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Detecting neurocognitive impairment in HIV-infected youth: Are we focusing on the wrong factors?

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Learning Objectives

At the conclusion of this activity, the participant will be able to:

1. Identify multiple approaches in assessing neurocognitive impairments in young adults living with HIV
2. Demonstrate how a neuropsychological battery is used to identify neurocognitive impairments in young adults living with HIV
3. Explore differences between virally suppressed and unsuppressed individuals

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Background

- Most individuals infected with HIV have some form of neurocognitive impairment, ranging from mild to moderate severity[1]
- HIV-associated neurocognitive disorders (HAND) are prevalent in between 15% to 50% of HIV-infected individuals[2]
- Not all neuropsychological tests are able to detect cognitive and memory impairments in HIV-infected individuals[3]
- Gender differences have been identified in screening for neurocognitive impairments (NCI). One study (n=2863) showed that 52% of HIV-infected women compared to 35% of HIV-infected men, screened positive for NCIs[4]

1. Clifford & Ances, 2013, *The Lancet.com/infection; 2. Vera, Ridha, Gilleece et al., 2017, Eur J Nucl Med Mol Imaging: 3. Barber et al., 2013, The Clinical Neuropsychologist; 4. Robertson, K., et al., 2014, AIDS Care*

Background (cont.)

Neurocognitive impairments in a mild form, can interfere significantly with:

- Quality of life
- Treatment adherence
- Cognitively demanding activities of daily living (e.g., employment, medication management, driving etc.)
- Executive functioning and planning
- Information processing speed
- Motor skills

Multiple ways to assess neurocognitive impairments

- The literature supports multimodal approaches for detecting NCI
  Clinical ratings (CR) and Global Deficit Score (GDS)[1]
- Neurocognitive testing can include assessment of at least two (2) or more of the following ability domains:
  - Cognitive domains (attention/information processing)
  - Language
  - Abstraction/Executive functioning
  - Memory (learning and recall)
  - Simple motor skills
  - Complex perceptual motor skill
- The clinical ratings (CR) approach is consistent with guidelines for the assessment of HAND classification, also known as the 'Frascati criteria'[2]

1. Blackstone et al., 2012, *The Clinical Neuropsychologist*; 2. Antinori et al., 2007, *Neurology*

Table 1. Disease severity and functional impact of neurocognitive impairment

Variable	Mild	Moderate	Severe
Test score results in at least 2 cognitive domains	At least 1 SD below the mean	At least 1 SD below the mean	At least 2 SD below the mean
Functional deficit	None	Mild difficulties with ADLs*	Markedly significant difficulties with ADLs

Adapted from - American Academy of Neurology, 1991; Antinori et al., 2007, *Neurology;* * ADLs - Activities of Daily Living

Clinical Ratings

- Clinical ratings involve using demographically corrected T-scores (test scores) from a standardized neuropsychological battery

  - Clinical ratings are assigned and scaled for all domains, ranging from 1 (above-average) to 9 (severely impaired)

  - Cut-off score of ≥ 5 – indicating mild impairment[1]
    - Individuals are classified as "Impaired" if impairment is in two (2) ability domains
    - Similarity with the Frascati method

[1] Blackstone et al., 2012, *The Clinical Neuropsychologist*

Table 2. T-scores converted to Deficit scores

T-score	Clinical Rating	Impairment description
≥ 55	1	Above average
45-54	2	Average
40-44	3	Low average
-	4	Borderline
35-39	5	Definite mild impairment
30-34	6	Mild-to-moderate impairment
25-29	7	Moderate impairment
20-24	8	Moderate-to-severe impairment
≥19	9	Severe impairment

Blackstone et al., 2012, *The Clinical Neuropsychologist*

Global Deficit Score

- Involves evaluating the number and severity of deficit performance throughout the neuropsychological battery
- Individual test scores from a neuropsychological battery are then converted into deficit scores, ranging from 0 (no impairment) to 5 (severe impairment)
- Deficit scores are averaged across all tests in the battery to create a GDS
- Detects mild HIV-neurocognitive impairment and patterns of deficits in domains

