An overview of the COMPASS-ND study of the Canadian Consortium for Neurodegeneration in Aging (CCNA)

Jennifer Fogarty, Ph.D.

Natalie Phillips, Ph.D.

Université Concordia University

LAWSON HEALTH RESEARCH INSTITUTE

Hôpital général juif Jewish General Hospital

INSTITUT LADY DAVIS DE RECHERCHES MÉDICALES / LADY DAVIS INSTITUTE FOR MEDICAL RESEARCH

CCNA Canadian Consortium on Neurodegeneration in Aging

CCNV Consortium canadien en neurodégénérescence associée au vieillissement

Objectives for Today's Session

- Review of training and quality control
- Orientation to cognitive test battery from screening visit (used for diagnostic purposes) and neuropsychology visit (used for clinical characterization)
- Familiarize people with the tests, the norms, and encourage discussion about research questions and collaborations
- Review of data from the release

Screening and Neuropsychology Test Battery Training

- Training Procedures:
  - Staff watch videos of Dr. Fogarty give the tests to a participant and then rate the participant's responses. These ratings are monitored and feedback is given.
  - Staff then administer the tests to another individual at their site, audio-record the session and score the tests. This administration is monitored and feedback is given.
  - For the screening visit, staff members can then test on their own but are asked to audio-record the cognitive measures. The recording is used to monitor the scoring of the cognitive measures.
  - For the neuropsychology visit, the first two participants are observed via secure video conference and feedback is given live. The session is audio-recorded and monitored.
  - From there on every participant is monitored in a similar fashion with audio-recording with the exception of the neuropsychology visit where staff members are eventually moved to partial monitoring.

Screening Visit

Domain	Measures
General Cognitive Screening	MoCA
Memory	CERAD Logical Memory Benson (Recall)
Visuoperceptual and Construction	Benson (Copy)

- MoCA is used for all diagnostic groups
- CERAD and Logical Memory are used for Controls, SCI, MCI, V-MCI and AD and Mixed Dementia groups
- Benson Figure is used for PD, PD-MCI and PDD, LBD and FTD groups

Neuropsychology Visit

Domain	Measures
Premorbid IQ	WAIS-III Vocabulary
Memory	Rey Auditory Verbal Learning Test Brief Visuospatial Memory Test CCNA-CIMA-Q Face Name Matching Digit Symbol (Incidental Recall) Envelope Test
Visuoperceptual and Construction	Birmingham Object Recognition Battery Judgement of Line Orientation Test Brief Visuospatial Memory Test (Copy)
Complex Attention and Executive Functioning	DKEFS Letter Fluency DKEFS Category Fluency Reitan Trail Making Test DKEFS Color Word Interference Test CCNA-CIMA-Q Sentence Interference Test CCNA-CIMA-Q Reaction Time Test
Processing Speed	WAIS-III Digit Symbol (Coding)
Working Memory	WAIS-III Digit Span Forward and Backward CCNA Reaction Time Test (n-back condition)
Speech and Language	NACC Word Reading Test NACC Semantic Word-Picture Matching Test NACC Semantic Associates Test NACC Northwestern Anagram Test NACC Sentence Reading/Repetition NACC Noun and Verb Naming Test Cookie Theft Picture Description

Cognitive Inclusion Criteria

Cognitive Intact Elderly	Subjective Cognitive Decline	Mild Cognitive Impairment	Vascular Mild Cognitive Impairment	Alzheimer's Disease	Mixed	Parkinson's Disease	Parkinson's Disease with Mild Cognitive Impairment	Parkinson's Disease Dementia	Frontotemporal Dementia	Lewy Body Dementia
CIE	**SCD**	**MCI**	**V-MCI**	**AD**	**Mixed**	**PD**	**PD-MCI**	**PDD**	**FTD**	**LBD**
All of the following:	All of the following:	One or more of the following:	One or more of the following:	Two or more of the following:	Two or more of the following:	All of the following:	All of the following:	All of the following:	No cognitive cutoffs	All of the following:
MoCA ≥25 Logical Memory: ≥9 for 16+ years of education ≥5 for 8-15 years of education ≥ 3 for 0-7 years of education CERAD >5	MoCA ≥25 Logical Memory: ≥9 for 16+ years of education ≥5 for 8-15 years of education ≥ 3 for 0-7 years of education CERAD >5	MoCA 13-24 Logical Memory: <9 for 16+ years of education <5 for 8-15 years of education <3 for 0-7 years of education CERAD <6 Global CDR score >0	MoCA 13-24 Logical Memory: <9 for 16+ years of education <5 for 8-15 years of education <3 for 0-7 years of education CERAD <6 Global CDR score >0	MoCA 13-24 Logical Memory: <9 for 16+ years of education <5 for 8-15 years of education <3 for 0-7 years of education CERAD <6 Positive response to the question "Has the candidate experienced any changes in personality of behavior"	MoCA 13-24 Logical Memory: <9 for 16+ years of education <5 for 8-15 years of education <3 for 0-7 years of education CERAD <6 Positive response to the question "Has the candidate experienced any changes in personality of behavior"	MoCA ≥25	MoCA 13-24	MoCA ≥25 with abnormal results on two or more of the following : Serial 7's Lexical Fluency or Clock Drawing Figure Copy Recall <3 words		MoCA 13-24

Premorbid IQ

WAIS-III Vocabulary

- Measures expressive vocabulary and crystallized intelligence
- Subset of the Weschler Adult Intelligence Scale, Third Ed.

- Procedure
  - Participant presented 17 words with increasing difficulty and asked to give a definition for each word
  - Words presented aurally and visually simultaneously by clinician

- Scores Derived
  - Responses scored based on specific criteria (0, 1, or 2)
  - Split half score of words correctly defined (0-34)
  - Raw score and age-scaled score
  - Normative data based on norms for healthy adults (WAIS-III Canadian Technical Manual)

Memory

Rey Auditory Verbal Learning Test (RAVLT)

- List-learning paradigm
  - Two word lists of 15 nouns

- Procedure
  - Initial recall
    - Recall of initial list (A1 – A5)
    - Recall of interference list (B1), followed by recall of the initial list (A6)
  - Delayed recall of List A (A7) and recognition after a 20-minute delay

- Scores derived:
  - Learning, interference, and recall trials: raw score and Z-score of total correct items, number of intrusions, number of repetitions.
  - Recognition: hits, false positives
  - Normative data based on age-specific norms for healthy adults (Schmidt, 1996)

Brief Visuospatial Memory Test (BVMT)

- Measures visual learning and memory

- Procedure
  - Initial Recall
    - 2 x 3 array of six line drawings for ten seconds
    - Three consecutive learning trials (Trials 1-3)
  - Delayed recall trial and recognition after 25 minutes

- Scores derived:
  - Drawings scored for accuracy and placement on the page
  - Raw scores, T-scores, and percentile equivalents for scores on Trials 1-3, total recall, learning, and delayed recall
  - Percent retained, recognition hits, false alarms, discrimination index, response bias
  - Normative data based on age-specific norms for healthy adults (Benedict, 1997)

CCNA-CIMA-Q Face-Name Association Task

- Measures associative recall
  - Adapted from Dr. Brambati's pilot task by CIMA-Q

- Procedure
  - Learning trials – names presented with faces
  - Initial recall – faces presented without names
  - Delayed recall trial after 20 minutes – faces without names
  - Recognition – for faces and names
    - Recognition choices: face associated with a new name never seen before, same name, or an incorrect name that was already presented

- Scores derived:
  - Immediate recall, delayed recall, delayed recognition

Envelope Test

- Measures prospective and retrospective memory
- Procedure
  - Participants are told that at a future time, they will be asked to write a name and address on an envelope, and that they are also to turn the envelope over, seal it and write their initials on the back.
  - Prospective memory
    - After 10 minutes, participants are given the name, address and phone number and asked to write this on the envelope.
  - Retrospective memory
    - Whether participant spontaneously recalls the additional instruction to write their initials on the back

- Scores derived:
  - Prospective score
  - Retrospective score

	Seals Envelope	Writes his/her initials on the back	Prospective Memory	Retrospective Memory
Responds within the delay, without a reminder	☐	☐	___ /2	___ /2
Responds, but after the delay, with a reminder	☐	☐		
No response	☐	☐		

Visuoperceptual and Construction

Birmingham Object Recognition Battery (BORB): Object Decision Task

- Measures object perception and knowledge

- Procedure
  - Participants are shown 16 animal drawings and 16 tool drawings
    - identify whether the object is real or unreal

- Scores derived:
  - Real score (out of 16)
  - Unreal score (out of 16)
  - Combined score and age-scaled score (out of 32)
  - Norms derived based from a small healthy population (N = 13, Humphreys & Riddock, 1993)

Judgement of Line Orientation Task

- Measures visuospatial perception and judgement

- Procedure
  - Participants are shown two lines and asked to match them to a series of lines in a fan orientation.
  - 15-item split-half version administered (odd items)

- Scores derived:
  - Total score
  - Age-dependent scaled score
  - Normative data based on age-specific norms for healthy adults (Benton et al., 1994)

Complex Attention and Executive Functioning

D-KEFS Letter Fluency

- Measures phonemic fluency

- Participants asked to generate words that begin with a particular letter as quickly as possible within a 60-second time window
  - Three trials, each with a different letter
  - Words cannot be names of people, places or numbers.

- Scores derived:
  - Raw score and age-scaled score
  - Repetition errors, set-loss errors
  - Normative data based on norms for healthy adults (Delis et al., 2001)

DKEFS Semantic (category) Fluency

- Measures sematic knowledge

- Procedure
  - Participants asked to generate as many words as they can according to specific categories (animals or boys names) as quickly as possible in a 60 second time period

- Scores Derived:
  - Raw score and age-scaled score
  - Repetition errors, set-loss errors
  - Normative data based on norms for healthy adults (Delis et al., 2001).

