

Conclusions: While neurocognitive dysfunction, substance abuse, and depression are all individually associated with medication adherence difficulty, patients with multiple disorders are at disproportionate risk for adherence failure.

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**B.W. BECKER, S.E. PANOS, J. JANG, A.L. GOODING, S.A. CASTEL-
LON, R.S. DURVASULA & C.H. HINKIN. Longitudinal Study of Neuro-
cognitive Function and Medication Adherence in HIV-Positive
Adults: Association with Apathy and Stimulant Use.**

Objective: Apathy, a common neuropsychiatric disturbance in HIV that can be reliably distinguished from depression, may be a marker of the direct neurophysiologic effects of HIV on frontostriatal circuits. These same circuits are involved in information processing speed and working memory and serve as an activation site for stimulants. Although stimulant use and neuropsychiatric disturbances have been independently associated with poor medication adherence, their combined effects on adherence and neurocognition have yet to be assessed.

Participants and Methods: Participants included 69 HIV-infected adults who underwent cognitive and psychiatric testing at study entry and then six months later. Medication adherence and stimulant use were assessed continuously using electronic monitoring devices and drug urinalysis screening. Participants were grouped based on stimulant use (Users vs Non-users) and presence of apathy (Apathy present vs. No apathy).

Results: A three-way (Stimulant use, Apathy, Time) mixed design ANCOVA with depression as a covariate revealed an interaction effect with stimulant users who endorsed apathy demonstrating significantly lower adherence rates than the other groups (37% adherent vs 70-81%, respectively). A three-way Stimulant X Apathy X Time interaction effect was found for information processing speed ($p = .001$) and working memory ($p = .02$) and were attributable to declines among stimulant users with apathy endorsement. Neuropsychological performance improved or remained stable in the other 3 groups.

Conclusions: The concurrent presence of apathy and stimulant use is a better predictor of medication adherence and neurocognitive decline than either disorder alone.

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**J. FOLEY, M. ETTENHOFER, M. WRIGHT, I. SIDDIQI, K. MASON,
H. MYERS, E. SINGER, S. CASTELLON & C. HINKIN. Effects of
Cerebrovascular Risk versus Age upon Cognitive Functioning in
HIV-1-Infected Patients.**

Objective: This study examined the additive effects of cerebrovascular risk factors, advancing age, and HIV-infection upon neurocognitive functioning. A secondary aim was to determine the impact of pharmacological control of cerebrovascular risk.

Participants and Methods: Participants included 98 HIV-seropositive adults (Age=44.2[7.6]; education=13.1[1.9]; AIDS=62.5%; Ln CD4 count=5.8[0.8], Ln viral load=8.1[2.4]). Participants were administered a comprehensive neuropsychological battery. Contributions of cerebrovascular risk, pharmacological control of risk, and age were examined using ANOVA and multiple regression.

Results: Older (>50 years) HIV+ performed worse than younger (< 39 years) HIV+ on processing speed ($p<0.01$; $\eta^2=0.10$), executive functioning ($p<0.01$; $\eta^2=0.07$), and learning/memory ($p=0.04$; $\eta^2=0.04$). Cerebrovascular risk was associated with slower processing speed ($p=0.02$; $\eta^2=0.06$). A hierarchical multiple regression analysis, conducted for the processing speed domain, indicated that only presence of cerebrovascular risks contributed significantly ($b=-2.071$; $p=0.04$) when controlling for age. There was no interaction effect. Follow up analyses indicated that pharmacologically controlled at-risk subjects performed

superior to uncontrolled at-risk subjects on processing speed ($p=0.01$; $\eta^2=0.27$) and learning/memory ($p=0.04$; $\eta^2=0.18$), with trend findings on executive functioning ($p=0.09$; $\eta^2=0.13$). We then compared uncontrolled at-risk participants and seropositive controls; results revealed superior performance among the controls on processing speed ($p<0.001$; $\eta^2=0.147$), learning/memory ($p=0.008$; $\eta^2=0.08$), and executive functioning ($p=0.04$; $\eta^2=0.05$).

Conclusions: Cerebrovascular risks appear to confer significant impact for HIV+ individuals, and this effect may be of greater consequence to processing speed reductions than advancing age. The impact of cerebrovascular risk upon cognitive functioning appears to be more pronounced and widespread in the absence of adequate pharmacological control.

