

ABCA7-50 Risk Cross-Comparison Regarding Aerobic Fitness Between Healthy Older African and African American Cohorts

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Background

- Aerobic fitness (and regular aerobic exercise) is a well-established contributor to cognitive health.
- Prior work on older African Americans suggests that the ABCA7 rs3764650 (ABCA7-50) risk genotype diminishes the neuroprotective effects of aerobic fitness on cognition (Berg et al., 2019).
- This relationship remains understudied within different African diaspora populations.

Objective

To explore whether the relationship between the ABCA7-50 risk genotype and aerobic fitness on cognition persists in a genetically related but distinct population: Yoruba Nigerians

Methods

Summary Statistics of Cohorts

Participants (N = 409)	Newark, African American Cohort (N=285)		Ibadan, Yoruba Nigerian Cohort (N=124)	
	Mean (N)	SD (%)	Mean (N)	SD (%)
Age (years)	70.89	6.51	70.06	0.41
Sex (female)	(186)	(69.7%)	(73)	(58.9%)
Systolic Pressure	139.68	20.35	142.99	22.61
Diastolic Pressure	78.41	10.12	84.72	13.26
VO ₂ Peak	12.91	1.54	11.77	1.33
Global Sleep Quality	7.80	3.33	6.22	2.89
ABCA7-50 Risk Genotype	(99)	(41.6%)	(58)	(47.9%)
ABCA7-80 Risk Genotype	(25)	(10.3%)	(25)	(20.5%)

Methods

- Participants of both cohorts donated saliva samples for genotyping and completed a battery comprising neuropsychological assessments (including a computerized generalization task: Stimulus Differentiation and Transfer Task (Image 1).

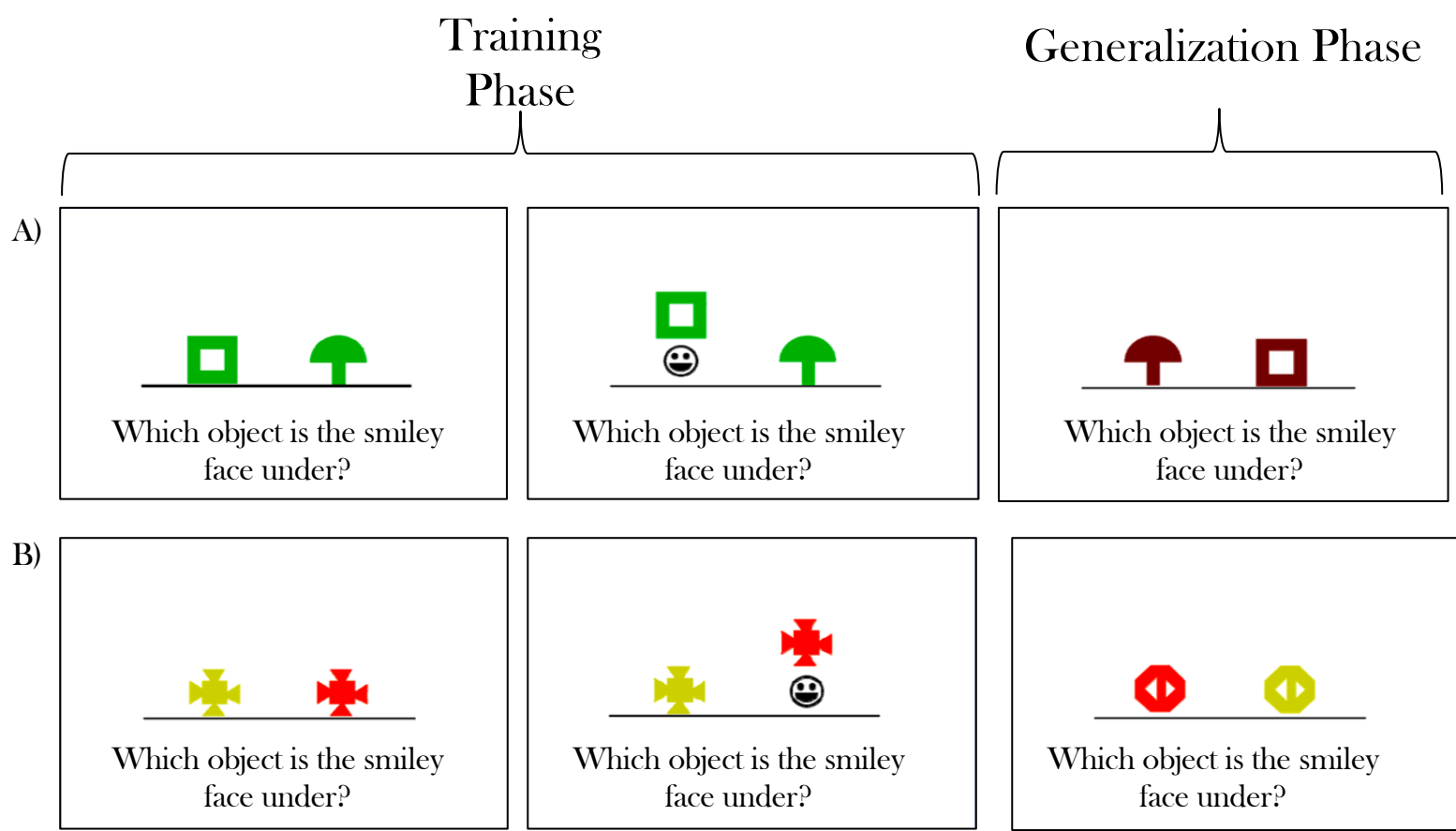


Image 1. Stimulus Differentiation and Transfer Task. The participants are presented 8 sets of paired stimuli during a training phase and then presented with novel stimuli pairs during the generalization of prior learning phase.

