

Longitudinal Association between Depressive Phenotype and Cognitive Impairment in Men with and without HIV

Nicole Armstrong, MPH

Department of Epidemiology

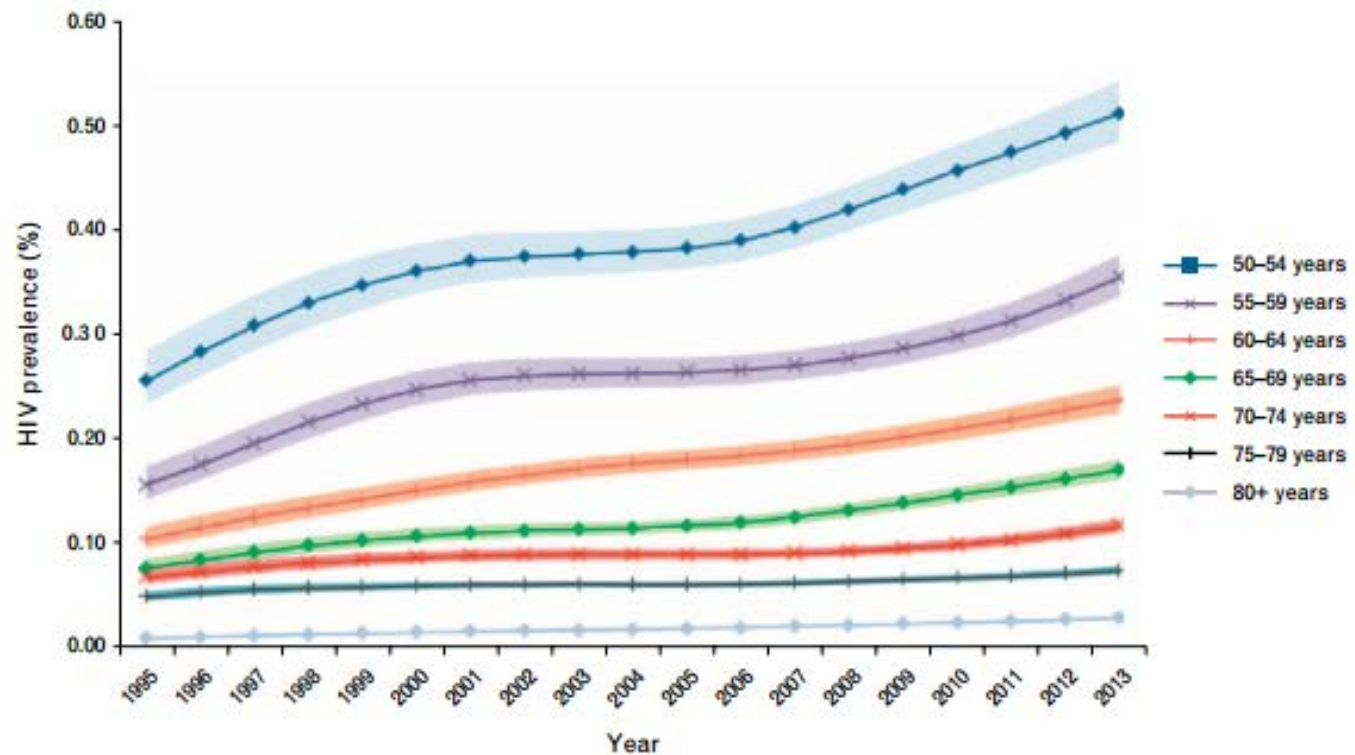
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Background