D-KEFS Colour-Word Interference

- Measures response inhibition, interference resolution, switching

- Procedure
  - Four conditions:
    1. Color naming
    2. Word reading
    3. Inhibition – Name ink colours in which colour words are printed in a different colour ink
    4. Inhibition/Switching – alternating between reading words and naming colours

- Scores derived:
  - For all four conditions: total uncorrected errors, total self-corrected errors, total time to complete and corresponding age-scaled score
  - Normative data based on norms for healthy adults (Delis et al., 2001)

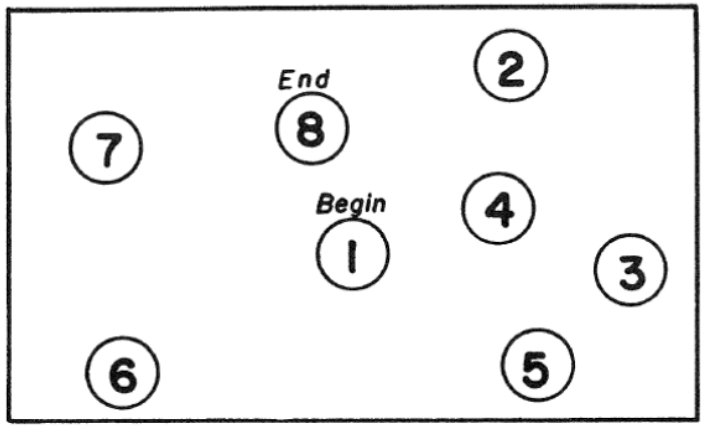
Trail Making Test

- Measures participants' ability to rapidly scan and sequence, attention switching

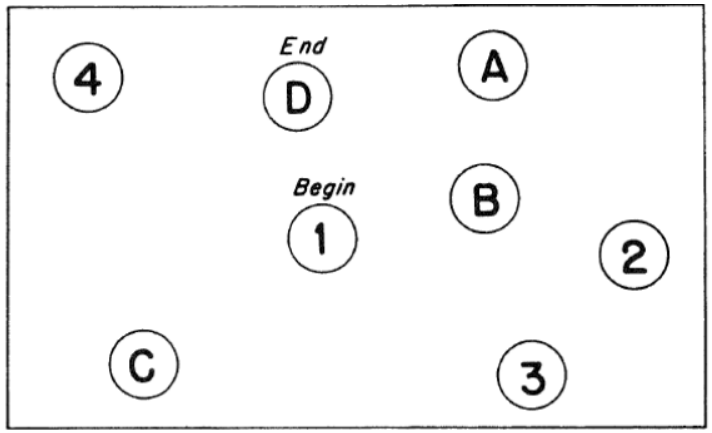
- Procedure
  - Part A: a series of dots containing numbers
  - Part B: a series of dots containing numbers and letters in an alternating series

- Scores derived:
  - Raw and scaled score for time to complete Parts A and B
  - Number of errors in Parts A and B
  - Normative data based on age- and education-specific norms for healthy adults (Tombaugh, 2003)

Part A Sample



Part B Sample



CCNA-CIMA-Q Sentence Inhibition Task

- Measures verbal inhibition
  - Adapted from Belanger & Belleville (2009)

- Procedure
  - Participants hear a series of 30 sentences, presented one at a time, in which the last word missing.
  - Participants required to give a word that fits at the end of the sentence (auto) or to give a word that is unrelated to the sentence (inhibition).

- Scores derived:
  - Correct responses for both auto (0 or 3 points) and inhibition (0, 1, or 3 points) word conditions
  - Response time

Phrase	Condition	Participant Response	Sample Responses		
			3 point	1 point	0 point
1. He crept into the room without a…	Auto		SOUND, NOISE, LIGHT, PEEP, WORD	n/a	BLUE, SUN, MOON
2. Bill hit his sister on the…	Auto		HEAD, ARM, NOSE, BUTT	n/a	MONKEY, YELLOW, ROOM
3. The lawyer feared that his client was…	Inhibition		SPOON, FORK, BLUE	CRAZY, SICK, INNOCENT, JUDGED, ABSENT, DEAD, VIOLENT, LYING	GUILTY
4. The dog chased our cat up the…	Inhibition		POTATO, PHONE, KETTLE	STREET, ROAD, TOWER OF PISA, GARDEN, CHICKEN, HILL, LADDER	TREE

Processing Speed

WAIS-III Digit Symbol-Coding

- Measures incidental learning
- Procedure
  - Symbol coding
    - 120 seconds to copy symbols paired with numbers as fast as they can
  - Incidental recall
    - Without the code, participants are required to recall the symbols which corresponded with each number.
  - Free recall
    - Boxes taken away, participants asked to remember as many symbols as they can

- Scores derived:
  - Raw score and age-scaled score
  - Incidental recall (pairing) raw score
  - Free recall raw score
  - Normative data based on norms for healthy adults (WAIS-III Canadian Technical Manual)

CCNA Reaction Time Task: Simple & Choice

- Measures reaction time and working memory
- Adapted by Joe Lindsay based on Bielak et al., (2010)

- Procedure
  - Computerized task with three conditions:
  - Simple RT: Participants instructed to press key as soon a green X appears on the screen
  - Choice RT: Participants shown a display with three squares and one colored X, instructed to press the key corresponding to X's location and color
  - N-back: Participants asked to indicate location of X seen on previous trial

- Scores Derived:
  - Reaction time

Working Memory

WAIS-III Digit Span Forward, Backward

- Measures attention span and working memory

- Procedure
  - Examiner reads series of number sequences of increasing length
  - Digits Forward: Participant asked to repeat digits in same order as presented
  - Digits Backward: Participants asked to repeated digits in reverse order

- Scores Derived:
  - Trial score (0 or 1) and item score (0, 1, 2)
  - Digit Span total score (forward and backward, 0-30)
  - Raw score and age-scaled score

Reaction Time Test

- Procedure
  - Computerized task with three conditions – the third condition is a measure of working memory
  - N-back: Participants asked to indicate location of X seen on previous trial

Speech and Language

Cookie Theft Picture Description

- Measures descriptive language
- Cookie Theft Picture of the Boston Diagnostic Aphasia Examination- Third Edition (BDAE-3) Complete Kit.

- Procedure
  - Participants shown a picture of a kitchen scene and asked to describe what they see
  - Administered after the Noun and Verb Naming Test

- Scores Derived
  - Not scored yet
  - Audio-recorded

NACC Northwestern Anagram Test

- Measures grammatical knowledge

	Target sentence	Transcribe word string order (errors only)	S Wh	O Wh
P1	Who is carrying the bride?		☐	--
1.	Who is chasing the cat?		☐	--

- Procedure
  - Participants are presented with a series of pictures demonstrating an action and given randomly arranged words on pieces of cardboard
  - Participants instructed to arrange words to make a sentence starting with “Who is” to describe each picture
  - Total of ten items, five “Subject Who” and five “Object Who” questions

- Scores Derived:
- Total target sentences for subject items (0-5), object items (0-5), and summed items (0-10)
- Percentage of target sentences for subject, object, and summed items

NACC Word Reading Test

- Measures language impairment

Regular Words

Words	Participant Response	Correct	Incorrect
BALL		☐	☐

- Procedure
  - Participants asked to read 15 regular and 15 irregular words from a stimulus card, verbatim responses recorded
  - Time limit of 10 seconds per word
  - No cues or prompting

Irregular Words

Words	Participant Response	Correct	Incorrect
EARTH		☐	☐

- Scores Derived:
- Total score for number regular and irregular words correctly spoken
  - Scoring based on whether words are spoken correctly or incorrectly
  - Regular and irregular words both given a total score of 0-15 based on number of completely accurate words
  - Audio recorded for future coding

NACC Sentence Repetition/ Reading Test

- Measures oral repetition and reading ability

Sentence	Correct	# omitted words
1. The cat ate the caterpillar.	☐	

- Procedure
- **Sentence Repetition**
  - Participants repeat five sentences (recorded) of increasing complexity
  - When sentences not accurately repeated, record number of omitted words

- **Sentence Reading**
  - Participants asked to read same five sentences, responses recorded verbatim
  - Number of omitted words recorded
  - Always given after, but not in succession with Sentence Repetition Task

- Scores Derived:
- Number of completely and accurately repeated sentences
- Number of completely and accurately read sentences
- Audio recorded for future coding

NACC Semantic Word-Picture Matching Test

- Measures word recognition and comprehension

Auditory stimulus	Participant's response	
1. dog	1	2
	3	4

- Procedure
  - Participants are presented with five different displays of four semantically related photos
  - Each display presented four times
  - Participants are instructed to point to the picture that matches the word read by the examiner
  - 10 second time limit for each, no cues or prompts

- Scores Derived:
  - Total correct out of the 20 words read by the examiner

NACC Noun and Verb Naming Test

- Measures ability to name actions and objects

Nouns for confrontation naming

Nouns	Frequency per million	Category	Response	Correct	Incorrect
GLOVE	1.8	clothing		☐	☐

Verbs for confrontation naming

Verbs	Frequency per million	Response	Correct	Incorrect
ZIP**	2.7		☐	☐

- Procedure
  - Participants asked to name 16 pictures of nouns and 16 pictures of verbs
  - Responses recorded verbatim, but only recorded for accuracy.
  - Inaccurate responses not prompted
  - 10 second time limit for participants to produce name

- Scores Derived:
  - Score for total number of verbs (0-16) and total number of nouns (0-16) correctly spoken.
  - Noun/verb ratio
  - No coding for specific types of error
  - Audio recorded and uploaded to LORIS