- Six-minute walk test: Participants are instructed to walk along a pre-measured 90-foot distance marked with cones at a normal pace for six minutes. The distance walked is then used to calculate the VO₂peak levels (Image 2).

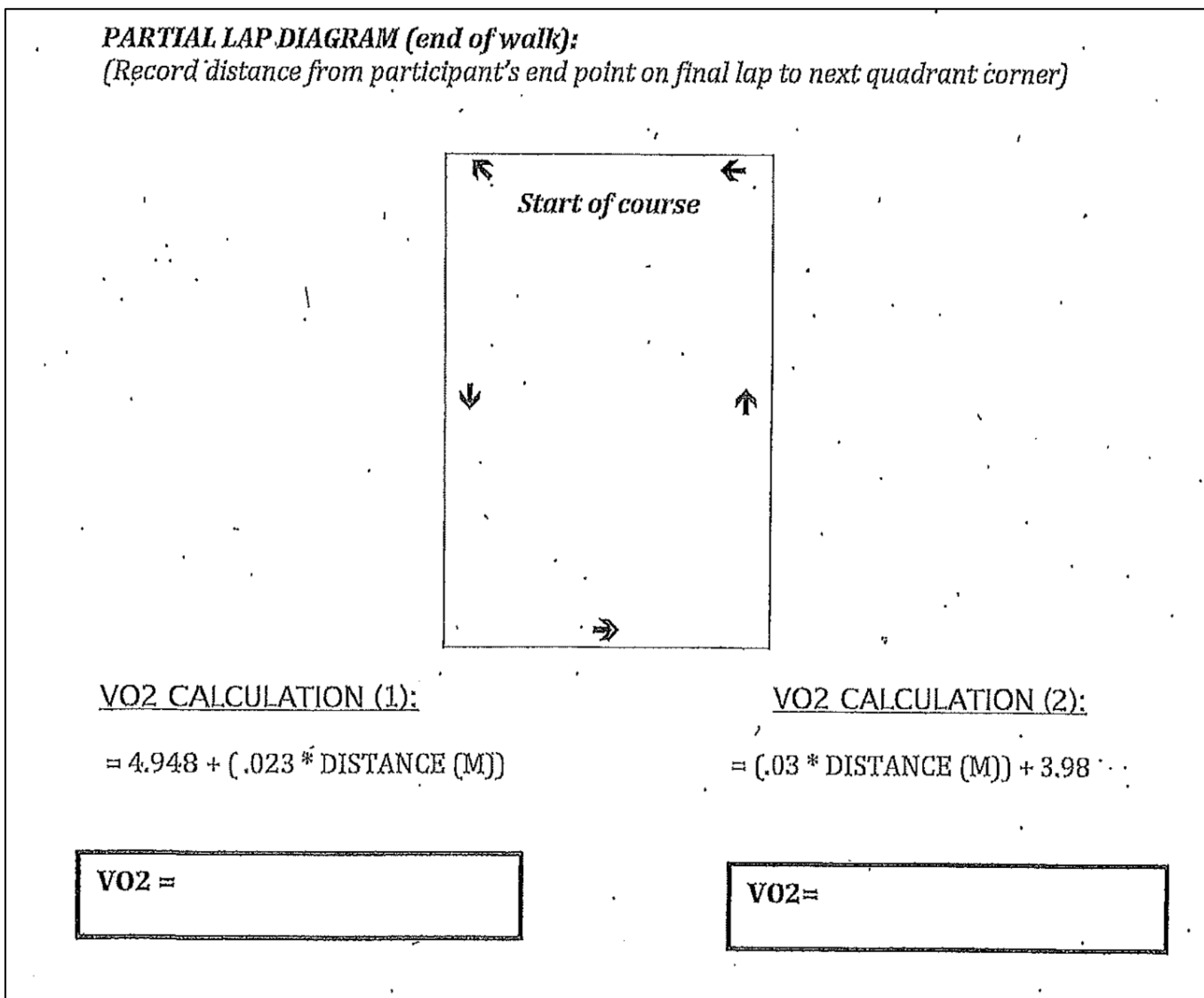


Image 2. Six-Minute Walk Test: Diagram of the partial lap used to track distance walked. Estimated VO₂peak calculations are shown at the bottom of the image.

Analyses

- Conditional effect analyses were conducted to accurately assess the relationship between aerobic fitness and cognition. See Figure 1 and Figure 2.

