Family history of cardiovascular disease is associated with self-reported cognitive function: the Emory Healthy Aging Study

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Background: Family history of cardiovascular disease (FHxCVD) is a CVD risk indicator that captures the influence of genetic and shared familial factors and is readily available to individuals and clinicians. Though CVD risk factors associate with greater risk of cognitive impairment, less is known about the association between FHxCVD and self-reported cognitive function. Evaluating this association may further elucidate links between cardiovascular and cognitive health.

Methods: The Emory Healthy Aging Study is a community-based prospective cohort study aimed at identifying predictors of healthy aging and age-related diseases. Participants are primarily residents of the Atlanta area, at least 18 years old, who completed an online baseline health survey. Information about demographic (age, self-reported race, gender), socioeconomic (education, household income), lifestyle (physical activity, smoking) and CVD risk factors (diabetes, hyperlipidemia, BMI, hypertension) and family health history were collected at enrollment. Family history of CVD was defined as self-reported history of coronary artery disease, myocardial infarction, or stroke for any biological parent or sibling. Self-reported cognitive function was measured using the validated Cognitive Function Instrument (CFI) and categorized into quartiles. Associations between FHxCVD and CFI score quartile were assessed using multinomial logistic regression, adjusting for demographic, socioeconomic, lifestyle and the participant's own CVD risk factors, as well as family history of any diagnosed cognitive impairment.

Results: We studied 6,115 participants (75% female, 84% white, 11% black, and 5% other self-reported race), without existing CVD, recruited between October 2015 and 2017. Mean age was 59±13 years and 61% reported a family history of CVD. Comparing extreme quartiles of CFI score, adjusted for demographic, socioeconomic, and lifestyle factors, plus family history of any diagnosed cognitive impairment, FHxCVD was associated with poorer self-reported cognitive function (OR=1.43; 95% CI (1.21, 1.70)). The OR after additional adjustment for CVD risk factors was not meaningfully different (OR=1.47; 95% CI (1.23, 1.76)). In the same fully adjusted model, the estimated OR for family history of any cognitive impairment was slightly larger: 1.54 (1.30, 1.83).

Conclusion: In this cross-sectional community sample, family history of CVD was associated with poorer self-reported cognitive function, and this association was of a similar magnitude as having a family history of cognitive impairment. Although longitudinal studies are needed, these results underscore the link between cardiovascular and cognitive health. Twin studies are needed to estimate the contribution of genetic and shared familial factors.

Construct Validity of Montreal Cognitive Assessment Index Scores in Cognitively Normal Adults

EMORY Healthy Brain Study

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EMORY UNIVERSITY SCHOOL OF MEDICINE

Introduction

- Increasing numbers of individuals are surviving into advanced ages, expanding the proportion of the population at risk for the development of Alzheimer's disease and other neurodegenerative disorders. Thus, there is great need for simple and effective tools for dementia screening.
- The Montreal Cognitive Assessment (MoCA) is a cognitive screen used to characterize global cognitive status. It has been shown to have high sensitivity for detecting individuals with Mild Cognitive Impairment (90%) and Alzheimer's Disease (100%)[1].
- Julayanont & colleagues have categorized the items of the MoCA into six domain-specific indices: Memory, Visuospatial, Executive, Attention, Language, and Orientation.[2]

Objective

- Current research has primarily focused on the MoCA Memory Index and its ability to act as a predictor of conversion from Mild Cognitive Impairment to Alzheimer's disease.[2]
- There is minimal research establishing the construct validity, reliability, and sensitivity of all six MoCA indices.
- We examined the relationship between performance on the MoCA indices and other established neuropsychological measures to determine the construct validity and clinical application of the MoCA indices.

Method

- Participants: 409 cognitively normal (M_{MoCA} = 26.51, SD_{MoCA} = 2.32) middle-aged and older adults (M_{age} = 62.59, SD_{age} = 7.00) completed comprehensive cognitive testing as part of their participation in the Emory Healthy Brain Study (EHBS).
- The EHBS is a prospective study of preclinical Alzheimer's disease and other chronic diseases of aging that aims to identify predictors of disease development through in-depth characterization of potential biomarkers within a cognitively normal sample of those at-risk for disease. The EHBS includes a comprehensive neuropsychological battery.
- We utilized correlation analyses to examine the construct validity of five of the six MoCA indices: memory, executive functioning, attention, language, and visuospatial.