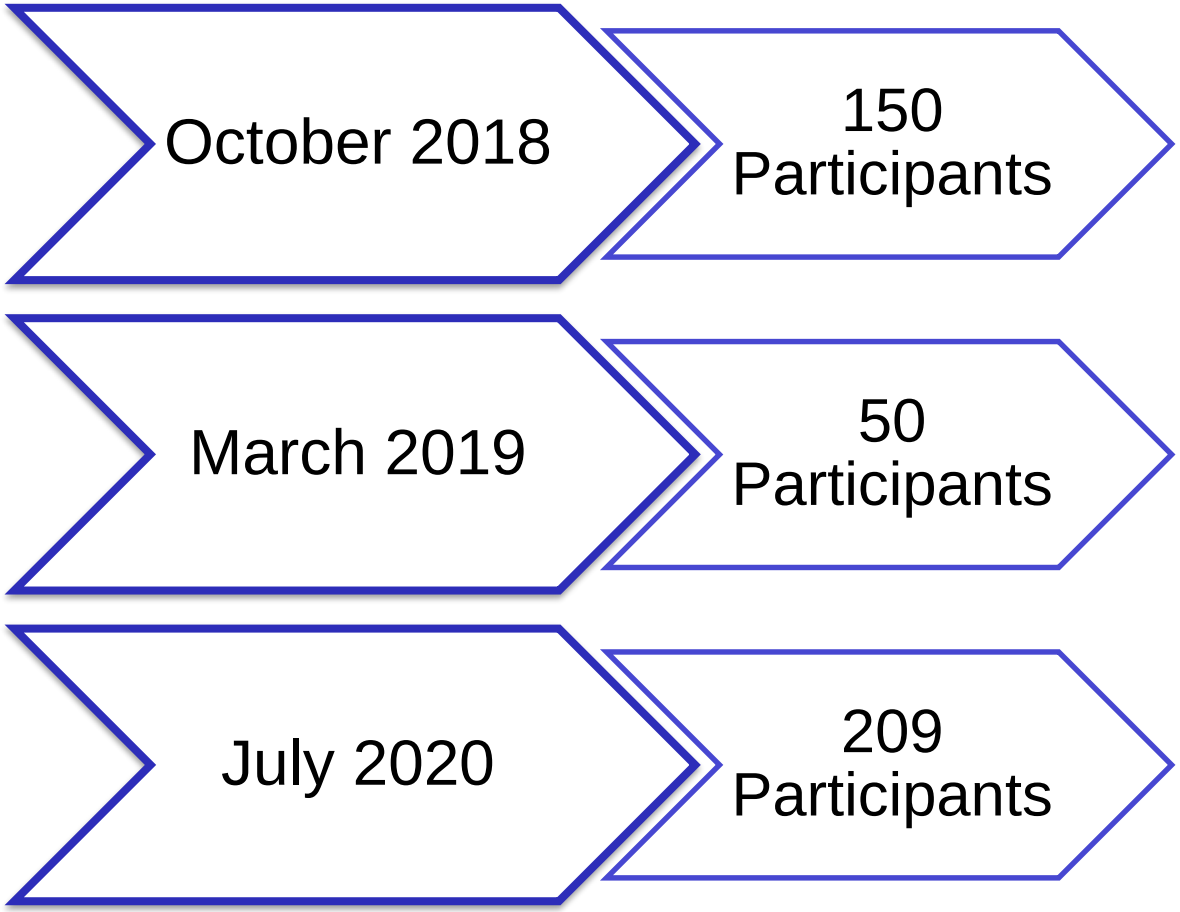
NACC Semantic Associates Test

- Measures semantic memory

	Target	Distracter	Category	
			Animals	Tools
Example 1	sweater • blanket	sweater • pillow	--	--
Example 2	sweater • chest	sweater • workbench	--	--
Example 3	sweater • dress	sweater • magnet	--	--

- Procedure
  - Participants presented with two pairs of pictures and asked to point to the pair that have a relationship
  - Total of 16 items.
- Scores Derived:
  - Total score of sum of correct items

Data Release Overview

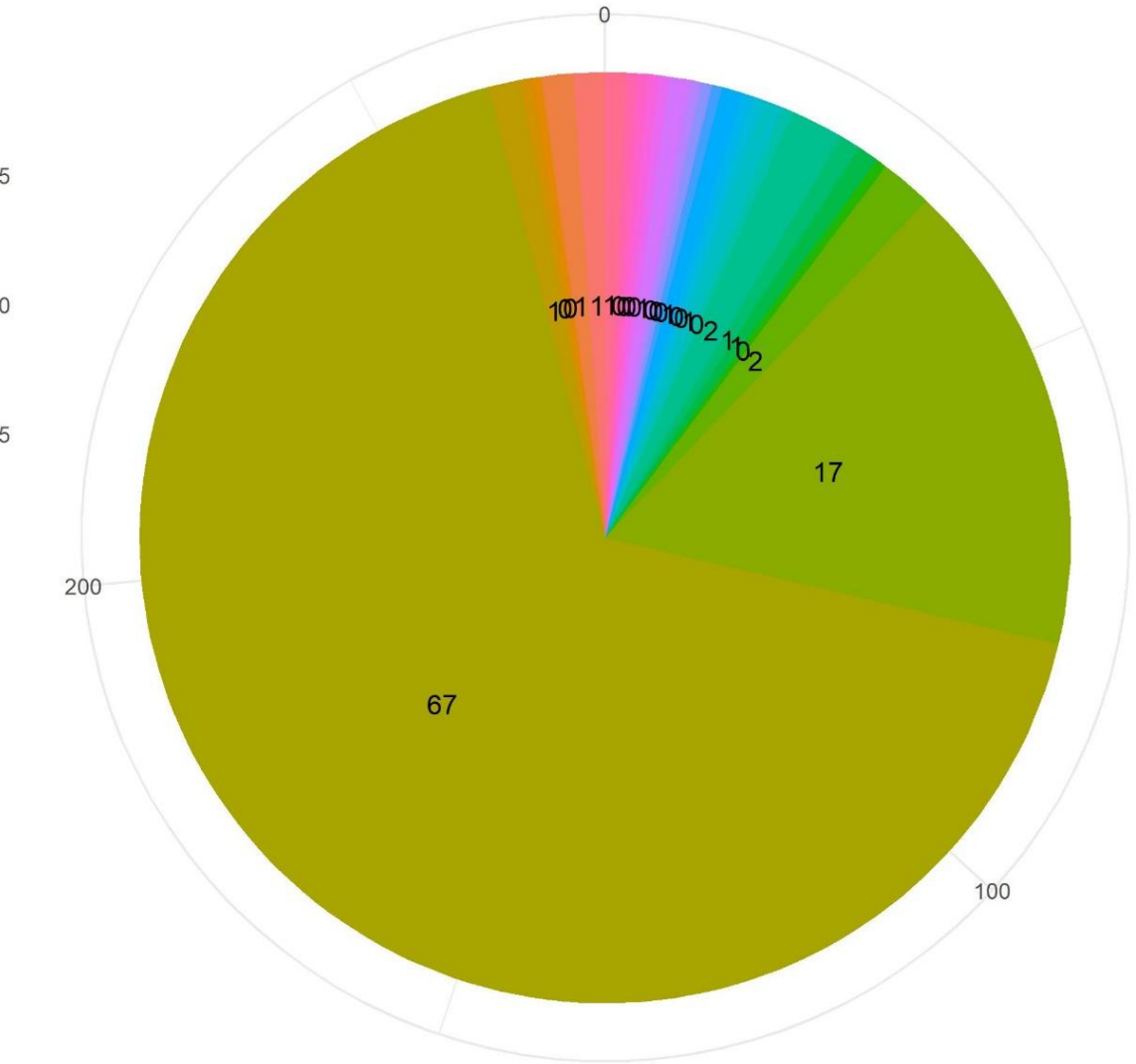


Demographics: All Groups

Group	n	W	M	Age		Education		MoCA	
		%	%	Mean	SD	Mean	SD	Mean	SD
CIE	10	100.0		71.2	6.8	14.8	4.3	28.4	1.4
SCD	56	76.8	23.2	70.0	6.9	17.0	3.1	27.3	1.9
MCI	104	44.2	55.8	71.4	6.4	15.7	4.0	24.0	3.0
V-MCI	64	35.9	64.1	77.3	4.7	15.3	3.5	23.3	3.5
AD	48	33.3	66.7	74.6	7.5	15.3	4.2	18.7	3.5
PD-MCI	25	20.0	80.0	71.4	7.6	15.8	3.5	22.0	4.0
PD	34	44.1	55.9	66.5	6.5	16.3	3.4	27.6	1.8
PDD	5		100.0	74.3	7.8	18.4	3.2	18.2	5.1
Mixed	39	48.7	51.3	78.3	5.1	14.5	3.2	18.1	3.2
FTD	12	50.0	50.0	64.3	7.7	14.5	3.8	21.3	3.8
LBD	12	16.7	83.3	73.3	4.7	14.3	5.7	19.1	4.3