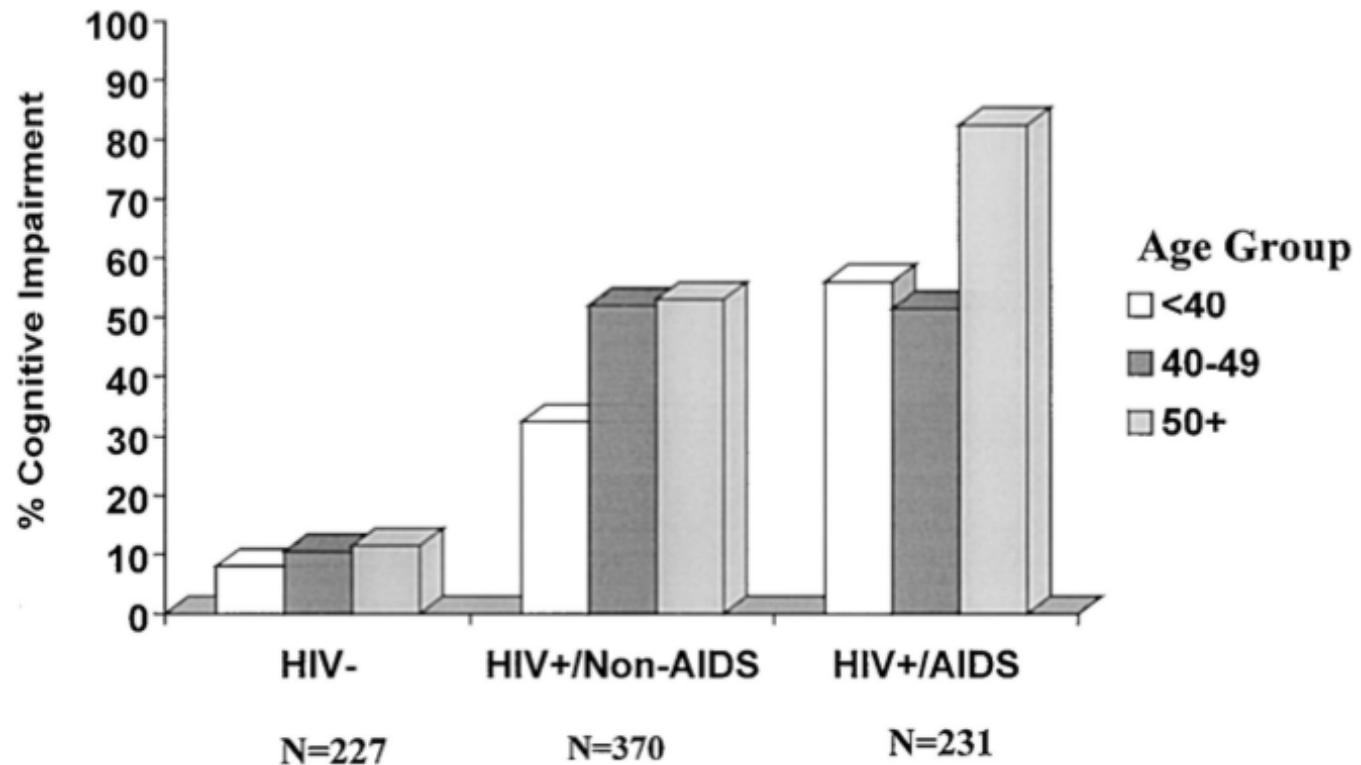
More than half of those living with HIV today are over 50 years of age.¹



