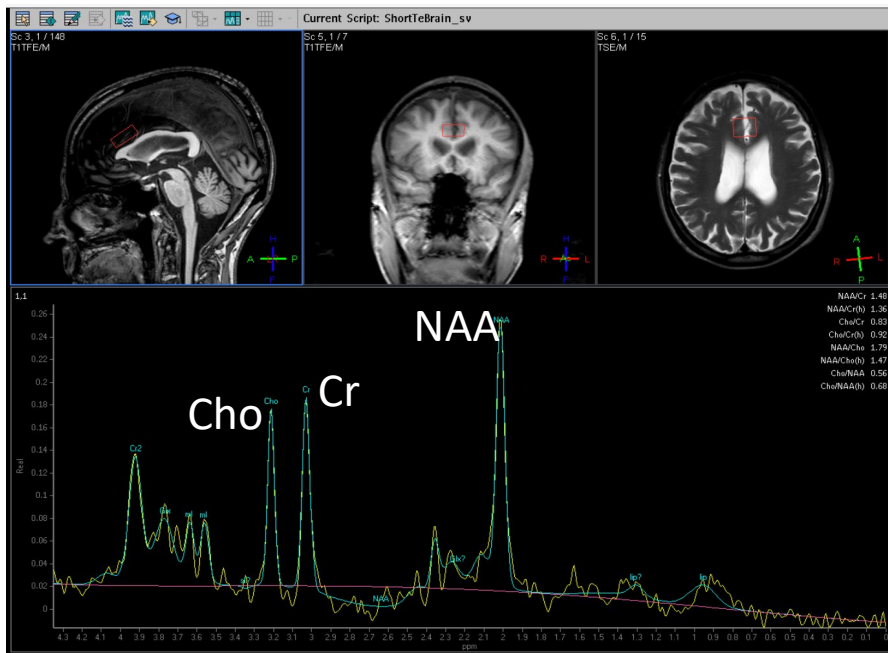
FLAIR: WM Disease



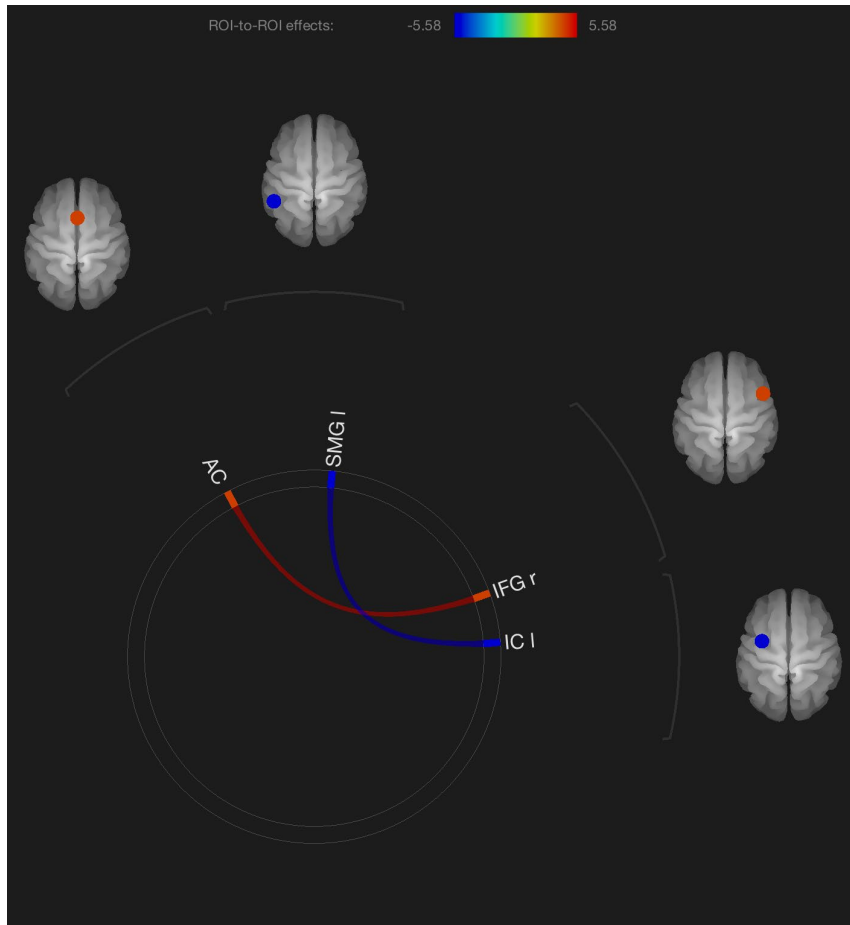
MR Spectroscopy



MR Spectroscopy

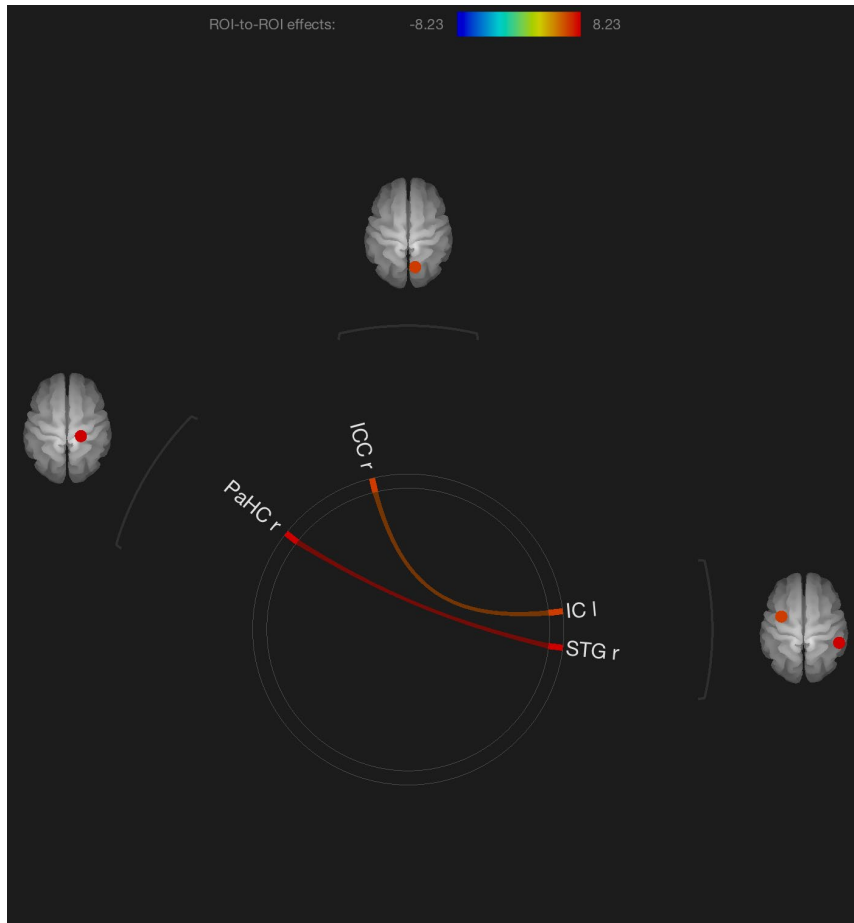


FUNCTIONAL CONNECTIVITY: PD MALE > FEMALE



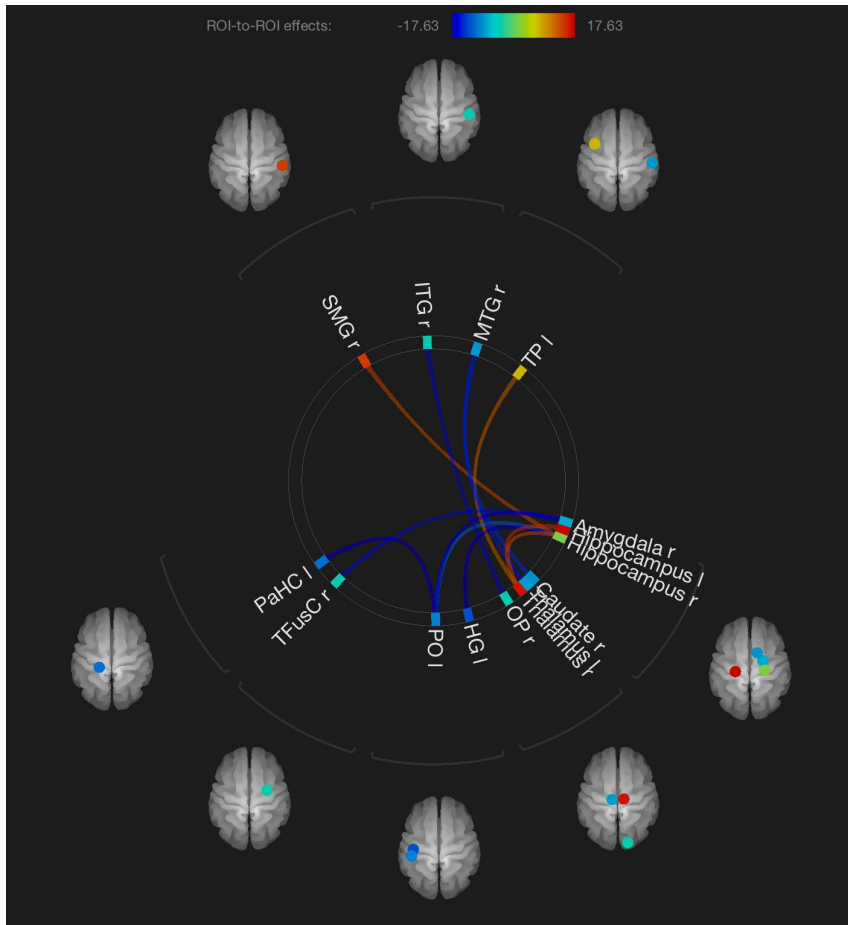
- AC, Anterior Cingulate Gyrus
- IFG r, Inferior Frontal Gyrus, Right
- SMG l, Supramarginal Gyrus, Left
- IC l, Insular Cortex Left

FUNCTIONAL CONNECTIVITY: PD MALE AND SDMT, SIMPLE EFFECT OF SDMT



- PaHC r, Parahippocampal Gyrus Right
STG r, Superior Temporal Gyrus Right
- ICC r, Intracalcarine Cortex Right
IC l, Insular Cortex Left

FUNCTIONAL CONNECTIVITY: PD FEMALE AND SDMT, SIMPLE EFFECT OF SDMT



- SMG r, Supramarginal Gyrus Right
- Hippocampus Left
- ITG r, Inferior Temporal Gyrus Right
- OP r, Occipital Pole Right
- MTG r, Middle Temporal Gyrus Right
- Caudate Right
- TP l, Temporal Pole Left
- Thalamus Left
- HG l, Heschl's Gyrus Left
- Hippocampus L
- PO l, Parietal Operculum Cortex Left
- PaHC l, Parahippocampal Gyrus Left
- Hippocampus L

TFusC r, Temporal Fusiform Cortex Right

CONCLUSIONS

- Men consistently had poorer performance than women in many cognitive domains
- Processing speed was associated with everyday function
- Brain imaging data is correlated with processing speed in PD





- Thank you to the American Parkinson Disease Association!