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

Jennifer Fogarty, Ph.D.
Natalie Phillips, Ph.D.
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

<table>
<thead>
<tr>
<th>Domain</th>
<th>Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Cognitive Screening</td>
<td>MoCA</td>
</tr>
<tr>
<td>Memory</td>
<td>CERAD</td>
</tr>
<tr>
<td></td>
<td>Logical Memory Benson (Recall)</td>
</tr>
<tr>
<td>Visuoperceptual and Construction</td>
<td>Benson (Copy)</td>
</tr>
</tbody>
</table>

- 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

<table>
<thead>
<tr>
<th>Domain</th>
<th>Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premorbid IQ</td>
<td>WAIS-III Vocabulary</td>
</tr>
<tr>
<td>Memory</td>
<td>Rey Auditory Verbal Learning Test</td>
</tr>
<tr>
<td></td>
<td>Brief Visuospatial Memory Test</td>
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<tr>
<td></td>
<td>CCNA-CIMA-Q Face Name Matching</td>
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<td></td>
<td>Digit Symbol (Incidental Recall)</td>
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<td>Envelope Test</td>
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<td>Visuoperceptual and Construction</td>
<td>Birmingham Object Recognition Battery</td>
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<td>Judgement of Line Orientation Test</td>
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<td>Brief Visuospatial Memory Test (Copy)</td>
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<tr>
<td>Complex Attention and Executive</td>
<td>DKEFS Letter Fluency</td>
</tr>
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<td>Functioning</td>
<td>DKEFS Category Fluency</td>
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<td>Reitan Trail Making Test</td>
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<td>DKEFS Color Word Interference Test</td>
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<td>CCNA-CIMA-Q Sentence Interference Test</td>
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<td>CCNA-CIMA-Q Reaction Time Test</td>
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<tr>
<td>Processing Speed</td>
<td>WAIS-III Digit Symbol (Coding)</td>
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<tr>
<td>Working Memory</td>
<td>WAIS-III Digit Span Forward and Backward</td>
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<td>CCNA Reaction Time Test (n-back condition)</td>
</tr>
<tr>
<td>Speech and Language</td>
<td>NACC Word Reading Test</td>
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<td>NACC Semantic Word-Picture Matching Test</td>
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<td>NACC Semantic Associates Test</td>
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<td>NACC Northwestern Anagram Test</td>
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<td>NACC Sentence Reading/Repetition</td>
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<td>NACC Noun and Verb Naming Test</td>
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<td>Cookie Theft Picture Description</td>
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<td>Cognitive Inclusion Criteria</td>
<td>Cognitive Intact Elderly</td>
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<tr>
<td>-----------------------------</td>
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<tr>
<td>CIE</td>
<td>SCID</td>
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<tr>
<td>All of the following:</td>
<td>All of the following:</td>
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<tr>
<td>MoCA ≥25</td>
<td>MoCA ≥25</td>
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<tr>
<td>Logical Memory:</td>
<td>Logical Memory:</td>
</tr>
<tr>
<td>≥9 for 16+ years of education</td>
<td>≥9 for 16+ years of education</td>
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<tr>
<td>≥5 for 8-15 years of education</td>
<td>≥5 for 8-15 years of education</td>
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<tr>
<td>≥3 for 0-7 years of education</td>
<td>≥3 for 0-7 years of education</td>
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<tr>
<td>CERAD &gt;5</td>
<td>CERAD &gt;5</td>
</tr>
<tr>
<td>Global CDR score &gt;0</td>
<td>Global CDR score &gt;0</td>
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</tbody>
</table>
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
• 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
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)
• 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
• 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)
• Measures semantic 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).
• 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)
• 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)
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

<table>
<thead>
<tr>
<th>Phrase</th>
<th>Condition</th>
<th>Participant Response</th>
<th>Sample Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. He crept into the room without a…</td>
<td>Auto</td>
<td>Sound, Noise, Light, PEEP, Word</td>
<td>n/a</td>
</tr>
<tr>
<td>2. Bill hit his sister on the…</td>
<td>Auto</td>
<td>Head, Arm, Nose, Butt</td>
<td>n/a</td>
</tr>
<tr>
<td>3. The lawyer feared that his client was…</td>
<td>Inhibition</td>
<td>Spoon, Fork, Blue</td>
<td>CRAZY, SICK, INNOCENT, JUDGED, ABSENT, DEAD, VIOLENT, LYING</td>
</tr>
<tr>
<td>4. The dog chased our cat up the…</td>
<td>Inhibition</td>
<td>Potato, Phone, Kettle</td>
<td>STREET, ROAD, TOWER OF PISA, CHICKEN, HILL, LADDER</td>
</tr>
</tbody>
</table>
Processing Speed
• 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
• 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
• 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
• 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
• Measures grammatical knowledge