Language status

Native Language of Participants
in percentages

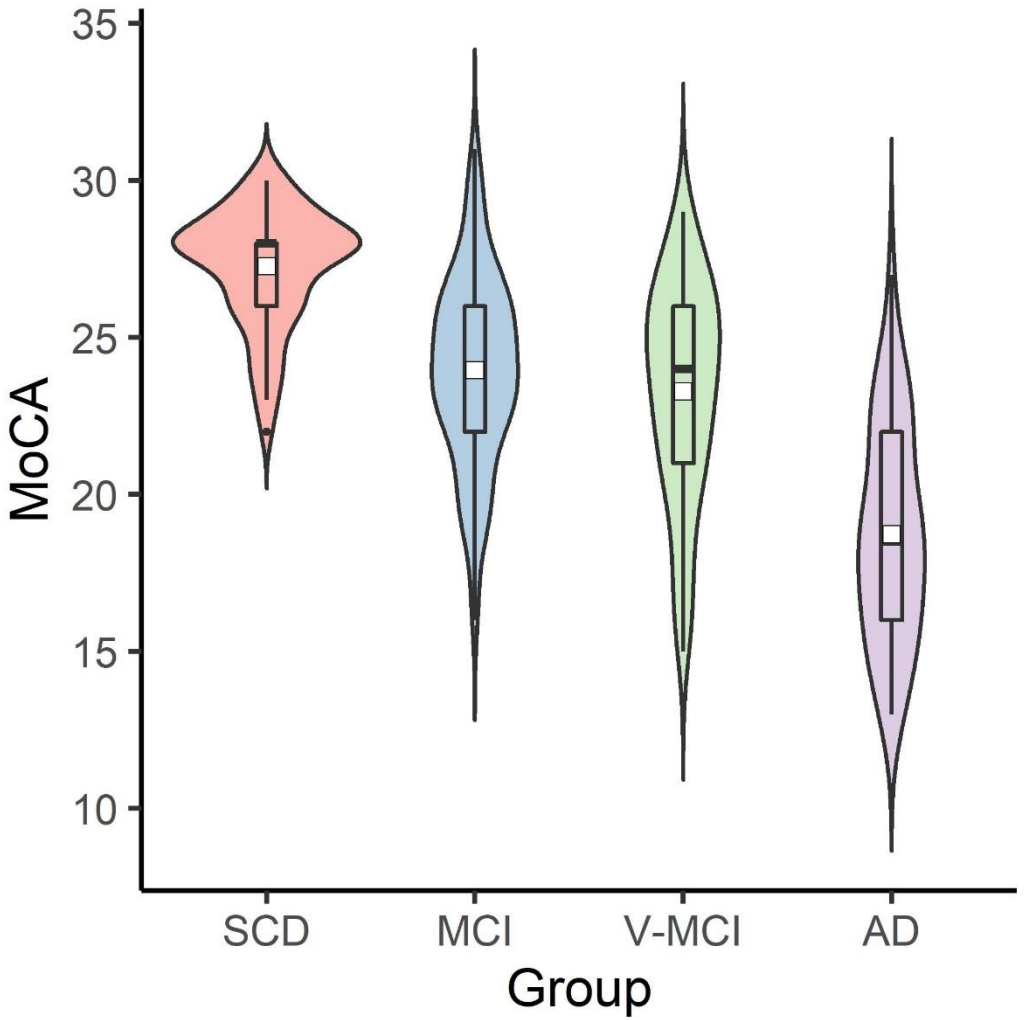


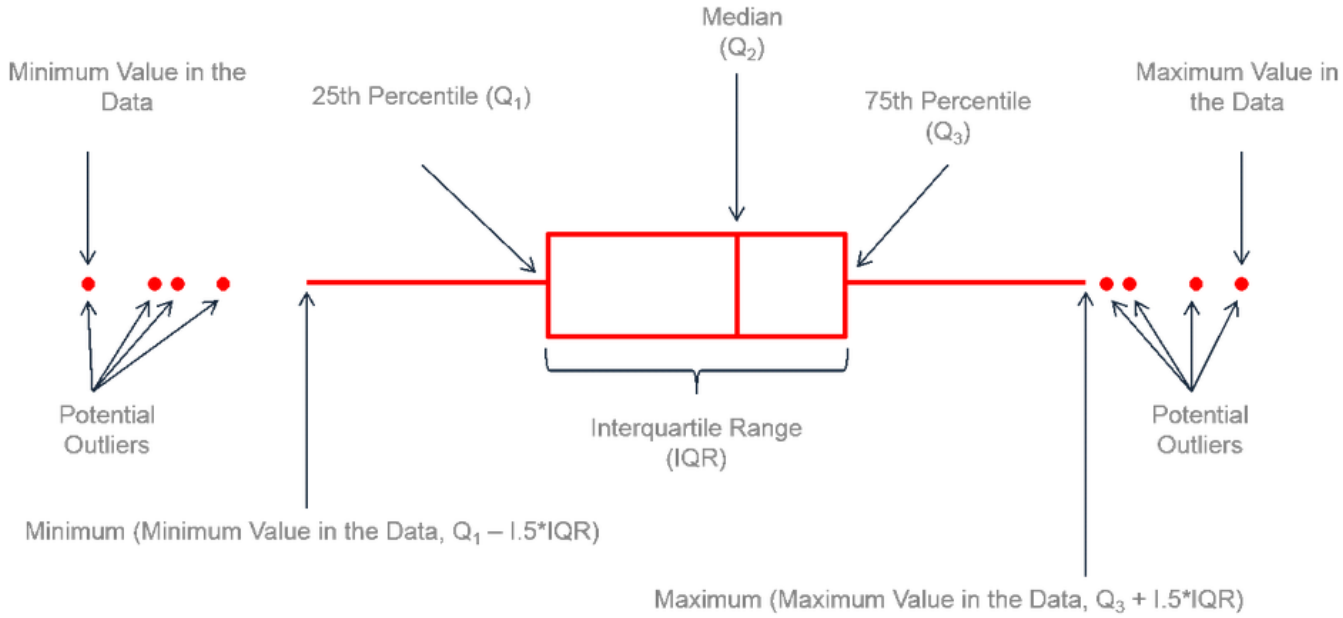
237 tested in English
35 tested in French
16 % tested in their non-native language

Type

- Arabic
- Cantonese
- Croatian
- Danish
- Dutch
- English
- French
- German
- Gujrati
- Hindi
- Hungarian
- Italian
- Norwegian
- Polish
- Portuguese
- Punjabi
- Romanian
- Russian
- Shanghainese (Chinese)
- Sirayaki
- Spanish
- Swiss
- Tagalog
- Transylvanian German
- Urdu
- Yiddish

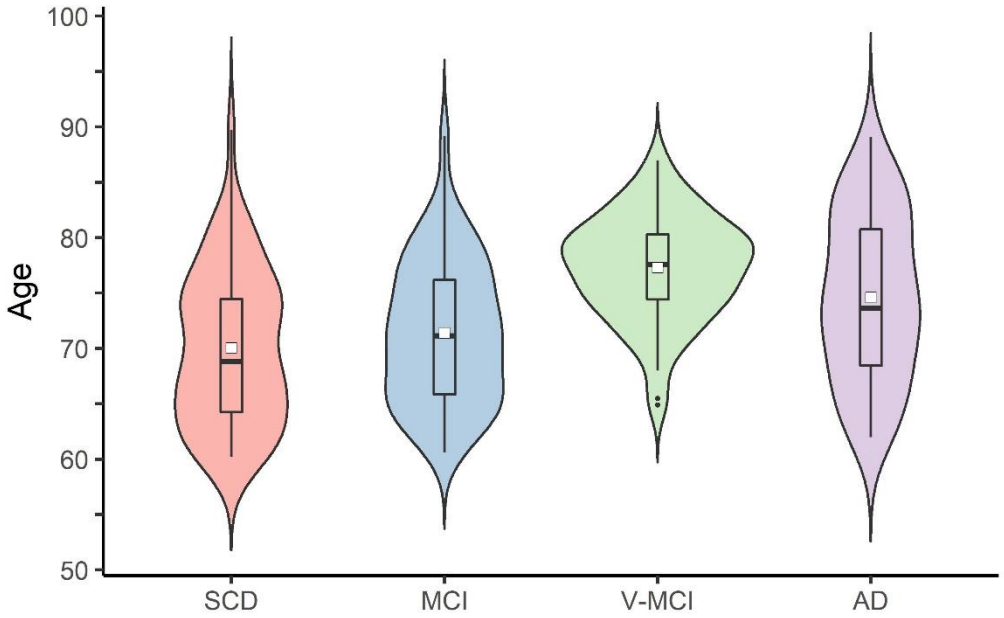
		N
SCD	Monolingual	24
	Multilingual	26
MCI	Monolingual	42
	Multilingual	50
AD	Monolingual	21
	Multilingual	24