Table 3. T-scores converted to Deficit scores

T-score	Deficit score	Impairment description
≥ 40	0	None (normal)
35-39	1	Mild impairment
30-34	2	Mild to moderate impairment
25-29	3	Moderate impairment
20-24	4	Moderate to severe impairment
≤ 19	5	Severe impairment

Blackstone et al., 2012, *The Clinical Neuropsychologist*

CR vs. GDS approaches

- Both approaches appear to detect mild, HIV-associated NCI
- CR approach requires impairment in at least two (2) ability domains, while the GDS considers numbers and severity of impairment across *all* measures
- GDS may be more "user friendly", whereas CR has more similarities with *the gold standard* (Frascati method)
- Research found a high degree of agreement between the two methods
- More people were classified as 'impaired' using the CR approach, suggesting CR may be more appropriate for detecting subtle levels of impairment

Blackstone et al., 2012, *The Clinical Neuropsychologist*

Other approaches in detecting neurocognitive impairment

- Carey et al., (2004)
  - Compared six neuropsychological measures most likely affected by HIV infection to determine diagnostic accuracy rates
  - Neuropsychological impairment was classified if demographically corrected T-scores fell below 40 on two (2) tests or below 35 on one (1) test

How to create a neuropsychological battery

- Little consensus over the makeup of an appropriate neuropsychological battery [1]
- Neuropsychological testing is time-consuming, costly, and education and language dependent[2]
- A growing demand exists for brief neuropsychological screening measures[3]
- Many neuropsychological tests for each domain
- Decision criteria: length of batteries and domains most likely affected by HIV infection[4]

1. Barber et al., 2013, *AIDS Care*; 2. Hueying, H., et al., 2012, *Exp. Ther Med; 3. Malloy, Cummings, Coffey, Duffy, & Fink,* 1997, *Journal of Neuropsychiatry & Clinical Neurosciences;* 4. Carey et al., 2017, *The Clinical Neuropsychologist*

Table 4. Neuropsychological Tests

Domains	Neuropsychological Tests/Tools
General neuropsychological impairment	International HIV Dementia Scale (IDHS); Montreal Cognitive Assessment Test (MoCA) HIV Dementia Scale (HDS); Brief Neuro-cognitive Screen
Attention/information processing speed	WAIS-IV - Digit span (Forward & Backward) / Trail-making Test – Part A; Stroop Color and Word Test; Paced Auditory Serial Addition Test (PASAT)
Language	Boston Naming Test
Memory (Learning and Recall)	Hopkins Verbal Learning Test-Revised; Brief Visuo-spatial Memory Test-Revised (BVMT)
Motor skills	Grooved Pegboard Test; Timed Gait Test
Psychomotor speed	WAIS-IV – Symbol Search; Trail Making Test – Parts A & B; Color Trails – Part 1
Executive functioning	Trail-making Test – Part B;

Exploratory investigation of a neuropsychological testing battery

- Population
- Tools used
- Procedures
- Results

Participants (n=27)

- Clients in a NYC Young Adult Infectious Diseases Clinic
- Perinatally acquired youth living with HIV – 22 (85.2%)
- Gender (predominantly male) – 17 (63%)
- Ages – mean 24.96 years, SD – 3.39, and Range is 19 – 34 years
- Ethnicity
  - Non-Hispanic Black – 18 (66.7%)
  - Hispanic – 9 (33.3%)
- Viral load
  - Suppressed – 23 (85.2%)
  - Unsuppressed – 4 (14.8%)

Clinical neuropsychological battery

- Three (3) neuropsychological tools and four (4) ability domains assessed:

  - **Memory** (visual) – Brief-Visuospatial Memory Test-Revised (BVMT-R)
  - **Visual-motor coordination** – Grooved Pegboard Test (Dominant & Non-dominant hand)
  - **Attention/Information Processing speed** – WAIS-IV (Digit span - Forwards & Backwards)
  - **Psychomotor speed** – WAIS-IV - Symbol Search

Procedures

- Raw test scores from each of the measures were converted to T-scores to create a standardized way of detecting impairments across measures
- Raw scores were converted to demographically corrected T-scores, adjusting for age, ethnicity, gender and education[1]
- Following Carey et al., 2004's neuropsychological screening battery criteria, impaired test performance was defined by T-scores in at least two (2) measures, falling below 40, or if a T-score for one (1) measure fell below 35, indicating mild-to-moderate impairment[2]
- Descriptive statistics (Means and SD) were used to determine which measures generated the greatest amount of impairment

