

Cardiovascular and lipid profile in *APOE*ε3 Christchurch (R136S) variant carriers within the Colombian *PSEN1*-E280A kindred

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Introduction //

APOE variants modulate Alzheimer's disease (AD) risk and influence lipid and cardiovascular profiles. The *APOE3* Christchurch (*APOE3Ch*; R136S) variant has been associated with resistance to autosomal dominant Alzheimer's disease, yet its systemic and cardiovascular effects remain poorly characterized. This is critical to inform the safety and translational potential of emerging *APOE3Ch*-targeted therapeutic strategies.

Objective //

To characterize the lipid and cardiovascular profiles of *APOE3Ch* carriers to explore its broader systemic implications.

Methods //

We studied 37 individuals from the Colombian *PSEN1*-E280A kindred stratified by *APOE3Ch* genotype (1 homozygote, 29 heterozygotes, 7 non-carriers), aged 19–77 years. Participants underwent standardized clinical assessments, fasting lipid profiles, and comprehensive cardiovascular phenotyping. Data were summarized using descriptive statistics and nonparametric tests, when appropriate.

Results //

Sociodemographic, cardiovascular and lipid profile data are presented in Tables 1 and 2. No notable differences were observed in arterial stiffness, ankle–brachial index, carotid Doppler, or Holter measures. Sympathovagal indices are presented in Figure 1. *APOE3Ch* carriers showed less favorable age-stratified lipid/risk indices than non-carriers. Exploratory analyses of six *PSEN1*-E280A carriers found no distinct or deleterious cardiovascular profile.

Conclusions //

Our findings provide a description of cardiovascular profiles in *APOE3Ch* carriers. Variations remained within or only slightly above established physiological ranges in heterozygous and were not accompanied by increased disease burden. A possible gene-dose effect suggests that *APOE3Ch* may exert a cumulative influence on systemic metabolism. These results offer a preliminary framework to inform cardiovascular biomarkers for future *APOE3Ch*-based therapies in AD.

Table 1. Sociodemographic and cardiovascular characteristics

	Homozygous <i>APOE3Ch</i> carriers (n=1)	Heterozygous <i>APOE3Ch</i> carriers (n=29)	<i>APOE3Ch</i> non-carriers (n=7)
Sex			
Female (%)	1 (100%)	15 (51.7%)	5 (71.4%)
Age			
Years [Q1, Q3]	77 [N/A]	42 [34, 50]	48 [39.5, 60.5]
Education			
Years [Q1, Q3]	1 [N/A]	7 [5, 11]	11 [3.5, 11]
Comorbidities (%)			
Hypertension	1 (100%)	7 (24.1%)	4 (57.1%)
Dyslipidemia	1 (100%)	6 (20.7%)	3 (42.9%)
Type 2 diabetes	0 (0%)	3 (10.3%)	1 (14.3%)
Hypothyroidism	0 (0%)	2 (6.9%)	2 (28.6%)
Heart failure	0 (0%)	0 (0%)	0 (0%)
IHD	0 (0%)	1 (3.4%)	0 (0%)
Vascular disease	0 (0%)	3 (10.3%)	1 (14.3%)
Obesity	0 (0%)	2 (6.9%)	1 (14.3%)
Polypharmacy (%)			
Yes	1 (100%)	3 (10.3%)	4 (57.1%)
Statin use (%)			
Yes	1 (100%)	4 (13.8%)	2 (28.6%)
Cardiovascular risk (Framingham)			
Median [Q1, Q3]	10.3 [N/A]	3.86 [1.13, 6.60]	2.47 [1.13, 22.5]
Missing (%)	0 (0%)	5 (17.2%)	2 (28.5%)

APOE3Ch: *APOE*ε3 Christchurch variant; Q1: first quartile; Q3: third quartile; IHD: Ischemic heart disease