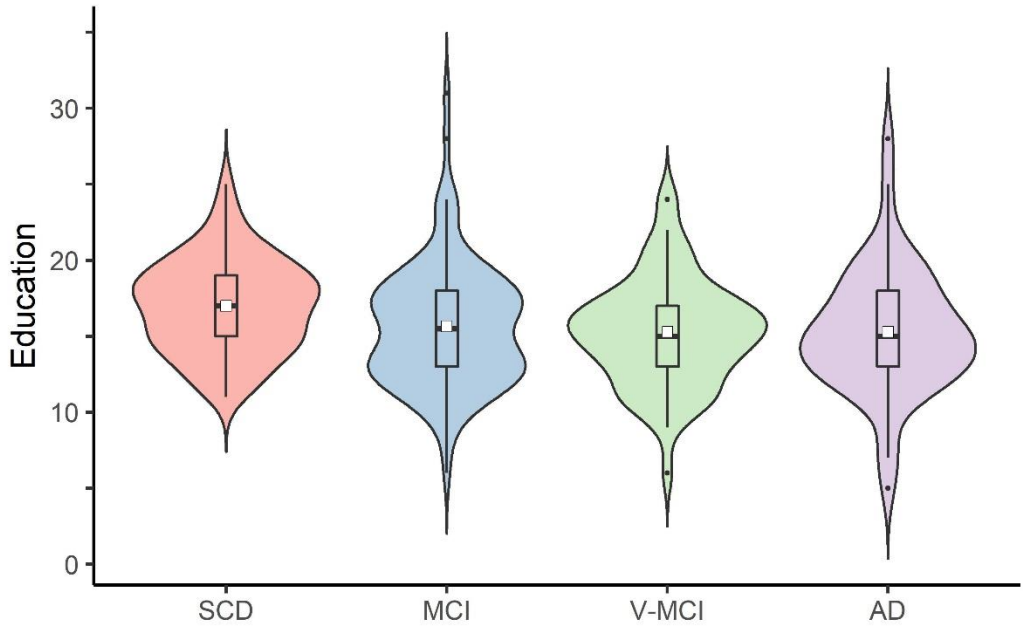




https://www.r-graph-gallery.com/boxplot.html

Demographics: SCD, MCI, V-MCI, AD

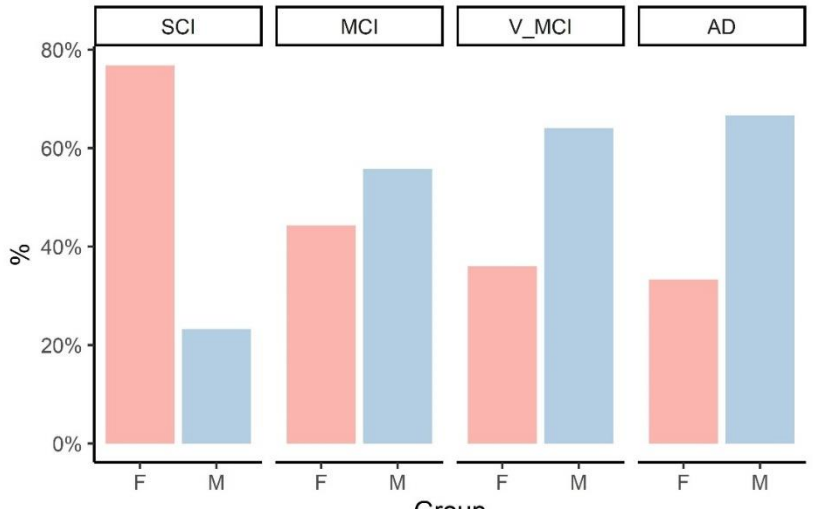




SCD = MCI
SCD < V-MCI

MCI < V-MCI

MCI < AD
V-MCI = AD

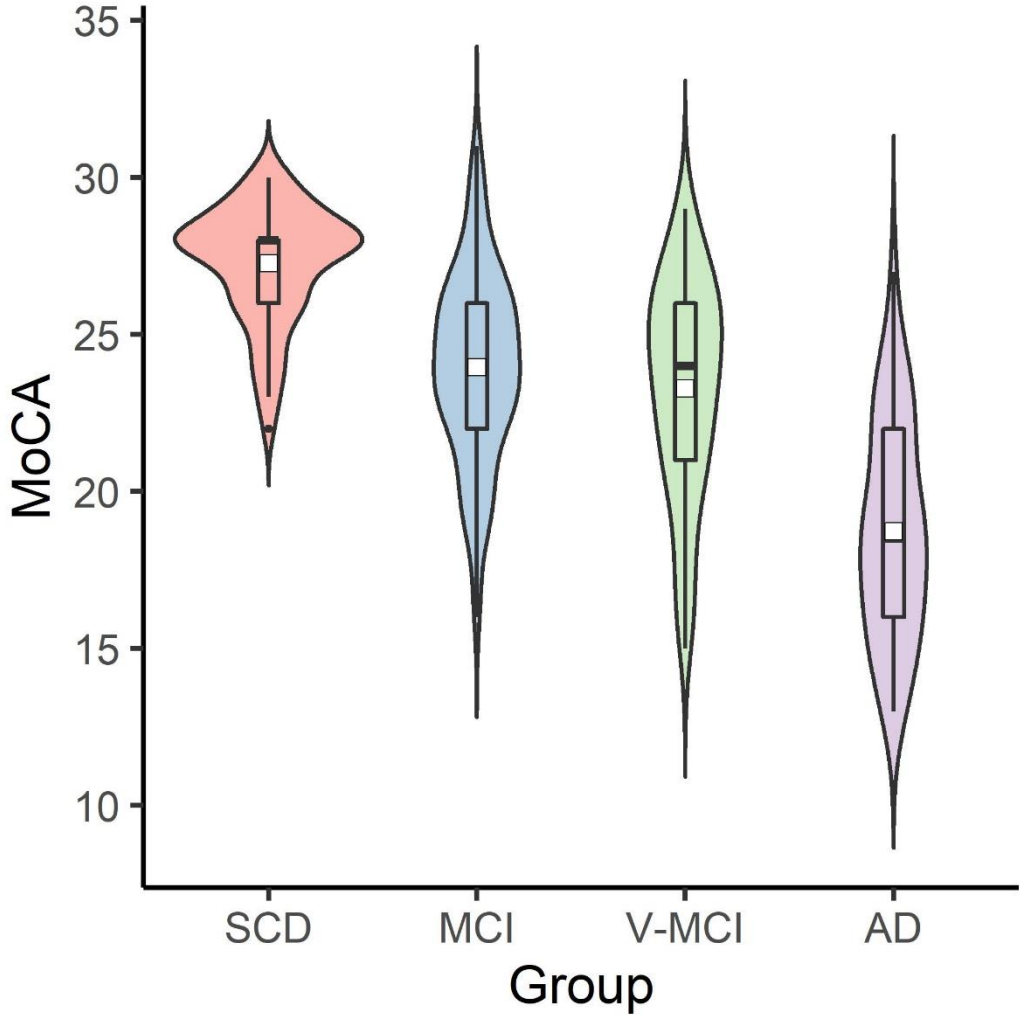


Women
Men

- Surprisingly little missing data
- We did not remove statistical outliers
- Sex
  - Groups currently not balanced on sex
  - Can be a significant predictor of cognitive function
- Language status may matter
  - Tested in L1?
  - Monolingual or multilingual?
  - Language equivalency of tests?
- Well-educated sample

- DV (cognitive variable) <- Group * Sex, Age, Education

MoCA



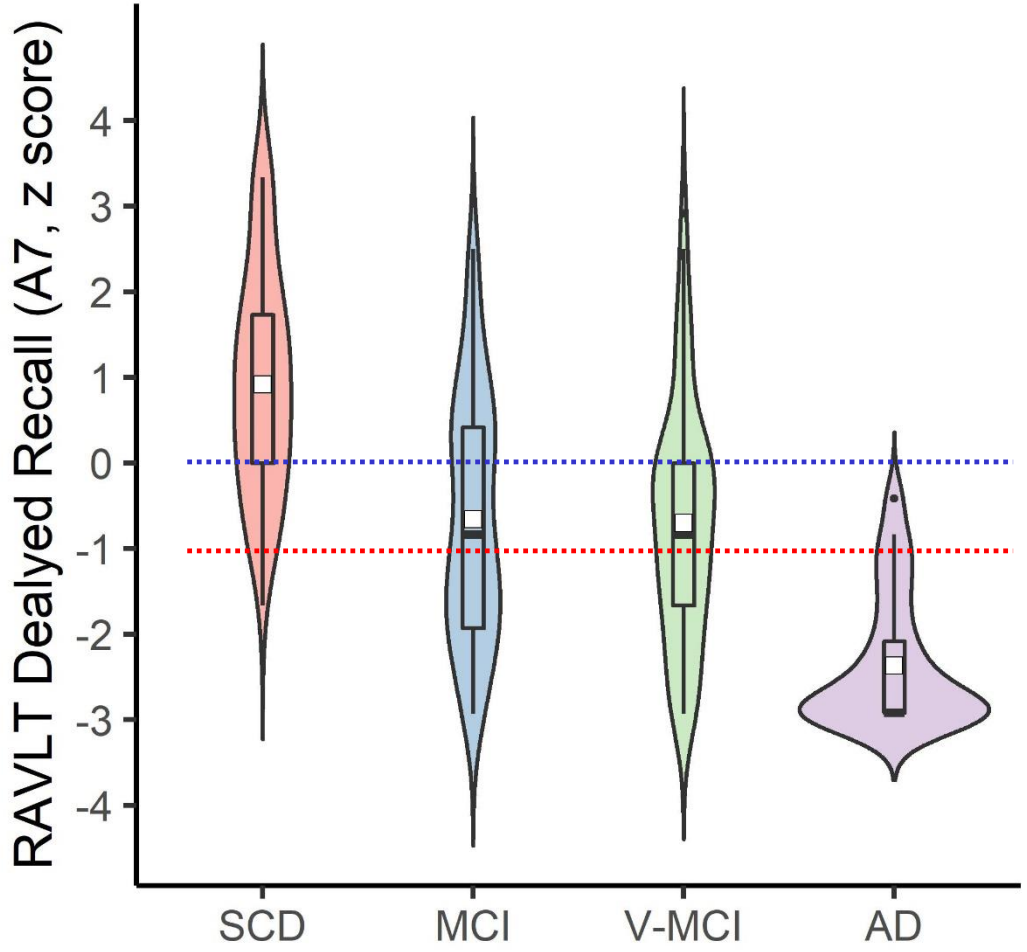
Amnestic MCI status

- Criteria
  - Score below ADNI education cutoff on Logical Memory 2, AND/OR
  - < 6 on CERAD delayed recall AND/OR
  - > 2/5 words recalled on MoCA delayed recall AND/OR
  - ≥ 0.5 or greater on CDR memory subsection

		Amnestic			
	Non-amnestic	Failed 1	Failed 2	Failed 3	Failed 4
MCI	4%	22%	39%	18%	16%
V-MCI	5%	21%	27%	26%	21%