1. Norman, et al., 2011, *J Clin Exp Neuropsychol; 2.* Carey et al., 2004*, The Clinical Neuropsychologist*

Table 5. Demographically corrected means and standard deviations of the measures

Variable	Mean (SD)	Range
*Memory – BVMT (n=17)	43.00 (10.20)	27 - 62
*Motor – Groove Pegboard		
Dominant hand (n= 19)	**34.11 (8.87)**	21 – 53
Non-dominant hand (n=19)	36.53 (10.68)	20 – 53
Attention – Digit span (n=18)	44.61 (9.51)	30 – 67
Psychomotor speed – Symbol Search (n=19)	35.16 (9.38)	20 – 53

*Used demographically corrected T-scores for these measures (Heaton, Grant & Mathews (1991); *Benedict, 1997*

Table 6. Impairment detected by measure

Measure	Patients with impairments (%) Demographically corrected	Patients with impairments (%) Non-demographically corrected
Symbol search (n=12)	63%	63%
*Grooved Pegboard – Dom. hand (n=10 vs. n=13)	53%	68%
Non-dominant hand (n=9 vs. n= 8)	47%	42%
*BVMT (n=4 vs. n=7)	24%	41%
Digit Span (n=2)	11%	11%

Impairment determined if patient scored 1.5 SD or lower on an individual measure

*Used demographically corrected T-scores for these measures (Heaton, Grant & Mathews (1991); *Benedict, 1997*

Table 7.
Virally suppressed vs. unsuppressed

Variable	Virally suppressed (n=23)	Unsuppressed (n=4)
	Means (SD)	Means (SD)
BVMT	42.30 (10.9)	45.25 (8.6)
Groove Pegboard **- Dominant hand**	**33.81 (9.5)**	35.67 (4.5)
- Non-Dominant hand	36.94 (11.3)	**34.33 (7.7)**
Digit span	45.38 (9.3)	47.0
Symbol search	**34.17 (8.6)**	53.0

Table 8. Demographic characteristics by impairment

Variable	No cognitive impairment N (%)	Impairment N (%)
Age (n=27)	9 (23)	18 (67)
Gender – Female (n=10) - Male (n=17)	2 (20) 7 (41)	8 (80) 10 (59)
Ethnicity - Non-Hispanic Black (n=18) - Hispanic (n=9)	 4 (22) 5 (56)	 14 (78) 4 (44)
Viral suppression - Virally suppressed (n=23) - Unsuppressed (n=4)	 7 (30) 2 (50)	 16 (70) 2 (50)

Results

- Using demographically corrected T-scores, for memory and motor functioning, ***mild to moderate*** neurocognitive impairment was noted in two (2) ability domains - motor and psychomotor speed (among suppressed individuals)
- When correcting for demographic variables, 24% of patients had visual memory impairments, compared to 41% using the published norms
- 63% of HIV-infected participants exhibited NCI in psychomotor speed
- 53% of participants exhibited impairment with the *dominant hand* of the motor test

Client characteristics affect NCI

- Consistent with the literature, a higher percentage of women (80%) than men (59%) were found to have neurocognitive impairments
- Ethnicity - Non-Hispanic Black participants (78%) exhibited impairments
- Sixty-seven percent (67%) of our sample exhibited overall neurocognitive impairments
- Seventy percent (70%) of virally suppressed patients still exhibited overall neurocognitive impairments

Summary

- Early neurocognitive screening an essential preventative measure to forestall long-term neurocognitive deficits
- Mild neurocognitive impairments continue to exist even in virally suppressed young adults living with HIV, and NCIs are risk factors for further neurocognitive deterioration
- Using demographically corrected T-scores are important when assessing the areas of visual memory and visual-motor coordination
- Results of neurocognitive assessments can help providers in assisting HIV-infected individuals learn skills to better manage and compensate for deficits
- A thorough medical and clinical evaluation should include assessment of ADLs, psychiatric symptoms (including mood and substance use disorders), and neuro-brain imagining tests, when detecting neurocognitive impairments

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Questions

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