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**C.A. BOUSMAN, M. CHERNER, J. ATKINSON, R.K. HEATON,
I. GRANT & I.P. EVERALL. Catechol-O-Methyltransferase, Exec-
utive Dysfunction, and Sexual Risk Behavior in the Context of HIV-
Infection and Methamphetamine Dependence.**

Objective: Catechol-O-methyltransferase (COMT) metabolizes prefrontal cortex dopamine (DA), a neurotransmitter involved in executive behavior; the Val158Met genotype has been linked to executive dysfunction, which might increase risky sexual behaviors favoring HIV transmission. We examined the influence of COMT genotype and executive functioning on sexual risk behavior among participants with or without HIV infection and methamphetamine dependence (METH+); both, conditions linked to DA disturbance and risk behavior.

Participants and Methods: 208 men (51 = METH+/HIV+; 67 = HIV-only; 46 = METH-only; 44 = Control) received a self-administered sexual behavior questionnaire that asked about the percent time they used a condom, engaged in oral, vaginal, anal and/or intoxicated sex, as well as the number of different sexual partners in the past year. All subjects were hepatitis C negative. An executive deficit score was derived from the Wisconsin Card Sorting Test, Trail Making Test Part B, and Halstead Category Test. COMT Val158Met polymorphism was assayed from blood-derived DNA.

Results: Linear regressions revealed that executive dysfunction significantly influenced number of sexual partners and additionally uncovered a genotype X executive dysfunction interaction ($p < .05$). Regressions stratified by COMT genotype revealed that the relationship between executive dysfunction and number of sexual partners was statistically significant ($p < .001$) for carriers of the Met/Met but not the Val/Met or Val/Val genotype.

Conclusions: COMT genotypic differences may moderate the influence of executive functioning on sexual risk-taking, supporting a role of DA metabolism in these behaviors. In the context of HIV and methamphetamine dependence, dopaminergic overactivity in the prefrontal cortex conferred by the Met/Met genotype appears to result in a liability for executive functioning and potentially associated risky sexual behavior.

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**D.F. TATE, S. ZHANG, M. SAMPAT, J. CONLEY, K. KERTESZ, S. RAN-
GARAJAN, T. RUSSELL, J. PRICE, D.H. LAIDLAW, L. TAYLOR, D. MC-
CAFFREY, C. GUTTMANN, T. FLANIGAN & K. TASHIMA. Para-sagittal
Corpus Callosum Fractional Anisotropy is Associated With Measures
of Attention and Motor Function Among HIV Infected Patients.**

Objective: HIV-associated white matter injury is a contributing pathological factor underlying cognitive dysfunction commonly observed in HIV-infected cohorts. Diffusion tensor imaging (DTI) has been shown to be sensitive to white matter abnormalities and cognitive dysfunction in this population. In this study, we examined the associations between fractional anisotropy (FA) acquired in the mid-sagittal (MSFA) plane, para-sagittal FA (PSFA) acquired from tractography results, and a broad range of cognitive function among an HIV-infected sample.

Participants and Methods: DTI and cognitive testing results from 21 ethnically diverse HIV-infected patients (mean age=41.28 years; education=12.85 years; 52% African American, CD4 count=406.29; 47% with undetectable viral loads) were examined. For each participant, we segmented the mid-sagittal corpus callosum (CC) into five functional related areas and calculated the average FA within each region. Using the segmented areas as seed points, we then generated tractography maps of fiber projections through each CC area. From these tractography maps, we calculated the average FA along the length of the streamtubes for a measure of PSFA. We then examined the relationship between MSFA, PSFA, and a summary cognitive performance z-score for five cognitive domains (attention, executive, motor, language, and memory).

Results: Consistent significant associations were noted between PSFA, attention ($p<0.007$), and motor ($p<0.02$) domains regardless of region examined. Executive, language, and memory domains were unrelated to PSFA ($p>0.10$). No significant associations between MSFA and cognition were noted ($p>0.09$). Fisher exact z-test comparisons demonstrated a significant difference in the magnitude of associations between PSFA and MSFA ($p<0.01$) for these two domains.

Conclusions: PSFA from tractography may provide more robust and reliable measures of tract integrity than MSFA. One explanation may be that PSFA captures additional spatial variability in cognitively relevant tract integrity.

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Invited Plenary: Reading the Genome for Genes for Reading

Speaker: Elena Grigorenko

1:45–2:45 p.m.

E. GRIGORENKO. Reading the Genome for Genes for Reading.

In this presentation, Dr. Grigorenko will provide an overview of the behavior- and molecular-genetic studies of reading ability and disability that are carried out in her laboratory. After contextualizing this work in the field in general, she will exemplify her laboratory's work by summarizing the results from research that utilizes different genetically informative designs, ranging from family segregation studies, through whole-genome screens and candidate-gene analyses, to single-case investigations. Dr. Grigorenko will conclude with a set of comments on how these studies enrich psychological theories of reading.