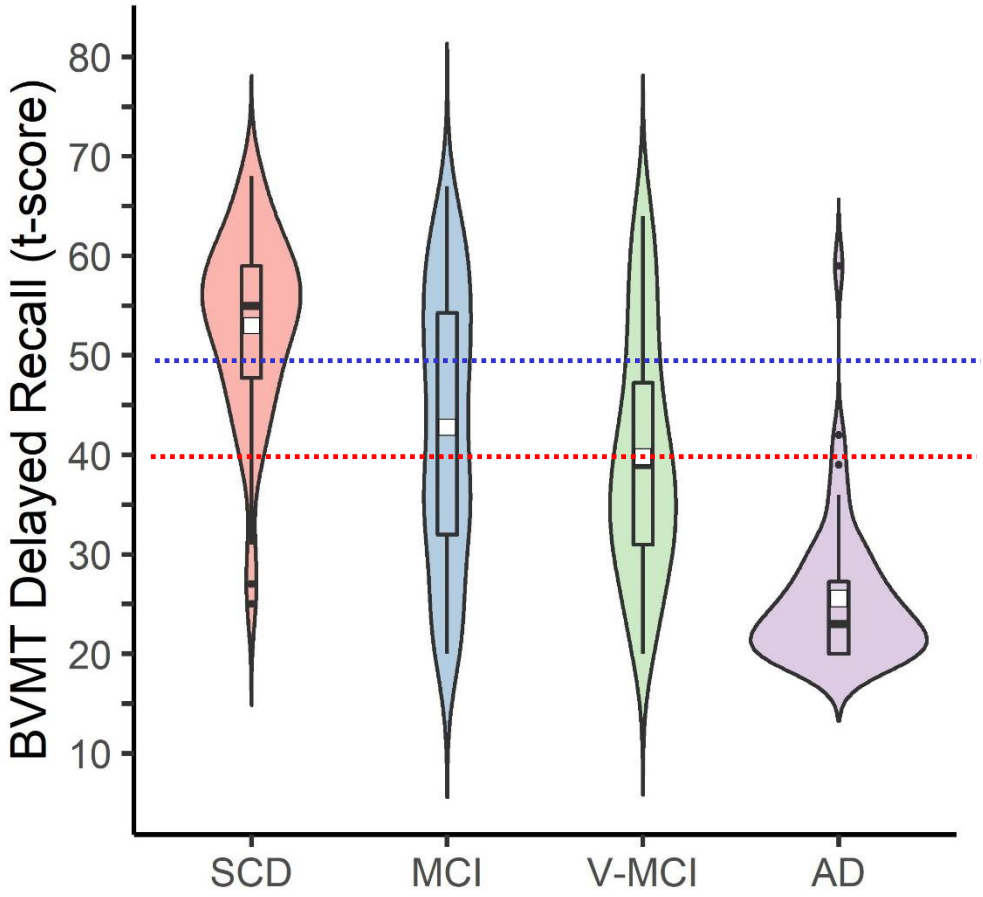
Learning and Memory

RAVLT Delayed Recall
Auditory Verbal Memory



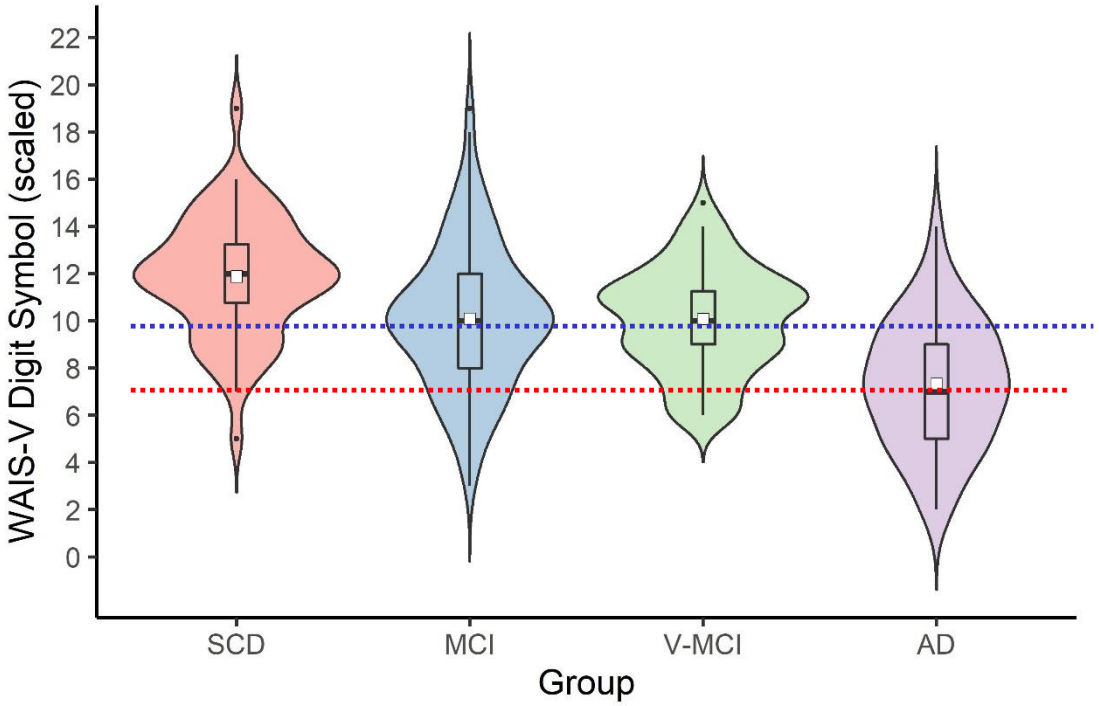
Predictors: Age Education Sex

BVMT Delayed Recall
Visual Memory



Predictors: Age Education Sex

Processing Speed

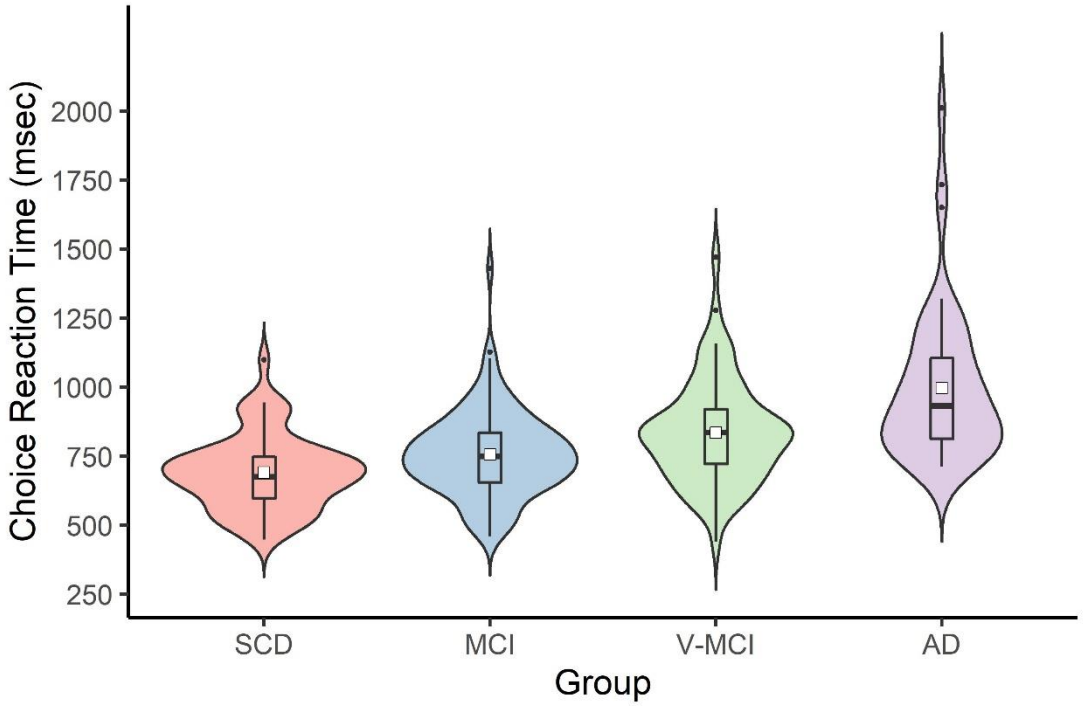


SCD > MCI
SCD > V-MCI

MCI = V-MCI

MCI, V-MCI < AD

Predictors: Age Education ***Sex***



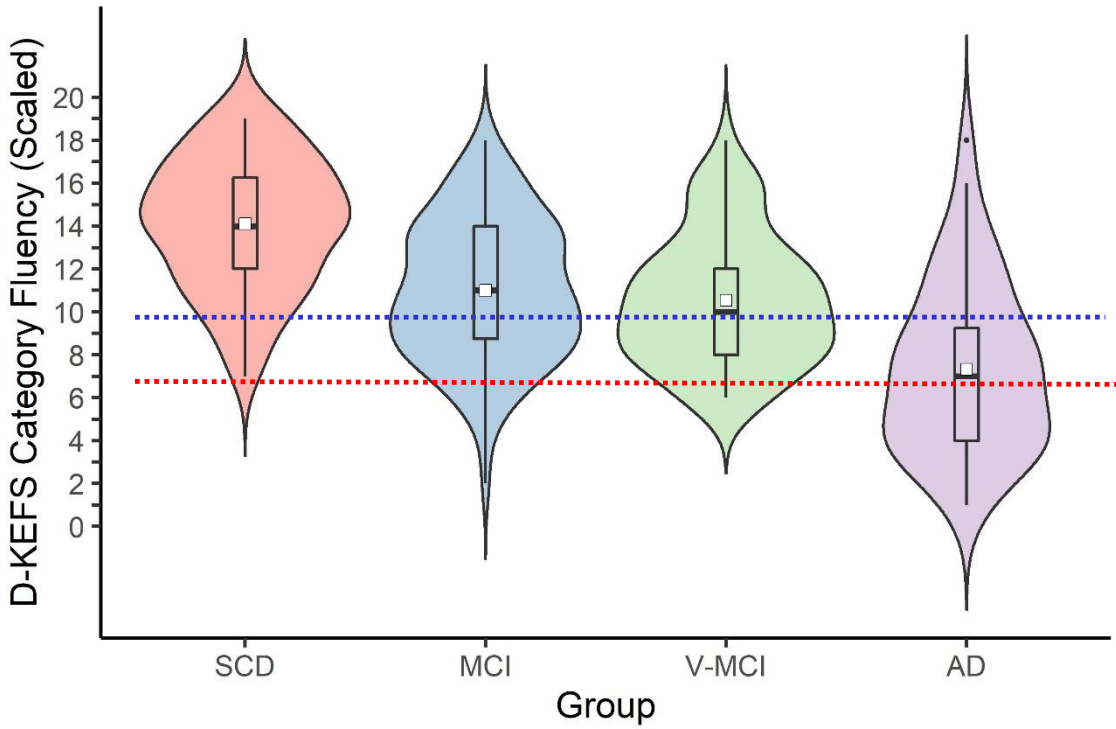
SCD = MCI
SCD < V-MCI

MCI ~ V-MCI

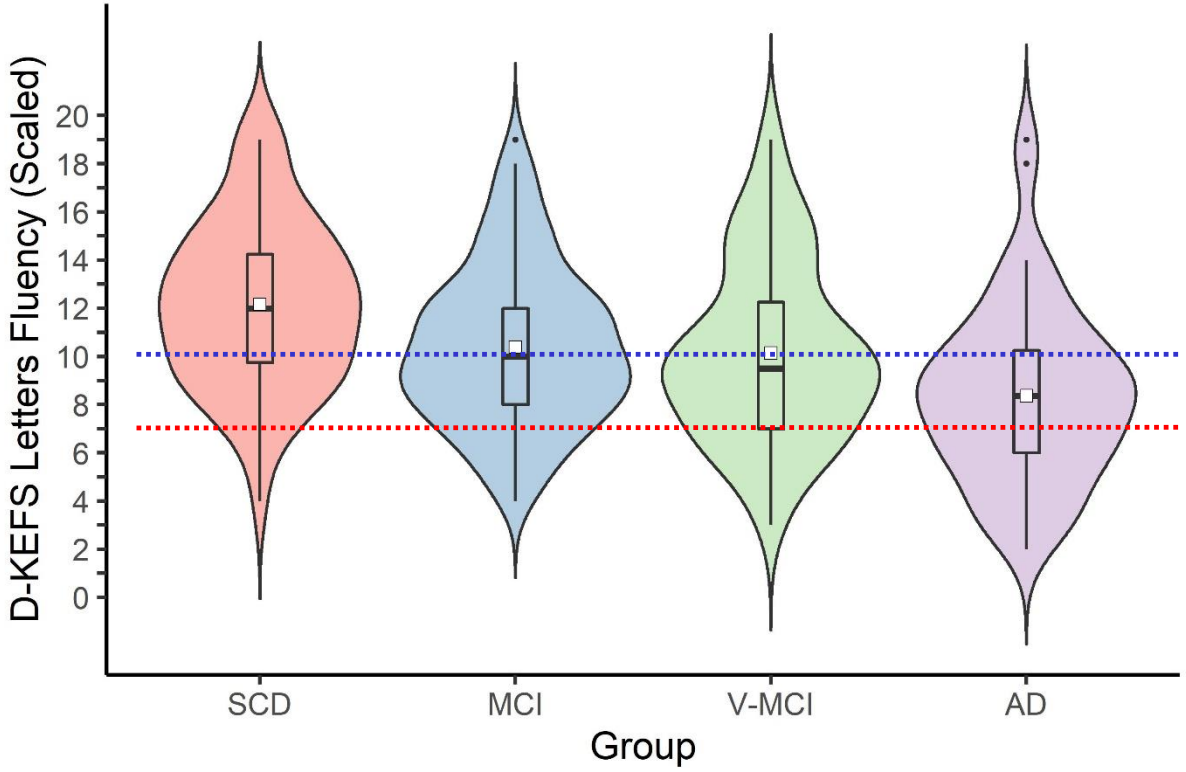
MCI, V-MCI < AD

Predictors: Age Education Sex