• 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

• 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

• 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
• Measures oral repetition and reading ability

• 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
• Measures word recognition and comprehension

• 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

**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
• Measures semantic memory

• 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
### Demographics: All Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>W</th>
<th>M</th>
<th>Age Mean</th>
<th>SD</th>
<th>Education Mean</th>
<th>SD</th>
<th>MoCA Mean</th>
<th>SD</th>
</tr>
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<tbody>
<tr>
<td>CIE</td>
<td>10</td>
<td>100.0</td>
<td></td>
<td>71.2</td>
<td>6.8</td>
<td>14.8</td>
<td>4.3</td>
<td>28.4</td>
<td>1.4</td>
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<td>SCD</td>
<td>56</td>
<td>76.8</td>
<td>23.2</td>
<td>70.0</td>
<td>6.9</td>
<td>17.0</td>
<td>3.1</td>
<td>27.3</td>
<td>1.9</td>
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<td>MCI</td>
<td>104</td>
<td>44.2</td>
<td>55.8</td>
<td>71.4</td>
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<td>15.7</td>
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<td>24.0</td>
<td>3.0</td>
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<tr>
<td>V-MCI</td>
<td>64</td>
<td>35.9</td>
<td>64.1</td>
<td>77.3</td>
<td>4.7</td>
<td>15.3</td>
<td>3.5</td>
<td>23.3</td>
<td>3.5</td>
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<td>AD</td>
<td>48</td>
<td>33.3</td>
<td>66.7</td>
<td>74.6</td>
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<td>15.3</td>
<td>4.2</td>
<td>18.7</td>
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<td>PD-MCI</td>
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<td>20.0</td>
<td>80.0</td>
<td>71.4</td>
<td>7.6</td>
<td>15.8</td>
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<tr>
<td>PD</td>
<td>34</td>
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<td>55.9</td>
<td>66.5</td>
<td>6.5</td>
<td>16.3</td>
<td>3.4</td>
<td>27.6</td>
<td>1.8</td>
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<tr>
<td>PDD</td>
<td>5</td>
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<td>74.3</td>
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<td>18.4</td>
<td>3.2</td>
<td>18.2</td>
<td>5.1</td>
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<tr>
<td>Mixed</td>
<td>39</td>
<td>48.7</td>
<td>51.3</td>
<td>78.3</td>
<td>5.1</td>
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<td>LBD</td>
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<td>83.3</td>
<td>73.3</td>
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<td>14.3</td>
<td>5.7</td>
<td>19.1</td>
<td>4.3</td>
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</tbody>
</table>
Language status

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

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<tr>
<th>Type</th>
<th>N</th>
<th>Monolingual</th>
<th>Multilingual</th>
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<td>26</td>
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<tr>
<td>MCI</td>
<td></td>
<td>42</td>
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</tr>
<tr>
<td>AD</td>
<td></td>
<td>21</td>
<td>24</td>
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</table>
https://www.r-graph-gallery.com/boxplot.html
• 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
Amnestic MCI status

• Criteria
  • Score below ADNI education cutoff on Logical Memory 2, \text{AND/OR}
  • < 6 on CERAD delayed recall \text{AND/OR}
  • > 2/5 words recalled on MoCA delayed recall \text{AND/OR}
  • \geq 0.5 or greater on CDR memory subsection

<table>
<thead>
<tr>
<th></th>
<th>Non-amnestic</th>
<th>Failed 1</th>
<th>Failed 2</th>
<th>Failed 3</th>
<th>Failed 4</th>
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<tbody>
<tr>
<td>MCI</td>
<td>4%</td>
<td>22%</td>
<td>39%</td>
<td>18%</td>
<td>16%</td>
</tr>
<tr>
<td>V-MCI</td>
<td>5%</td>
<td>21%</td>
<td>27%</td>
<td>26%</td>
<td>21%</td>
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</tbody>
</table>
Learning and Memory

RAVLT Delayed Recall
Auditory Verbal Memory

BVMT Delayed Recall
Visual Memory

Predictors: Age, Education, Sex

Predictors: Age, Education, Sex
**Processing Speed**

**Predictors:** Age, Education, Sex

- **WASI-V Digit Symbol (scaled)**
  - SCD > MCI
  - SCD > V-MCI
  - MCI = V-MCI
  - MCI, V-MCI < AD

- **Choice Reaction Time (msec)**
  - SCD = MCI
  - SCD < V-MCI
  - MCI = V-MCI
  - MCI, V-MCI < AD
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.ccna17.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

- BVMT total recall score
- RH Entorhinal cortical thickness

**BSIT category**
- Anosmia
- Hyposmia
- Normal

**Frequency (%)**
- SCD
- MCI
- AD

- *r = 0.40*
- *r = 0.31*
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
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.Philips@concordia.ca, Jennifer.Fogarty@lhsc.on.ca
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