Interactions between physical fitness and genetics on behavioral and biological markers of Alzheimer's risk in older African Americans

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Dual Missions



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⇒1. Community Engagement for Public Health:

Offer brain health and Alzheimer's prevention programs for older African Americans in the greater Newark area.

Our Community Engagement Team: Senior Leadership

Housing



Glenda Wright Director of Public and Subsidized Housing Relations

Churches



Rev. Glenn Wilson Director of Church Relations (Pastor, Pilgrim Baptist Church)

Retention



Delores Hammonds

Director of Participant Satisfaction and Retention

Together, they bring almost 200 years of collective experience with local African American communities.

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Louche Powell



Jerome Perkins



Catherine Willis



Rev. Vivian Cook



Rev. Sandra Rock



Gills



Arcande Oyono

Our Community Engagement: Overview

- 1. Long-term investment in community health.
- 2. Share the wealth: Grant funds support community.
- 3. "80/20 rule": 80% public health; 20% recruitment.
- 4. Outreach to multiple African American communities.
- 5. Varied and frequent programming: 1x or 2x / week.
- 6. Men require distinct, focussed, and indirect outreach.
- 7. Partner input via "Community Stakeholders Board."

Bottom line: There is <u>no</u> quick, easy, or cheap way to successfully recruit older African Americans to aging research.



Dual Missions

1. Community Engagement for Public Health: Offer brain health and Alzheimer's prevention for older African Americans in the greater Newark area.

⇒ 2. Neuroscience and Brain Health Research:

Through university-community collaborations, conduct research on aging, brain health, and Alzheimer's prevention.

Pathways to Healthy Aging in African Americans

A University-Community Collaboration



Since 2015, over 500 older African Americans from greater Newark have joined our program for two reasons:

- 1. Improve their own brain health and reduce risk of dementia.
- 2. Support research on healthy aging.

Made possible by support from multiple grants from the NIH's National Institute on Aging (R01AG053961; R01AG08211), the NJ Department of Health, and private donors.

Who is Eligible to Participate?

- Identify as African American or Black. (regardless of where you or your parents were born)
- Age 60 <u>or older.</u>
- Speak English fluently.

- DAY 1: 30 minutes. (NJ Medical School): Saliva for genetics. Blood tests for brain health, immune health, and diabetes.
- DAY 2: 2.5 hours: Cognition, health, fitness, and lifestyle assessments.



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- **Optional:** 4 days of home sleep monitoring.



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- DAY 2: 2.5 hours: Cognition, health, fitness, and lifestyle assessments.
- Day 3: 1.5 hours: MRI Brain Imaging and EEG (brain waves).
- **Optional:** 4 days of home sleep monitoring.

REPEAT: *Return every two years (every year once 80+).*

What have we learned from our "Pathways" cohort ?



Fitness & Exercise



How We Measure Physical Fitness



6 Minute Walk: How far can participants walk in 6 mins?

• Estimates maximal oxygen consumption (VO2 Max)

Physical Fitness Does NOT Correlate with Standard Neuropsychological Measures of Cognition



If standard neuropsychological measures of memory and cognition do not correlate (in our cohort) with fitness, what measure might ?



Our Computational Models Suggested a Functional Dissociation of Subregions

(Gluck & Myers, 1995; Meeter, Gluck, & Myers, 2005)



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PREDICTION: Pre-Symptomatic/Preclinical AD May Only Affect Representation (Encoding) of New Learning: <u>NOT "Episodic" Event Memory Storage</u>



What behavioral measures will be sensitive to changes in how new learning is encoded/ represented in the brain ?



Generalization: The transfer of past learning to new situations.



Damage to the Hippocampus Impairs Generalization of Learning

(Gluck & Myers, 1993, 2001)



Generalization Task Schematic

4 Shape Rules (Color irrelevant)

4 Color Rules (Shape irrelevant)



Mild HA in Aging: Generalization Transfer Deficits

Myers, Kluger, Golomb, Ferris, de Leon, Schnirman, & Gluck. J. Geriatric Psychiatry and Neurology (2002)



Which brings us back to ask — If standard neuropsychological measures don't correlate with physical fitness, will GENERALIZATION ?



Physical Fitness

DOES Correlate with Rutgers Generalization Tasks, Measuring Generalization of Learning



Physical Fitness,

DOES Correlate with Rutgers Generalization Tasks, Measuring Generalization of Learning



ABCA7 and Alzheimer's Disease

ABCA7 affects the transport of proteins in the brain, amyloid- β (A β).

Two Single Nucleotide Polymorphisms at different places in ABCA7 Gene:

ABCA7 (rs115550680). "ABCA7-80"

Specific to African Americans: Risk allele rarely found in those of European descent Risk allele: <u>Almost double risk (100% increase) for AD in African Americans</u>



ABCA7 (rs3764650). "ABCA7-50"

Risk allele found in both those of European and African descent, especially women. Risk allele: Increases risk about 20%

ABCA7-50 Gene Modulates: Fitness-Generalization Relationship



Interim Summary

Carriers of the <u>non-risk</u> ABCA7-50 variant showed a strong correlation between physical fitness and generalization — *but not standard neuropsychological tests of memory*.

