

Watering flowers in the rain: The elusive nature of executive dysfunction in HIV

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ABSTRACT

Individuals infected with human immunodeficiency virus (HIV) frequently experience both neurocognitive and psychiatric dysfunction. Apathy is a prominent neuropsychiatric symptom associated with HIV and is related to neurologic dysfunction. In contrast, depression is independent of neurocognitive impairment in HIV. This case report illustrates the importance of behavioral observations from family members of HIV-positive (HIV+) individuals as a valuable source of information. These behavioral observations can be particularly important in rural resource-limited settings, where cognitive testing is often limited to standardized mental status examinations.

Key words: Apathy, behavior, depression, HIV, impairment, neurocognitive

Introduction

It is well documented that human immunodeficiency virus (HIV) enters the central nervous system early after infection and may result in decrements of cognitive, behavioral, and motor performance. Neurocognitive impairment occurs in approximately 30 to 50% of asymptomatic individuals receiving highly active antiretroviral therapy (HAART).^[1] Even mild cognitive impairment is associated with difficulty taking medications and reduced vocational functioning.^[2] The specific pattern of neuropsychological deficits associated with HIV involves multiple cognitive domains, including processing speed, learning/memory, psychomotor skills, attention/working memory, and executive function. These cognitive deficits are attributed to damage to the frontostriatal circuitry.^[3,4] HIV-positive (HIV+) individuals with executive dysfunction often display a flat affect and apathy caused by damage to this region of the brain. It is important to differentiate behavior and affective changes associated with HIV because

apathy, but not depression, is associated with cognitive dysfunction.^[5,6] Thus, apathy among HIV-infected individuals may reflect HIV-associated neurologic dysfunction, which is not amenable to treatment with antidepressant medications. This may seem a minor problem, since antidepressants are usually not harmful from a medical perspective; however, from a resource perspective, this can be wasteful, with some HIV+ individuals being prescribed expensive medications without benefit.

Cognitive impairment and depression often coexist in HIV.^[7] Depression does not affect neuropsychological function in HIV-infected individuals,^[8] but it can impact quality of life and adversely impact medication adherence.^[9,10] Previous research has shown that a single question about depressed mood has a sensitivity of 85 to 90% for major depression,^[11] and adding a second question about anhedonia increases the sensitivity to 95%.^[12] Two screening questions from a focused interviewing guide, the Mood Module of the Primary Care Evaluation of Mental Disorders, can help to elicit symptoms of depression.^[13] This shortened screening instrument, The Patient Health Questionnaire-2 (PHQ-2), was designed for use by healthcare workers without formal training in psychiatry, takes only a few minutes (<5 minutes) to administer and score, can be easily interpreted, and has been translated into multiple languages. It is particularly appealing for use in busy, understaffed clinics in rural settings.

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Executive functions can be difficult to measure, even with sophisticated neuropsychological tests. Poor insight is often a component of executive dysfunction, so directly asking patients if they are experiencing cognitive problems may be misleading. It is important to obtain information from family/friends who are familiar with the patient's behavior. A cross-cultural investigation demonstrated that executive dysfunction is relatively robust to cultural differences. And the willingness of the family members to report such symptoms did not differ between cultures, which suggest that the construct of the dysexecutive syndrome has validity across cultures.^[14]

Case Report

A 42-year-old HIV+ man presented for neuropsychological

testing because of unusual behavior observed by his family over the past 3 to 4 years, which included decreased social awareness, occasional inappropriate comments, and "odd" behaviors. According to the family, these behaviors had gradually worsened, and most recently, he was observed "watering flowers in the rain." The patient himself appeared apathetic and did not understand his family's concern or why they thought his behavior was strange. He was employed full-time as a church pastor, but had recently been asked to take a medical leave due to concerns about his unusual behavior. Consistent with his apathetic demeanor, he had little reaction to this major change in his vocational status. There was no significant medical or psychiatric history prior to the HIV diagnosis. Since his diagnosis with HIV 7 years previously, he had been successfully treated with HAART, with no history of opportunistic infections.

Table 1: Neuropsychological test and performance (percentiles and ranges)

Neuropsychological tests		Percentile	Range
Cognitive screening	Mini-Mental status exam 29/30	NA	Normal
Intelligence Quotient ¹	Verbal IQ 133	99	Very superior
	Performance IQ 130	98	Very superior
	Full scale IQ 135	99	Very superior
Learning/memory	Visual span forward	50	Average
	Visual span backward	37	Average
Verbal memory ²	Logical memory I	25	Average
Visual memory ²	Logical memory II	37	Average
Verbal learning ³	Visual reproduction I	37	Average
	Visual reproduction II	50	Average
	Total learning	16	Low average
	Delayed recall	25	Average
	Recognition	75	Average
Language	Boston naming	73	Average
	Token test ⁴	33	Average
Visual spatial	Benton judgment of line orientation	72	High average
	Benton facial recognition	72-85	High average
Fine motor speed ⁵	Dominant hand	27	Average
	Non-dominant hand	27	Average
Executive functions	Letter (total correct)	5	Impaired
	Category (total correct)	2	Impaired
Visual sequencing	Trail making A	2	Impaired
Set shifting/problem solving ⁷	Trail making B	6	Impaired
Figural fluency ⁸	Categories	2-5	Impaired
	Total errors	8	Impaired
	Perseverative errors	9	Impaired
	Total unique designs	19.1	Low average
Selective attention ⁹	Total speed	7	Impaired
	Total accuracy	58	Average
Academic achievement ¹⁰	Word reading	77	>12.9 Grade Level
Affect/emotional functioning	Beck depression inventory	NA	Minimal
	Beck anxiety inventory	NA	Minimal