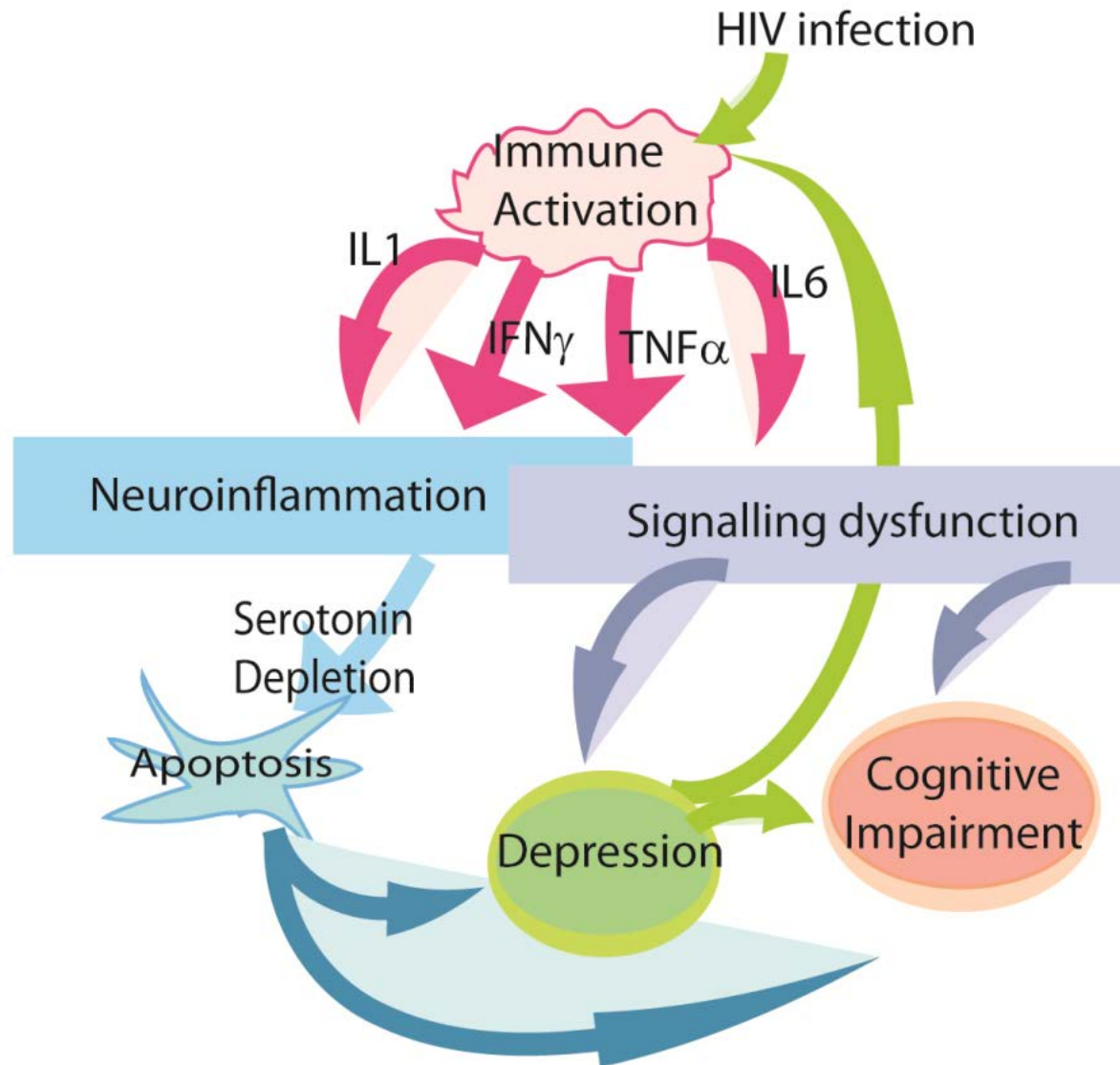
1. Mahy M et al. AIDS. 2014;28(Suppl 4): S453-S459..

Background

There is a trend in increasing prevalence of cognitive impairment with age and HIV severity status.²



Background



Study Aim and Hypothesis

- To determine whether men with a depressive phenotype have an increased risk of having cognitive impairment over time, especially if they are HIV-infected.

HYPOTHESIS: HIV-infected men with a depressive phenotype will be at increased risk of cognitive impairment over time.



Method

STUDY SAMPLE:

- 567 HIV+ and 360 HIV- men from the Multicenter AIDS Cohort Study (MACS) from 2000 onward with 5+ follow-up visits



DEPRESSIVE PHENOTYPE:

- Center for Epidemiologic Studies-Depression (CES-D) of 16 or greater for three consecutive visits

COVARIATES:

- Baseline age, number of comorbidities at baseline, race, level of education, HIV status, CD4 count (<200, 200-350, 350+) and log-transformed viral load
- Time since index visit and time squared



Cognitive Impairment Measures

Trail Making Test Part B

Patient's Name: _____

Date: _____

Trail making test A

Performance: _____

A rectangular frame containing 25 numbered circles (1-25) scattered across the area. The circles are arranged in a non-linear pattern, with some clustered together and others isolated.