Results

- Among low-risk individuals in the Newark cohort, higher VO₂peak was associated with fewer generalization errors ($\beta = -2.93$, $p = .04$), whereas no association was observed among high-risk carriers ($\beta = 2.90$, $p = .35$), replicating prior findings that genetic risk diminishes the neuroprotective value of fitness (Figure 1).
- In contrast, within the Yoruba cohort, while aerobic fitness independently predicted cognition ($\beta = -5.02$, $p = .01$), with higher VO₂peak associated with fewer errors, no moderating effect of ABCA7-50 was observed ($\beta = -2.57$, $p = .50$) (Figure 2).

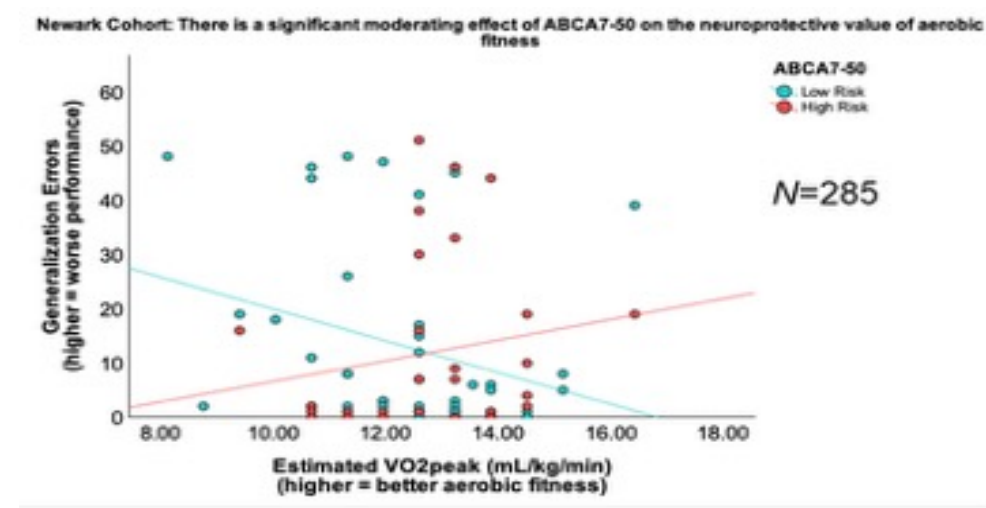


Figure 1. We replicated our prior published finding in a larger sample: ABCA7 high risk genotype diminishes the neuroprotective value of aerobic fitness in older African Americans.

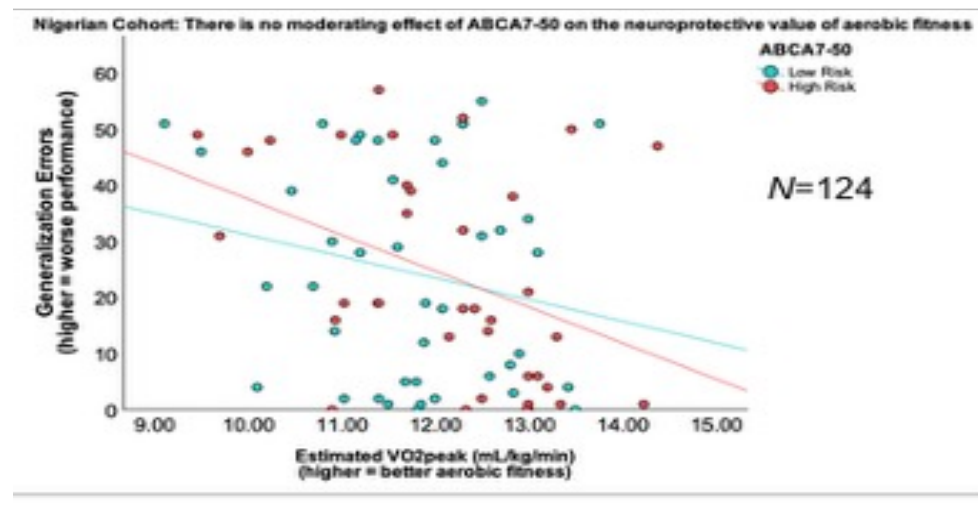


Figure 2. Unlike the Newark cohort, there was no significant moderating effect of ABCA7-50 high risk variant on the neuroprotective value of aerobic fitness in an older Yoruba cohort.

Discussion

- These findings demonstrate that the influence of ABCA7-50 genotype on aerobic fitness is not consistent across populations with common ancestry.
- Genetic variation in the Newark cohort likely reflects African American heterogeneity, whereas West African populations may likely be more genetically homogeneous.
- The more active lifestyles observed in both populations further highlight the role of modifiable factors in cognitive health. Together, these results establish the need for expanded comparative research to define how genetic and lifestyle factors jointly shape Alzheimer's disease risk across diverse populations.
- Future work should extend to Western African populations, given their historical linkage through the transatlantic slave trade.

Acknowledgements

Funding Source: 1R01AG053961 (NIH/NIA)

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