Executive Function: D-KEFS Verbal Fluency

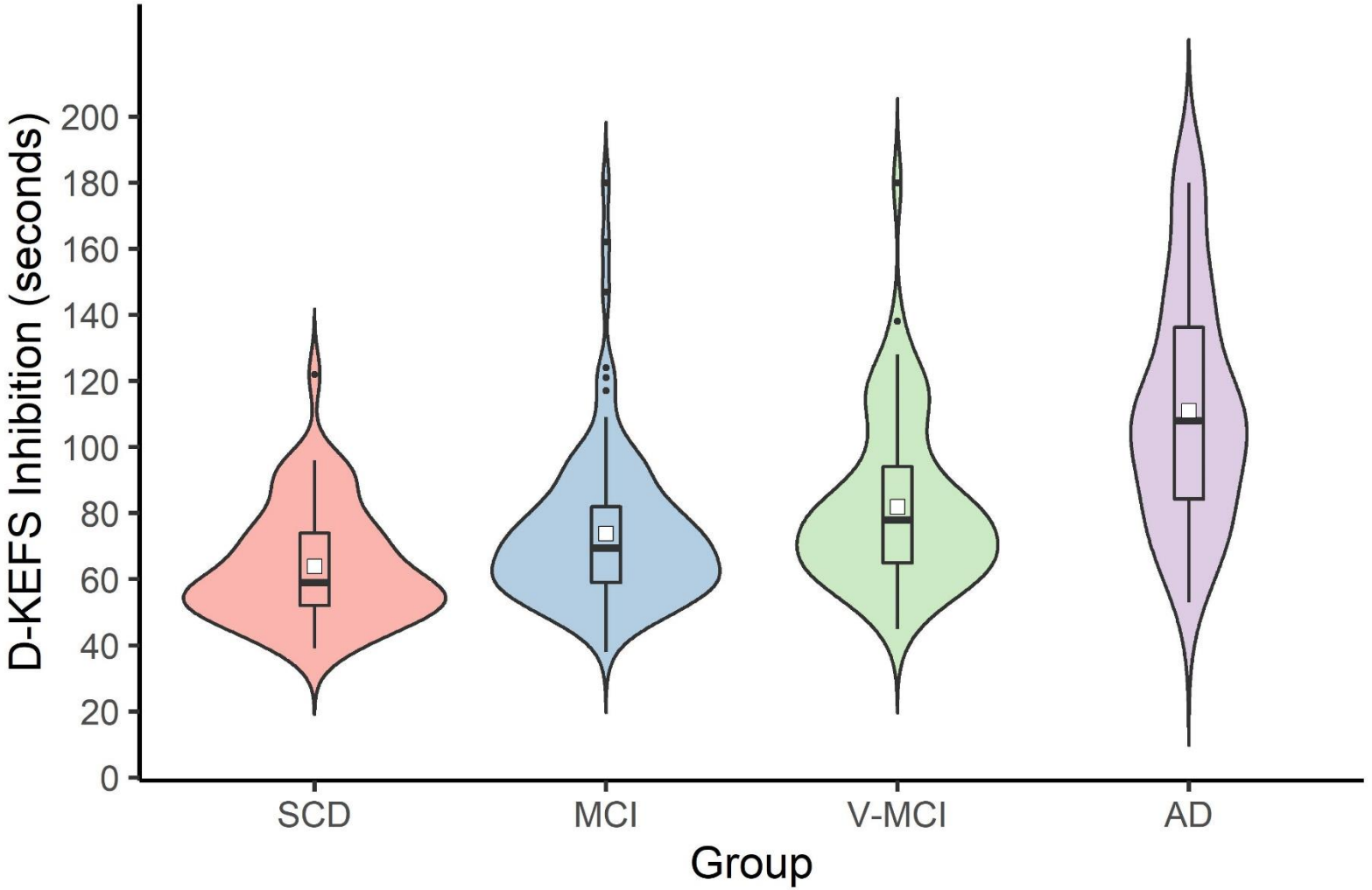


Age ***Education*** Sex



Age ***Education Sex***

Executive Function: D-KEFS Stroop



Age ***Education*** Sex

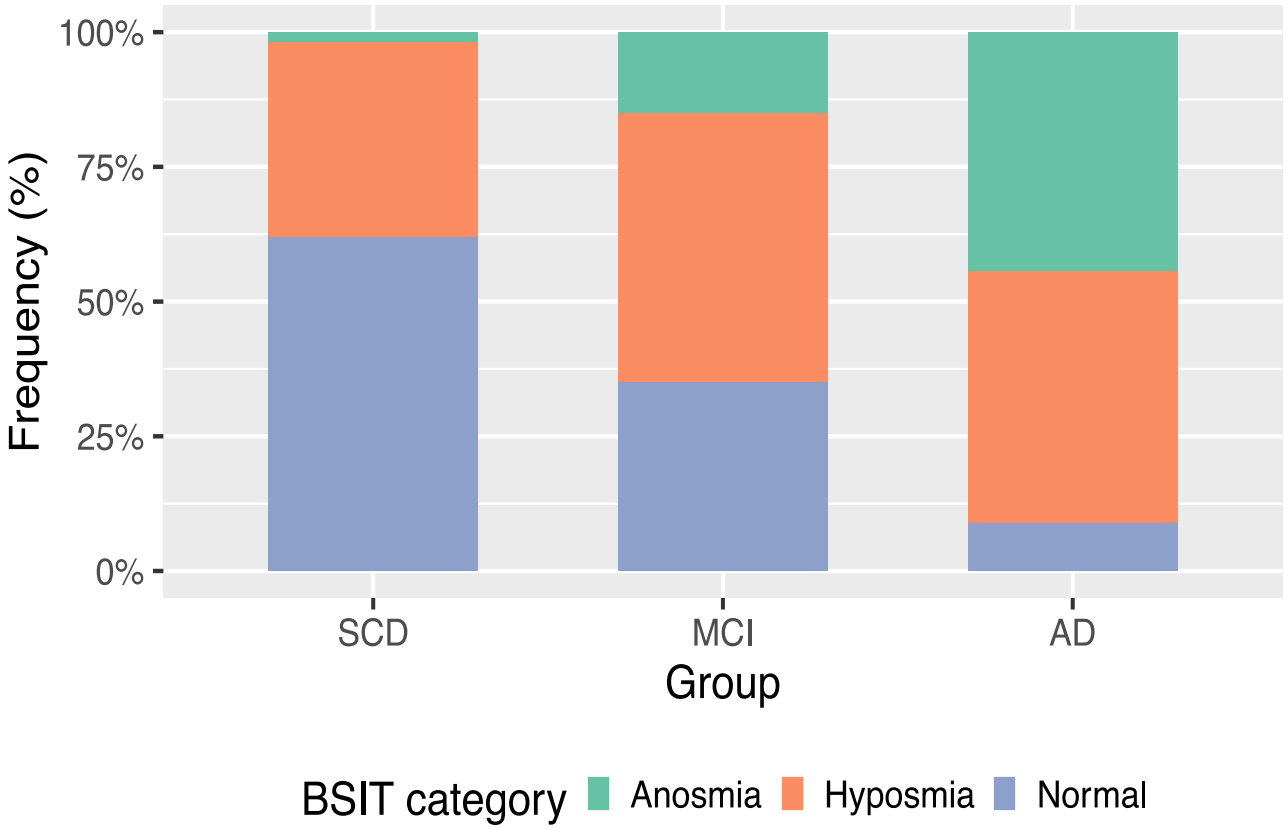
Team 17: Research at the Sensory-Cognitive Interface

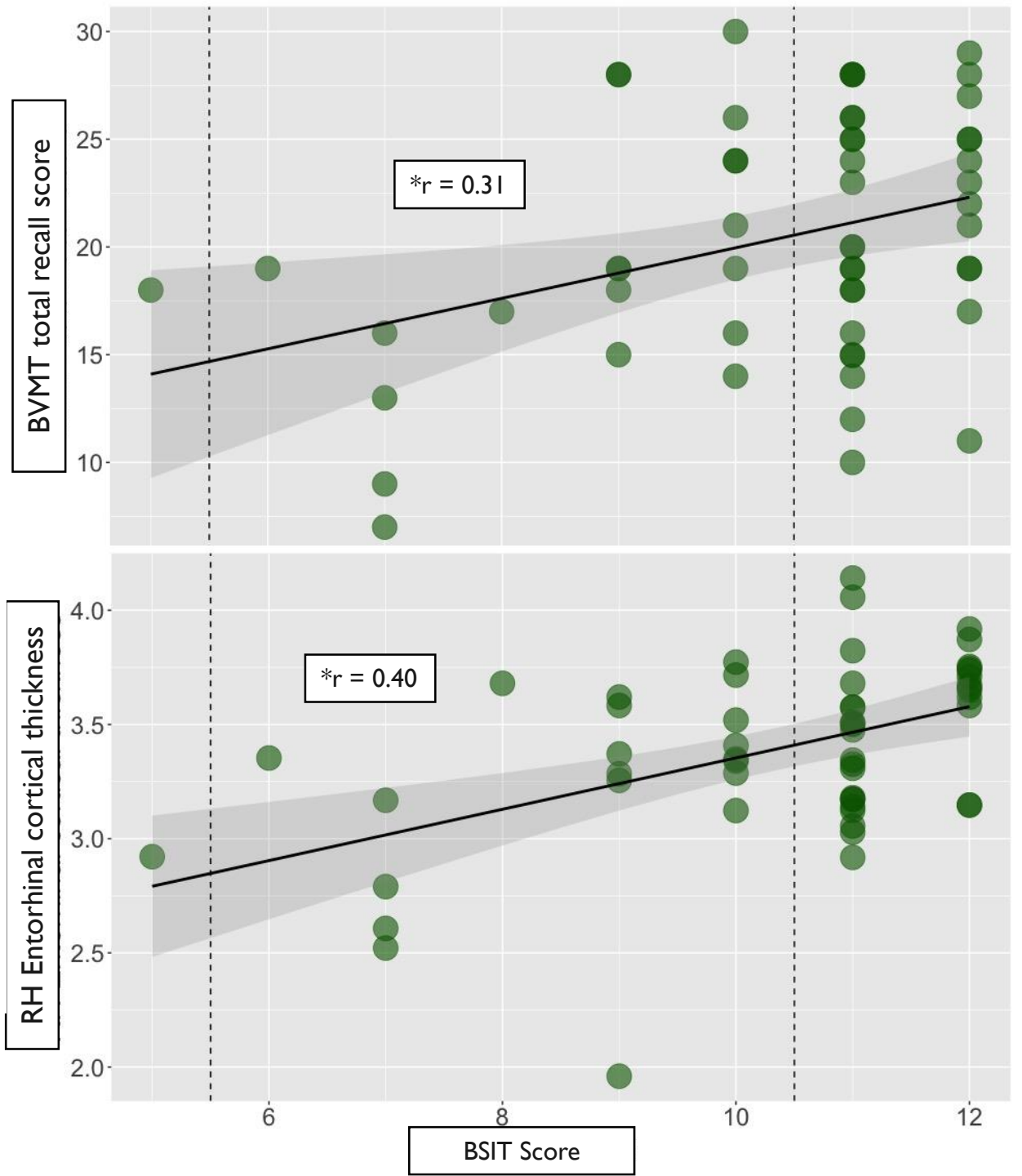
www.ccnateam17.ca

Olfaction
Hearing: pure tone screening
speech-in noise
Vision: acuity
contrast sensitivity

psychology, medicine (otolaryngology), hearing and vision sciences, speech/language pathology, rehabilitation, gerontology, public health