A rectangular frame containing a sequence of letters and numbers arranged in a path. The path starts at circle 8 and ends at circle 10. The sequence is as follows:

- 8: 8
- 9: 9
- 10: 10
- 11: 1
- 12: 2
- 13: 3
- 14: 4
- 15: 5
- 16: 6
- 17: 7
- 18: 8
- 19: 9
- 20: 10
- 21: 11
- 22: 12
- 23: 13
- 24: 14
- 25: 15



Statistical Analyses

1. Linear random effects models among HIV+ and HIV- men
 - Adjusted for covariates
 - Inclusion of interaction terms:
 - HIV status and depressive phenotype
 - Depressive phenotype and time
2. Linear random effects models only among HIV+ men
 - Adjusted for covariates, CD4 count, and log-transformed viral load



Characteristics of Study Sample

	Depressive Phenotype		p-value for difference
	Yes N=335	No N=592	
Age, in years, mean (SD)	38.4 (8.0)	39.4 (9.4)	0.0969
Race, n (%)			0.0006
Non-white	227 (67.8)	333 (56.3)	
White	108 (32.2)	259 (43.8)	
Education, n (%)			0.0014
Less than college	210 (62.9)	308 (52.0)	
College graduate or more	124 (37.1)	284 (48.0)	
Number of Comorbidities, n (%)			<0.001
0	43 (12.8)	193 (32.6)	
1-2	241 (71.9)	372 (62.8)	
3+	51 (15.2)	27 (4.6)	

Characteristics of HIV+ Sample

	Depressive Phenotype		p-value for differences
	Yes N=227	No N=340	
Viral Load, copies per mL, mean (SD)	32,642.2 (113,513.2)	15,529.1 (58,050.7)	0.0246
CD4 Count, cells per mm³, mean (SD)	521.0 (281.3)	551.3 (285.4)	0.2372



Results – Trail-making Test Pt. A

Fixed Effects	Estimate	95% CI
Depressive Phenotype	1.08	(1.04, 1.12)
Number of Comorbidities		
1-2 vs. 0	0.97	(0.94, 0.99)
3+ vs. 0	0.95	(0.90, 1.00)
HIV Positive	0.96	(0.93, 0.99)
White vs. Non-White	0.91	(0.88, 0.95)
College Graduate Vs. Not	0.84	(0.81, 0.87)
Baseline Age*	1.01	(1.01, 1.01)
Time since Index Visit, in Years	0.95	(0.95, 0.96)
Time Squared	1.00	(1.00, 1.00)



Results – Trail-making Test Pt. B

Fixed Effects	Estimate	95% CI
Depressive Phenotype	1.12	(1.07, 1.18)
Number of Comorbidities		
1-2 vs. 0	0.98	(0.95, 1.01)
3+ vs. 0	0.96	(0.91, 1.02)
HIV Positive	0.99	(0.96, 1.02)
White vs. Non-White	0.84	(0.80, 0.88)
College Graduate Vs. Not	0.78	(0.74, 0.81)
Baseline Age*	1.01	(1.01, 1.01)
Time since Index Visit, in Years	0.95	(0.95, 0.96)
Time Squared	1.00	(1.00, 1.00)



Results – Symbol Digit Modalities Test

Fixed Effects	Estimate	95% CI
Depressive Phenotype	-1.84	(-3.76, 0.07)
Number of Comorbidities		
1-2 vs. 0	0.58	(-0.20, 1.37)
3+ vs. 0	0.81	(-0.71, 2.32)
HIV Positive	0.40	(-0.82, 1.62)
White vs. Non-White	4.81	(3.34, 6.28)
College Graduate Vs. Not	6.92	(5.47, 8.38)
Baseline Age*	-0.34	(-0.42, -0.26)
Time since Index Visit, in Years	0.32	(0.17, 0.47)
Time Squared	-0.02	(-0.04, -0.01)
HIV Positive * Depression	-2.39	(-4.46, -0.33)



Summary of Results

- Men with a depressive phenotype took **8%** and **12% longer** on the Trail-Making Tests Pt. A and B respectively than men without a depressive phenotype across time after adjusting for covariates.
- Among men who are HIV negative and adjusting for other covariates, men with a depressive phenotype had **1.84 fewer digit-symbol pairs** on the Symbol Digit Modalities Test than men without a depressive phenotype.