Those with the <u>risk</u> ABCA7-50 variant showed no significant advantage to being more physically fit.

IMPLICATIONS: ABCA7-50 risk genotype may diminish the neuroprotective value of aerobic fitness.

Which leads us to ask:

Does the ABCA7-50 gene also impact the effects of exercise on cognition and brain health ?



<u>That is:</u> Can we help these people with low fitness and low cognition improve both?



Physical Fitness

Methods

- Lifestyle and physical fitness assessment, and cognitive testing.
- 5-months of 2x weekly cardio-dance aerobic exercise
- Re-assessments after the intervention.

To better understand our exercise Intervention, we will invite you after this session to join us for a short cardio-dance fitness break (plus coffee if you wish!) AS PREDICTED: After a 20-week aerobic exercise intervention, only carriers of the low risk ABCA7 genotype showed exerciserelated cognitive improvements

AS PREDICTED: After a 20-week aerobic exercise intervention, only carriers of the low risk ABCA7 genotype showed exerciserelated cognitive improvements



Interim Summary

Older sedentary African Americans with the high-risk variant of ABCA7-50 showed less cognitive benefit (improvements in generalization) from the cardio-dance intervention than those with the low-risk ABCA7 genotype.

IMPLICATIONS: Different people (with different genetic variations) may require different and <u>personalized</u> "prescriptions" of exercise interventions to reduce risk for Alzheimer's disease.

Which leads us to ask:

How does exercise rewire our brains to improve cognition ?



We Measure "Dynamic MTL Connectivity" with fMRI

Do a 10 minute resting-state fMRI scan.

Start Scan

Time in resting-state fMRI

10 min.

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Divide 10 minutes into 20 30-second slices

- Do graph-theoretic network analysis for each of the 20 slices.
- Measure the strength (stability) of connections between key subregions of the medial temporal lobe (MTL).

Ask: How rigid or dynamic are these graph networks across the 10 minutes (20 30-second slices)?

We Measure "Dynamic MTL Connectivity" with fMRI

Flexible Dynamic Connectivity in MTL = Healthy



Rigid Dynamic Connectivity in MTL = Cognitive Decline



Start Scan

Time in resting-state fMRI

10 min.

How does a five-month cardio-dance exercise intervention change MTL Dynamic Network Flexibility ?



Results: Exercise (5 months, Cardio-fitness 2x week) Increases MTL Dynamic Network Flexibility



Linking Brain Changes to Cognitive Improvement: Across Both Intervention and Control Participants, Increased Network Flexibility After 5 months was Associated With Increased Cognitive Performance on Generalization



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Interim Summary

Exercise promotes MTL-region "flexibility" and may prevent increases in synchronicity ("rigidity") across subregions, protecting against cognitive decline.

Current Directions..

Exercise and Brain Health

2023: A new randomized clinical trial with active comparator group (R01AG08211):

- 1. Which aspects of brain function can be improved by regular exercise, and which exercise routine is best?
- 2. What accounts for individual differences in why some people benefit more (or less) from exercise?
- 3. Does exercise prevent (or reverse?) the neuropathology of Alzheimer's disease or are the cognitive benefits only compensatory? (Tau, A/B, NfL)

And finally.....

What else are we learning from our "Pathways" cohort



New Paper

Sleep and Brain Health

<u>Finding #1:</u> Good Quality (Self-Reported) Sleep Eliminates the Cognitive Deficits Associated with ABCA7-80 High-risk Genotype



Pilot Data:..

Digital Sleep Monitoring (w/ B. Mander, UC-Irvine)



Current Directions...

Brain Pathology Using New Blood Tests (w/ H. Zetterberg & K. Blennow, Sweden)

Higher levels of plasma P-Tau 231 and 181 are associated with poorer generalization performance.



Generalization



Current Directions. (w/ P. Fitzgerald-Bocarsly, Rutgers Immunology)

Lower scores on generalization were associated with higher senescence in CD8 T cells, $\beta = -.002$, p < .001

Generalization Acquired Generalization Task Predicted Value .90 0 .80 .70 .60 .50 0 .40 .30 60 80 0 20 40 100 **CD8+ T cell Senescence**

Longitudinal Prediction of Decline

Rutgers Generalization Task performance and medial temporal lobe network flexibility predict episodic memory decline over two years

Current Directions..



Socio-Environmental Influences on Brain Health

(w/ A. Santana, Rutgers School of Criminal Justice)

Using Geographic-Info-Systems (GIS) technology we can compute the number of abandoned buildings within 300 feet of each participant.



Current Directions..



Covariates appearing in the model are evaluated at the following values: Facquisition = .67925995058, Age = 67.73, Education_yrs = 13.654

Error bars: 95% CI

For More Info



www.brainhealth.rutgers.edu

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