Results

Table 1. EHBS Participant Characteristics

	M	*SD*	%
Demographic Variables (N = 409)			
Age (years)	62.59	7.00	
Gender (% female)			75.8
Race (%)			
Asian			1.2
Black or African American			11.5
White or Caucasian			84.4
Other			2.9
Ethnicity (% Non-Hispanic)			97.1
Education	16.48	2.21	
Handedness (% Right)			90.2
MoCA	26.51	2.32	

Table 2. Components of the MoCA Indices by Domain and Associated Neuropsychological Measures from the EHBS Battery

MoCA Index	MoCA Components	Study Battery
Memory (MIS)	Delayed recall; Category-cued recall; Multiple choice-cued recall	Rey-Osterrieth Immediate Rey-Osterrieth Delay Rey-Osterrieth Recognition
Executive (EF)	Digit Span; Mini-Trails; Clock drawing; Serial 7s; Letter A tapping; Abstraction; Letter fluency	Trail-Making Test B FAS Number Span Backward
Attention (ATTN)	Serial 7s; Letter A tapping; Sentence repetition; Digit Span; Immediate word recall	Trail-Making Test A Number Span Forward Number Span Backward
Language (LANG)	Animal picture naming; Sentence repetition; Letter fluency	Multilingual Naming Test Animal Fluency FAS
Visuospatial (VS)	Cube drawing; Clock drawing; Animal picture naming	Rey-Osterrieth Figure Copy Judgment of Line Orientation

Table 3. Participant Performance Scores on the EHBS Neuropsychological Battery

Test Name	*M*	*SD*	*Range*
Animal Fluency	21.53	4.89	4-42
JoLO	25.16	3.95	8-30
MINT	30.78	1.74	17-32
MoCA	26.51	2.32	19-31
RCFT Copy	31.68	3.79	10-36
RCFT Immed	17.49	6.46	0-35
RCFT Delay	16.55	6.11	0-34
RCFT Rec	20.35	1.90	13-24
NS Backward	7.19	2.24	0-14
NS Forward	8.73	2.52	0-14
TMT-A	34.58	12.50	0-108
TMT-B	74.07	33.61	20-300
FAS	43.12	11.53	3-79

Table 4. Correlations Among Cognitive Measures and MoCA Indices

Test Name	Animal Fluency	JoLO	MINT	RCFT Copy	RCFT Immed	RCFT Delay	RCFT Rec	NS Back	NS Fwd	TMT-A	TMT-B	FAS
$MoCA_{MIS}$	.162**	.068	.063	.126*	.164**	.152**	.162*	.190**	.103*	-.195**	-.176**	.166**
$MoCA_{EF}$	.238**	.305**	.241**	.290**	.136**	.115*	.080	.226**	.176**	-.208**	-.302**	.388**
$MoCA_{Attn}$	.186**	.343**	.207**	.238**	.171**	.153**	.114*	.299**	.272**	-.180**	-.299**	.159**
$MoCA_{Lang}$	.276**	.202**	.215**	.101	.065	.057	.107*	.254**	.193**	-.149**	-.191**	.409**
$MoCA_{VS}$	.174**	.326**	.207**	.436**	.222**	.196**	.219**	.127*	.062	-.221**	-.299**	.125*

**. Correlation is significant at the 0.01 level (2-tailed).
*. Correlation is significant at the 0.05 level (2-tailed).

Results & Conclusions

- Despite statistically significant correlations between the MoCA indices and other well-established measures of domain functioning, there is weak evidence of construct validity for the indices. Effect sizes are weak and reveal limitations in the MoCA's ability to accurately characterize domain functioning.
- The MoCA memory index was weakly correlated to the Rey Complex Figure Test immediate (r = .16), delayed (r = .15) (p_s < .01), and recognition (r = .16) trials (p < .05). The language index was moderately correlated to F-A-S letter fluency (r = .41), but only weakly correlated to Animal Fluency (r = .28) and the MINT (r = .22) (p_s < .01).
- The MoCA indices do not adequately relate to performance on full-length cognitive tests of the same domains, suggesting that evaluation of index scores cannot reliably predict performance across all domains of neuropsychological functioning.
- Current research examining the MoCA indices has shown moderate to strong correlations between MoCA indices and standardized domain scores within a cognitively impaired sample[3]. Additionally, Cecato *et al.* found that specific items from the MoCA could discriminate between healthy controls and Alzheimer's disease patients, as well as between those with Mild Cognitive Impairment and Alzheimer's disease[4].
- Our research supports the notion that comprehensive neuropsychological testing is needed to accurately assess the domains of cognitive functioning during the preclinical phase of disease in order to detect early and subtle signs of change.
- Future research on the MoCA indices should utilize cognitively heterogeneous samples of individuals to better understand the clinical usefulness of the indices to differentiate populations and predict future decline.

*** References available on handout.**

Mental Health and Demographic Characteristics, but Not Parental History, Influence Subjective Ratings of Cognitive Functioning

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Introduction

- As our population ages, more individuals are seeing their loved ones succumb to Alzheimer's disease (AD). Children of adults with AD are more likely to report subjective concerns[1]. The strongest predictors are factual knowledge of the disease and negative self-assessments of memory[2].
- There is an increased risk for the development of AD in African Americans[3], as well as decreased factual knowledge about the disorder[4]. However, previous research on subjective cognitive decline has focused primarily on Caucasian populations.
- Subjective memory complaints have also been linked to depression and overall mental health[5].