Results – Trail-making Test Pt. A – HIV+

Fixed Effects	Estimate	95% CI
Depressive Phenotype	1.09	(1.04, 1.14)
Number of Comorbidities		
1-2 vs. 0	0.96	(0.89, 1.04)
3+ vs. 0	0.91	(0.82, 1.01)
White vs. Non-White	0.90	(0.86, 0.95)
College Graduate Vs. Not	0.87	(0.83, 0.91)
Baseline Age*	1.01	(1.01, 1.01)
Time since Index Visit, in Years	0.96	(0.95, 0.97)
Time Squared	1.00	(1.00, 1.00)
CD4 Count		
201-499 vs. ≤ 200	0.98	(0.96, 1.00)
≥ 500 vs. ≤ 200	0.98	(0.96, 1.01)
Log-transformed Viral Load	1.00	(1.00, 1.01)



Results – Trail-making Test Pt. B – HIV+

Fixed Effects	Estimate	95% CI
Depressive Phenotype	1.12	(1.05, 1.19)
Number of Comorbidities		
1-2 vs. 0	0.98	(0.90, 1.07)
3+ vs. 0	1.03	(0.92, 1.16)
White vs. Non-White	0.84	(0.78, 0.89)
College Graduate Vs. Not	0.81	(0.76, 0.86)
Baseline Age*	1.01	(1.01, 1.01)
Time since Index Visit, in Years	0.95	(0.94, 0.96)
Time Squared	1.00	(1.00, 1.00)
CD4 Count		
201-499 vs. ≤ 200	0.99	(0.96, 1.01)
≥ 500 vs. ≤ 200	0.98	(0.95, 1.00)
Log-transformed Viral Load	1.00	(0.99, 1.00)



Results – SDMT –HIV+

Fixed Effects	Estimate	95% CI
Depressive Phenotype	-4.31	(-6.15, -2.47)
Number of Comorbidities		
1-2 vs. 0	0.70	(-1.62, 3.01)
3+ vs. 0	3.43	(0.26, 6.59)
White vs. Non-White	5.40	(3.49, 7.31)
College Graduate Vs. Not	5.73	(3.80, 7.66)
Baseline Age*	-0.34	(-0.45, -0.23)
Time since Index Visit, in Years	0.22	(0.03, 0.48)
Time Squared	-0.02	(-0.04, 0.00)
CD4 Count		
201-499 vs. ≤ 200	0.06	(-0.56, 0.67)
≥ 500 vs. ≤ 200	0.11	(-0.57, 0.78)
Log-transformed Viral Load	0.04	(-0.12, 0.20)



Summary of Results

- After adjusting for covariates, men with depressive phenotype took **9%** and **12%** longer to complete the Trail-Making Tests Pt. A and B respectively than men without depressive phenotype among HIV+ men.
- After adjusting for covariates, men with depressive phenotype had **4.31 fewer digit-symbol pairs** on Symbol Digit Modalities Test than men without depressive phenotype among HIV+ men.



Conclusions

- Men with a depressive phenotype were at elevated risk for cognitive impairment than men without a depressive phenotype.
 - Results suggest slower psychomotor speed and worse executive function.
- The effect of depression on cognitive impairment was stronger among HIV-positive men only in Symbol Digit Modalities Test.



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3. Sacktor N, Skolasky RL, Cox C, et al. Longitudinal psychomotor speed performance in human immunodeficiency virus-seropositive individuals: impact of age and serostatus. *Journal of NeuroVirology*. 2010;16:335-341.
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Questions?

Thank You!