1 Wechsler Intelligence Scale-Third Edition (WAIS-III); 2 Wechsler Memory Scale-Third Edition (WMS-III); 3 California Verbal Learning Test-Second Edition (CVLT-II); 4 Multilingual Aphasia Test Battery; 5 Grooved Peg Board Test; 6 Delis-Kaplan Executive Function System (D-KEFS); 7 Wisconsin Card Sorting Test; 8 Ruff Figural Fluency; 9 Ruff 2 and 7 Selective Attention Test; 10 Wide Range Achievement Test-Fourth Edition (WRAT-4)

Table 2: Behavior ratings

Family rating scale (spouse)	T-score	Percentile
Apathy before	45	31
Disinhibition before	43	24
Executive dysfunction before	55	69
Total before	48	42
Apathy after	115	>99.9
Disinhibition after	78	99.9
Executive dysfunction after	117	>99.9
Total after	121	>99.9
Self-rating form (patient)		
Apathy before	52	58
Disinhibition before	33	4
Executive dysfunction before	50	50
Total before	46	34
Apathy after	72	98
Disinhibition after	35	7
Executive dysfunction after	58	79
Total after	60	84

Frontal Systems Behavior Scale (FrSBs).^[15] Scores represent Family Rating (completed by spouse) and Self-Rating (completed by patient). Ratings are for the patient's behavior before and after HIV diagnosis

Table 3: The patient health questionnaire-2

The Patient Health Questionnaire-2 (PHQ-2) ^[13]	Scores: 0 Not at all 1 Several days 2 More than half the days 3 Nearly everyday
Over the past two weeks, how often have you been bothered by any of the following problems:	
1. Feeling down, depressed, or hopeless	
2. Little interest or pleasure in doing things	
Total Score	/6
A cut-off score of >3 indicates possible depression	Depression: _____ Yes _____ NO

The PHQ-2 is an effective and valid approach for screening symptoms of depression. The response to each item is scored from 0 to 3, thus the scores can range from 0 to 6

Biomarkers were consistently within normal limits, including CD4 cell counts and an undetectable viral load (<50). At the time of testing, he was fully oriented and denied cognitive or emotional problems. Speech was fluent, and the patient demonstrated an excellent vocabulary consistent with his postgraduate education. Affect was noticeably flat, he appeared unconcerned and apathetic, and initiation was poor. Based on these changes in affect, he had been diagnosed 3 years previously with depression and prescribed antidepressant medication. There was no improvement in his thinking or affect with the antidepressant medication, so it was discontinued 6 months prior to neuropsychological assessment.

The patient was cooperative throughout several hours

of standardized neuropsychological testing. Testing revealed exceptionally high Intelligence Quotient (IQ) scores (Very Superior range) and intact performance on tests of language, attention/working memory, visuospatial perception, and constructional skills. Learning and memory scores were in the average range for the patient's age and education level, which were considered relative impairments in comparison with his high IQ scores. He was slow on a measure of sustained attention and executive dysfunction was evident on tests of visual sequencing, verbal and figural fluency, and problem solving/set shifting [Table 1]. In addition, a structured behavior rating scale revealed an increase in executive dysfunction since diagnosis with HIV [Table 2]. A self-report measure of depression did not confirm the diagnosis of depression. The patient's flat affect, apathy, and poor initiation were attributed to executive dysfunction rather than depression.

Discussion

Since formal neuropsychological testing is often not feasible for individuals infected with HIV in rural settings, this case demonstrates the value of interviewing family members about changes in behavior. Apathy has been associated with cognitive impairment in HIV, specifically executive dysfunction. Thus, family observations may be important in making predictions about performance on executive tasks and by extension, in everyday situations. Recent guidelines^[16] support the use of standardized mental status examinations, such as the International HIV Dementia Scale^[17] to diagnose HAND in regions where neuropsychological testing is not available. Although not a replacement for cognitive testing, information from family can provide important supplemental information. It takes only a few minutes to ask family members questions targeted at a range of problems commonly associated with executive dysfunction, such as planning problems, lack of insight, apathy and lack of drive, shallowing of affective responses, motivational changes, and lack of concern. This information, combined with two screening questions about depressed mood and anhedonia, may help to distinguish depression from apathy among individuals with HIV. As a first step to screen for depression, the PHQ-2 has demonstrated validity^[13] [Table 3]. In a study that screened for depression in 580 patients in a primary care setting, a cut-off score of >3 on the PHQ-2 had a sensitivity of 82.9 and specificity of 90.0.^[13] Differentiation of apathy due to executive dysfunction from depression is of great importance, not only clinically, but also to ensure judicious allocation of scarce medical resources. Since cognitive and psychiatric

symptoms associated with HIV may vary over time, serial monitoring is recommended.^[18]

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