Objective

We examined predictors of subjective cognitive complaints in Caucasian and African American older adults. We hypothesized that parental history and psychological functioning would predict subjective ratings on the Cognitive Function Instrument (CFI).

Method

- Older adult (M_{age} = 64.37, SD_{age} = 7.99) participants completed an online health history questionnaire as part of a prospective study of preclinical MCI and AD.
- Participants provided basic demographic information and family medical history, and rated their current symptoms.
- Overall CFI score was regressed onto the following predictors in a standard multiple regression: scores from the Generalized Anxiety Disorder 7-item scale (GAD-7), Patient Health Questionnaire depression scale (PHQ-8), ratings of overall physical (0-4) and mental health (0-4), age, race, and parental history.
- Participant characteristics for the full sample are included in the table. Only those participants with a complete CFI (N = 3984) were included in the regression analysis.

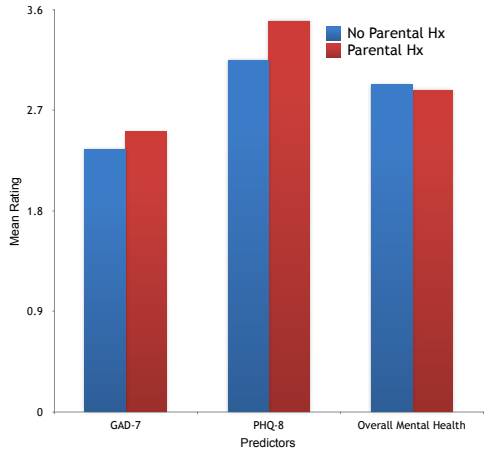
This data comes from the Emory Healthy Aging Study which is funded by the Goizueta Foundation.

Results

Participant Characteristics

Demographics	Participants		
	Range	(%)	M (*SD*)
Age	50 - 90		64.37 (7.99)
Female	-----	(76.0%)	-----
Male	-----	(23.7%)	-----
Education (≤15 Years)	0 - 22	(23.5%)	-----
Education (>15 Years)	0 - 22	(76.4%)	-----
Model Predictors			
GAD_total	0 - 21		2.15 (3.17)
PHQ_total	0 - 23		3.07 (3.70)
CFI_total	.0 – 14.0		1.96 (2.13)
Overall Physical Health	.00 – 4.00		2.77 (0.88)
Overall Mental Health	.00 – 4.00		2.98 (0.84)

Subjective Symptom and Health Ratings in Those With vs. Without a Parental History of AD



Note: ***Groups are significantly different, $p < .05$.

Mean ratings of self-reported symptoms using GAD-7, PHQ-8, and Overall Mental Health questions.

- The full regression model explained 36.5% of the variance in CFI score, $F(8,3975) = 285.37$, $p < .001$.
- The following were significant predictors: age, race, GAD-7, PHQ-8, and mental health rating.

Results (Cont.)

- 58.7% reported no parental history of AD or related memory problems, while 41.3% endorsed parental history for at least one parent.
- Neither parental history nor Overall Physical Health predicted CFI score.
- African Americans were more likely to report subjective cognitive complaints.

Table 2. Parameter Estimates of Predictors of CFI

Initial Visit Predictors	*B*	SE	Sig.
GAD-7	.092	.012	< .001
PHQ-8	.205	.011	< .001
Overall Mental Health	-.423	.041	< .001
Overall Physical Health	-.068	.037	.065
Age	.029	.002	< .001
Race	.495	.086	< .001
Parental History	.064	.059	.277

Conclusions

- Parental history did not predict perceptions of cognitive decline. Instead, minority race, older age, and greater psychological symptomatology were significant predictors.
- The finding of greater subjective cognitive complaints in African Americans differs from previous research[4], and may indicate success in more proactive self-monitoring. It has been hypothesized that subjective memory complaints could be a risk factor for developing AD[6].
- Those with psychological symptomatology are at a higher risk of perceived cognitive decline. These individuals should be monitored to determine if the subjective cognitive decline is a manifestation of the first signs of AD, or if it is more simply a side effect of a mental health disorder.

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Preliminary Assessment of a Flanker Smartphone App: Reliability, Feasibility, and Construct Validity

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EMORY Healthy Aging Study

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Introduction

- The widespread use of smartphones has led investigators to adopt this accessible technology for cognitive research (Defau et. al, 2011) through development of mobile applications that assess cognitive functioning (Dahmen, et. al., 2017; Ruggeri et. al., 2016).
- Remote cognitive assessment offers many benefits, including increased accessibility to large, heterogeneous samples and earlier detection of cognitive decline (Bauer et. al, 2012).
- We developed a smartphone app version of the computerized Flanker assessment to measure processing speed, visual attention, and inhibition.
- An ongoing pilot study assesses the reliability, construct validity, and feasibility of our mobile application ('Arrows').