Correspondence: *Elena Grigorenko, Child Study Center, Yale University, 230 South Frontage Road, P.O. Box 207900, New Haven, CT 06520-7900. E-mail: elena.grigorenko@yale.edu* **Paper**

Session 6: Alzheimer's, Aging, and Apolipoprotein E

1:30–3:00 p.m.

C.E. GLEASON, N.M. DOWLING, W.L. WHARTON, J.S. ROWLEY, A. LA RUE, B.P. HERMANN, S. ASTHANA & M.A. SAGER. **Cognitive performance of hormone therapy users and nonusers at-risk for Alzheimer's disease.**

Objective: Previous reports suggest that only women without a genetic risk factor for Alzheimer's disease (AD), the APOE4 allele, benefit cognitively from menopausal hormone therapy (HT). We examined the influence of HT use and two risk factors for AD, APOE4 genotype and parental history (PH) of AD, on a 5-factor cognitive profile.

Participants and Methods: 531 postmenopausal women enrolled in the Wisconsin Registry for Alzheimer's Prevention (WRAP), reported their past or current use of HT. Cognitive performance of women who used or are using HT (N=335, mean age=54.8) was compared to women who never used HT (N=196, mean age=57.2) in relation to APOE4 and PH status. General linear models were used to compare groups defined by HT use by APOE4 status and then by PH with age, education, and depression score entered as covariates in each model.

Results: Comparisons of HT users and nonusers revealed that women without the APOE4 gene on HT outperformed women naive to HT on verbal and visuospatial abilities factors. Likewise, comparing women with and without PH of AD revealed again that women exposed to HT outperformed women naive to HT on verbal ability and visuospatial tests, regardless of PH status. In both comparisons, the two groups did not differ on memory, working memory and speed-flexibility factors.

Conclusions: Verbal and visuospatial task performance was significantly different between HT users and nonusers for the APOE4 negative women, such that HT users outperformed nonusers; PH on the other hand did not appear to influence cognitive response to HT.

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J.L. WOODARD, R.C. GREEN, S.M. JAZWINSKI, J. ARNOLD, P. MARTIN, L.S. MILLER, A. DAVEY, M. BURGESS & L.W. POON. **Apolipoprotein E ε4 Adversely Impacts Cognitive and Functional Status in Caucasian Centenarians but not in African American Centenarians.**

Objective: Although it is associated with greater risk of Alzheimer's disease (AD), several studies suggest that the apolipoprotein E (APOE) ε4 allele does not affect cognition in late life. We investigated whether functional and cognitive performance differs between APOE ε4 carriers and non-carriers in participants from the Georgia Centenarian Study.

Participants and Methods: Using a population-based sample, 244 centenarians or near-centenarians between 98 and 108.6 years of age (M-age=100.5 years, 21% African American; 85% female) were recruited. Participants completed the Mini-Mental State Examination, Severe Impairment Battery, Fuld Object Memory Evaluation (episodic memory and right-left discrimination), Behavioral Dyscontrol Scale (executive functioning), motor speed assessment, and Direct Assessment of Functional Status (ability to perform basic and instrumental daily living skills). APOE genotyping was performed from a serum sample.

Results: Allele frequencies for the ε2, ε3, and ε4 alleles were 0.120 ± 0.017 , 0.802 ± 0.040 , and 0.078 ± 0.027 for Caucasians and 0.154 ± 0.069 , 0.683 ± 0.089 , and 0.163 ± 0.071 for African Americans, respectively. More African Americans were ε4 carriers relative to Caucasians (30.8% vs. 14.6%, Fisher's Exact Test $p=.013$). Only among Caucasians, ε4 carriers demonstrated significantly ($p<.05$) lower performance than non-carriers on all measures; Cohen's d effect sizes ranged from .43 to .73. ε4 status did not differentiate cognitive or functional performance for African Americans ($p's>.05$; d's: .11 to .39).

Conclusions: The APOE ε4 allele occurs with greater frequency among African American centenarians. Among Caucasian centenarians only, ε4 carriers performed more poorly on tests of cognitive and functional performance. At least among Caucasians, the deleterious impact of APOE appears to persist well beyond 80 years of age.

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N.M. WISDOM, J.L. CALLAHAN & K.A. HAWKINS. **The Effects of Apolipoprotein E on Nondemented Cognitive Functioning: A Meta-Analysis.**

Objective: Nearly twice as many participants are represented in the current literature than were available at the time of the last major meta-analytic neurocognitive examination of Apolipoprotein E (ApoE) ep-