Acknowledgments

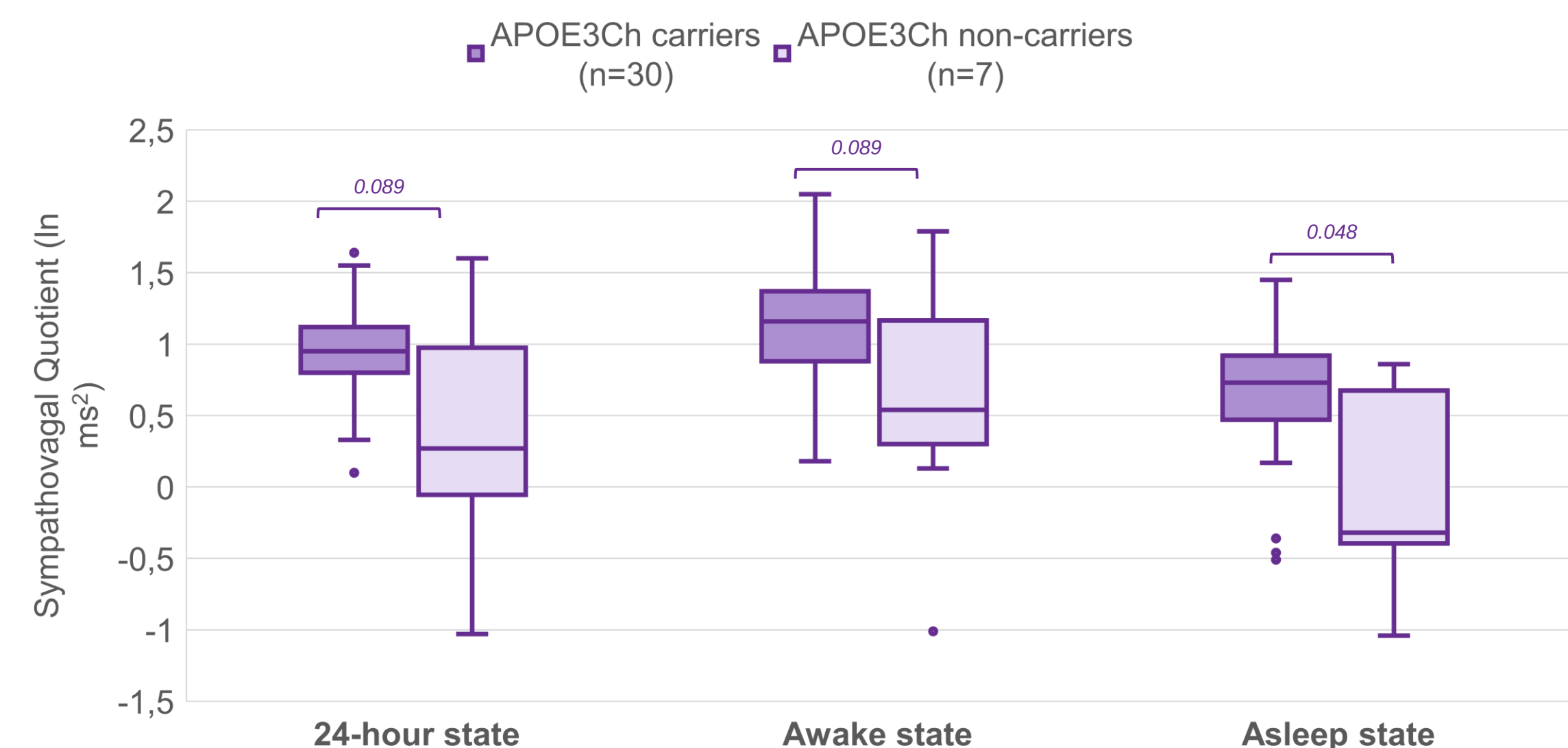
The authors thank the participants of the Resist Alzheimer's Project for making this work possible and honor Dr. Francisco Lopera's lifelong dedication to advancing Alzheimer's disease and related dementia research. A gift from Coefficient Giving and Remondi Family Foundation made this work possible.

Table 2. Lipid profile in *APOE3Ch* carriers versus non-carriers

	Homozygous <i>APOE3Ch</i> carriers (n=1)	Heterozygous <i>APOE3Ch</i> carriers (n=29)	<i>APOE3Ch</i> non-carriers (n=7)	Laboratory reference range (mg/dL)
Total Cholesterol (mg/dL)				
Median [Q1, Q3]	511.8 [N/A]	183.6 [162.2, 218.9]	172.6 [163.5, 172.9]	0 - 200
Missing (%)	0 (0%)	5 (17.2%)	2 (28.5%)	
Triglycerides (mg/dL)				
Median [Q1, Q3]	691.9 [N/A]	154.9 [106.2, 260.3]	121.7 [108.6, 151.6]	0 - 150
Missing (%)	0 (0%)	5 (17.2%)	2 (28.5%)	
LDL (mg/dL)				
Median [Q1, Q3]	317.6 [N/A]	112.8 [85.7, 137]	101.5 [99.8, 112.7]	0 - 100
Missing (%)	0 (0%)	5 (17.2%)	2 (28.5%)	
HDL (mg/dL) - Female				
Median [Q1, Q3]	55.7 [N/A]	52.9 [47.7, 61.5]	50.8 [46.8, 54.1]	> 50
Missing (%)	0 (0%)	4 (36.3%)	1 (25%)	
HDL (mg/dL) - Male				
Median [Q1, Q3]	N/A	37.2 [32.8, 43]	46.6 [N/A]	> 40
Missing (%)		1 (7.6%)	1 (50%)	

APOE3Ch: *APOE*ε3 Christchurch variant; Q1: first quartile; Q3: third quartile; N/A: Not Applicable; mg/dL: milligrams per deciliter.

Figure 1. Sympathovagal Quotient in *APOE3Ch* carriers versus non-carriers



References //



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GNA RESEARCH CAPABILITIES