Method

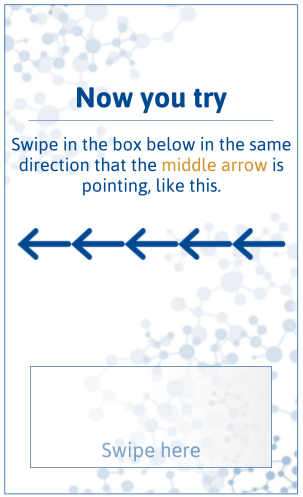
- Cognitively normal non-Hispanic Caucasian and African-American middle-aged and older adult smartphone users (N = 64) participated in a validation study of smartphone applications developed for remote cognitive assessment.
- Participants completed the original Flanker assessment and the novel Arrows application as well as other cognitive measures: Montreal Cognitive Assessment (MoCA), Wide Range Achievement Test-Word Reading subtest (WRAT), and Symbol-Digit Modalities Test (SDMT).
- Arrows reaction times were correlated to Flanker reaction times as well as other neuropsychological measures to assess reliability and construct validity. A paired samples t-test evaluated the difference between congruent and incongruent trial reaction times.
- Feasibility of the Arrows app was assessed through a self-report scale.

Participants

Table 1. Participant Characteristics

	Range	*M*	*SD*	%
Demographic Variables (N = 64)				
Age (years)	[45-75]	61.27	7.49	
Education (years)	[12-20]	16.52	2.32	
Gender (% female)				89.1
Race (% of sample)				
African American (N = 35)				54.7
Non-Hispanic Caucasian (N = 29)				45.3
Handedness (% Right)				85.9
Phone Model (% iPhone)				60.9

This project was supported by the Emory Healthy Aging Study, which is funded by the Goizueta Foundation, as well as through an NIH/NIA R03 grant (1R03AG055810).



Results

Table 2. Correlations Between Arrows and Neuropsychological Measures

Test Name	Flanker Mean RT	Flanker Congruent trials	Flanker Incongruent trials	MoCA Total	MoCA Attention	MoCA Visuospatial	MoCA Language	SDMT Total
Arrows Mean reaction time	.352**	--	--	-.295*	-.099	-.397**	-.149	-.221
Arrows Congruent trials	--	.362**	--	--	--	--	--	--
Arrows Incongruent trials	--	--	.316*	--	--	--	--	--

** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).
Note: all reaction times are presented in milliseconds.

Table 3. Feasibility Ratings

Feasibility Assessment	Mean Rating (1-5)
I think that I would like to use this app frequently.	3.75 (1.07)
I found the app unnecessarily complex.	1.48 (.71)
I thought the app was easy to use.	4.36 (1.06)
I think that I would need tech support to use this app.	1.22 (.49)
Most people would learn to use this app quickly.	4.11 (.98)
I needed to learn a lot of things before using this app.	1.36 (.72)

Note: Ratings were on a 1-5 scale, on which: 1= Strongly disagree, 2 = Disagree, 3 = Neutral, 4 = Agree, and 5 = Strongly agree.

Results (cont.)

- The time difference between congruent (*M* = 1295.67 ms, *SD* = 466.65) and incongruent trials (*M* = 1283.22 ms, *SD* = 524.91) was not statistically significant, $t(62) = .29$, $p = .77$.
- There was significant agreement between overall, congruent, and incongruent trial reaction times on the Flanker and Arrows tasks.
- Mean reaction time on Arrows trials was significantly related to performance on the MoCA, and in particular, the visuospatial index of the MoCA. Mean reaction time on Arrows was not related to the SDMT total score, the MoCA attention index, or the MoCA language index.
- Participants rated the app as easy to understand and use.

Conclusions & Future Directions

- There is preliminary evidence for task reliability given the relationship between Arrows and Flanker reaction times. However, total performance scores between the two tasks cannot be evaluated since the majority of our sample obtained a perfect score on Arrows, suggesting that it differs in difficulty level from the Flanker.
- There is currently no difference in reaction time between congruent and incongruent trials on Arrows. This may be related to user response style (one-handed responding) that is specific to smartphone use.
- Arrows was significantly related to overall cognitive functioning and visuospatial skills. Arrows was not significantly related to cognitive tasks assessing language, attention, and executive functioning. These relationships provide initial evidence of convergent and discriminant construct validity.
- Future research will incorporate task modifications to increase the overall difficulty of Arrows to allow for greater performance variability and the detection of performance differences between diagnostic groups.
- Future research will also assess the reliability, feasibility, and construct validity of additional app-based measures of cognition (pictured below).