Plan Overview

A Data Management Plan created using DMPTool-Stage

Title: Global and local ancestry modulate APOE association with Alzheimer's neuropathology and cognitive outcomes in an admixed sample

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Funder: National Institutes of Health (nih.gov)

Grant: R01AG17917

Template: NIH-GDS: Genomic Data Sharing

Project abstract:

Dementia is more prevalent in Blacks than in Whites, likely due to a combination of environmental and biological factors. Paradoxically, clinical studies suggest an attenuation of *APOE* e4 risk of dementia in African ancestry (AFR), but a dearth of neuropathological data preclude the interpretation of the biological factors underlying these findings, including the association between *APOE* e4 risk and Alzheimer's disease (AD) pathology, the most frequent cause of dementia. We investigated the interaction between African ancestry, AD-related neuropathology, *APOE genotype,* and functional cognition in a postmortem sample of 400 individuals with a range of AD pathology severity and lack of comorbid neuropathology from a cohort of community-dwelling, admixed Brazilians. Increasing proportions of African ancestry (AFR) correlated with a lower burden of neuritic plaques (NP). However, for individuals with a severe burden of NP and neurofibrillary tangles (NFT), AFR proportion was associated with worse Clinical Dementia Rating sum of boxes (CDR-SOB). Among *APOE* e4 carriers, the association between AFR proportion and CDR-SOB disappeared. *APOE* local ancestry inference of a subset of 309 individuals revealed that, in *APOE* e4 noncarriers, non-European *APOE* background correlated with lower NP burden and, also, worse cognitive outcomes than European *APOE* when adjusting by NP burden. Finally, *APOE* ε4 was associated with worse AD neuropathological burden only in a European *APOE* background. *APOE* genotype and its association with AD neuropathology and clinical pattern are highly influenced by ancestry, with AFR associated with lower NP burden and attenuated *APOE ε4* risk compared to European ancestry.

Start date: 12-31-2018

End date: 12-31-2023

Last modified: 07-20-2022

Copyright information:

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Part of the genomic data (genotyping with microarray) was generated with funds from NIH R01AG17917. The subset of data used in the current project and corresponding publications is being shared in anonymized, de-identified formats. To recover the linkage between this dataset and the original NIH R01AG17917 full dataset or other phenotypic data produced by USP on these individuals, a request must be submitted and approval will be registered in a Data Access Agreement.

Datasets can be directly accessed by researchers and institutions. Individual level phenotypic data with corresponding sample identifiers can be requested to corresponding researchers, approved and data will be shared after Data Access Agreement is signed by both parties.

Dataset of genomic data associated with this project is being submitted to the University of São Paulo Data Repository (https://metabuscador.uspdigital.usp.br/)

Dataset is expected to be deposited before August 2022 and available for download after publishing article (expectation August 2022).

Data from all subjects is anonymized and de-identified as requirements of Brazilian local and national ethical committees (CEP/CONEP). This project was approved by the FMUSP IRB under code 22262613.0.0000.0065 upon written consent of the knowledgeable informants.

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The dataset is approved for research purposes only. Phenotypic data access is subject of approval under reasonable request.