Olfaction


100%
75%
50%
25%
0%
Frequency (%)
SCD
MCI
AD
Group
BSIT category
Anosmia
Hyposmia
Normal

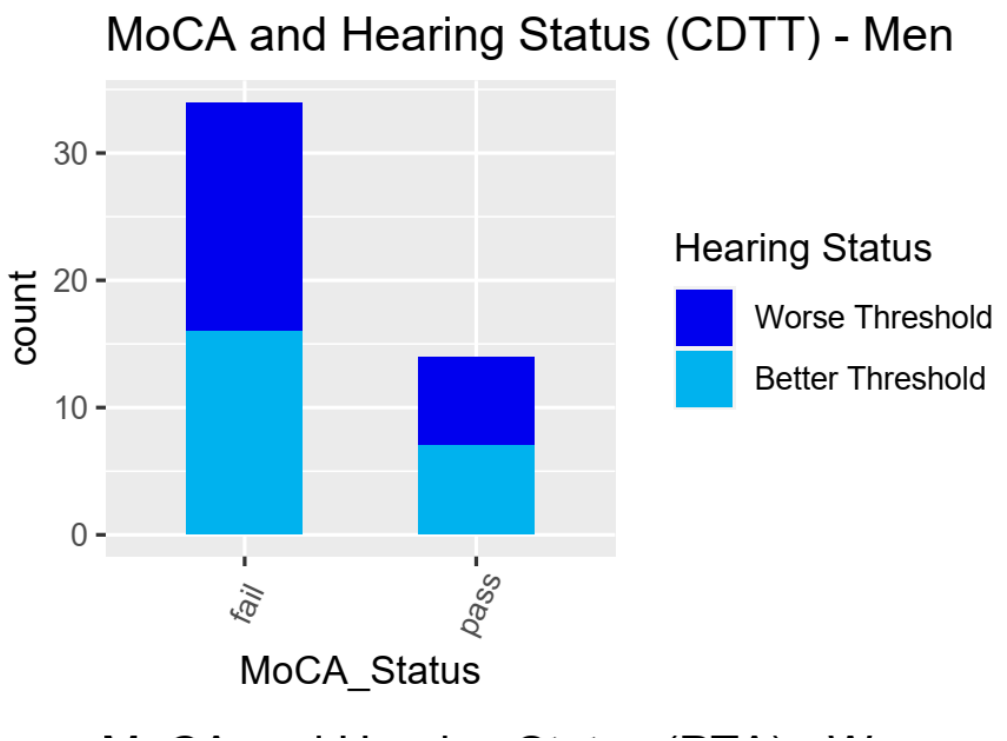

BVMT total recall score
*r = 0.31
30
25
20
15
10
RH Entorhinal cortical thickness
*r = 0.40
4.0
3.5
3.0
2.5
2.0
6
8
10
12
BSIT Score

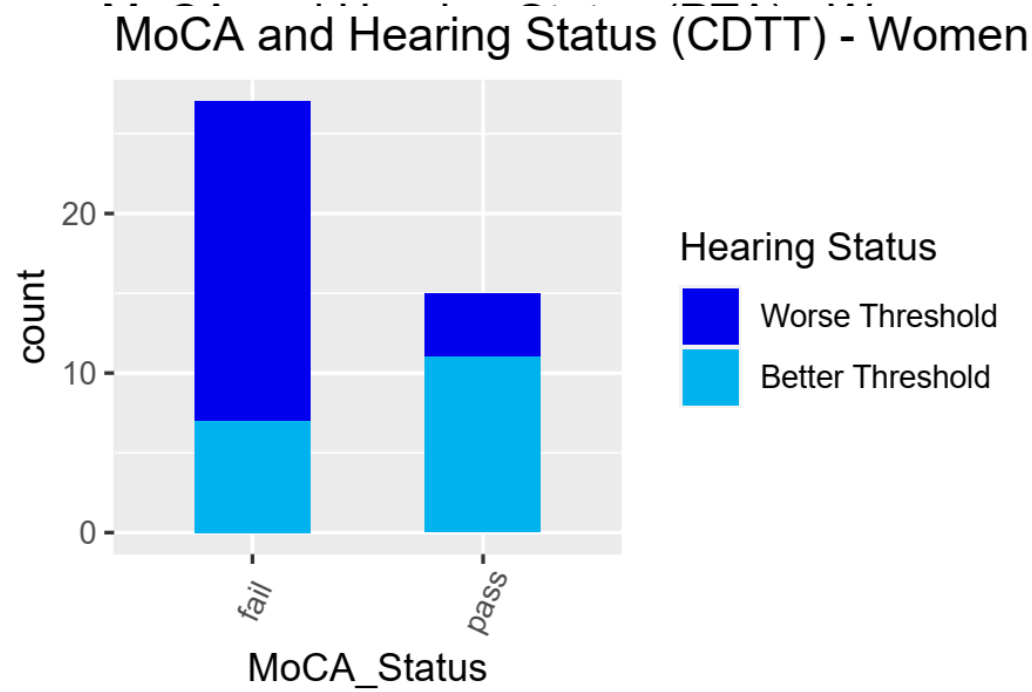
Sex-differences in Auditory-Cognitive associations

- COMPASS-ND Amnestic MCI (N=101)
  - No sex group or hearing group differences in
  - age, education, depression, social activity, hypertension, smoking, diabetes

- Women with hearing loss (PTA) were more likely to fail (<26) the MoCA relative to those with normal hearing.
  - No differences in men

- Women with poor suprathreshold hearing (CDTT) were more likely to fail the MoCA relative to those with good suprathreshold hearing
  - No differences in men



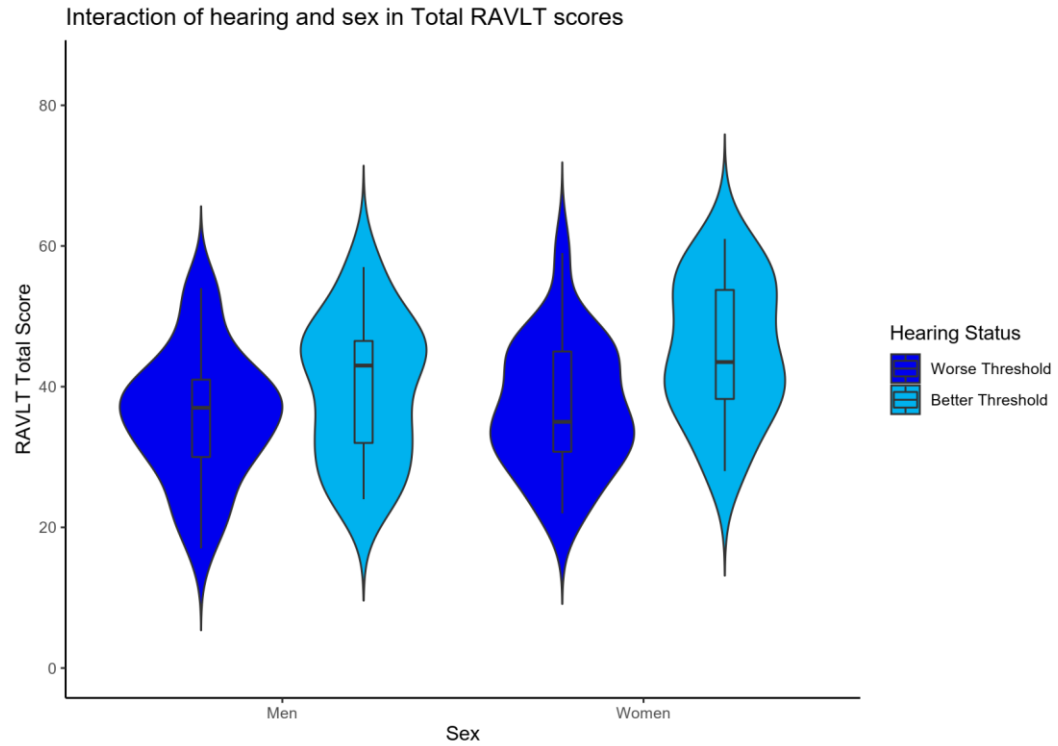


Al-Yawer, Pichora-Fuller, Wittich, Mick, Giroud, Rehan, & Phillips, in preparation

Sex-differences in auditory-cognitive associations

- Women with better suprathreshold hearing outperformed their poorer hearing peers
  - RAVLT and BVMT-R
  - No differences in men

- 50% of persons age 75+ have hearing loss (Mick et al., 2021)
- Auditory-cognitive associations appear to vary by sex
- Potential mechanisms need to be identified



Al-Yawer, Pichora-Fuller, Wittich, Mick, Giroud, Rehan, & Phillips, in preparation

Final comments

- Well-educated sample
- Majority of MCI meet criteria for aMCI, with many impaired in other domains of cognitive function
- Sex differences, possible language differences, sensory status
- Variable by variable or composite scores?
- Currently, scores are age/education corrected published norms
  - We will be able to express scores, standardized against our own normal controls
- Manuscript describing the neuropsychology test battery and preliminary results being drafted
- Please start using the data!
  - Work with the neuropsychologist on your team/platform
  - Reach out to us, we are happy to collaborate
    - Natalie.Phillips@concordia.ca, Jennifer.Fogarty@lhsc.on.ca

Acknowledgements

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- LORIS team
- Staff members in the COMPASS-ND investigator sites
- Phillips lab and CCNA Team 17
- Original neuropsychology development group
  - Drs. Anderson, Belleville, McLaughlin, Tierney, Troyer
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LAWSON HEALTH RESEARCH INSTITUTE

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- Thank you