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A study to determine the role of genetic differences and environmental exposures as risk factors for dementias and parkinsonism in Nigeria

Submission date
03/03/2023

Recruitment status
No longer recruiting

Registration date
07/03/2023

Overall study status
Completed

Last Edited
06/03/2023

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Environmental exposures and genetic (inherited) factors can increase the risk of developing neurodegenerative disorders. The most prevalent and burdensome of these disorders are Alzheimer's disease and related dementias (ADRD) and Parkinson's disease and atypical parkinsonisms (PDAP). The accompanying disability and increased risk of death indicate a need to find modifiable risk factors that can be incorporated into lifestyles through population-wide strategies. Despite much progress in other populations, very little is known about the contributions of environmental and genetic factors to these conditions in Nigeria and sub-Saharan Africa. This study proposes to address this gap by studying the environmental exposures and genetic differences in persons with ADRD and PDAP, compared to healthy volunteers of similar age, gender, education and ethnicity. The specific individual and combined effects of possible environmental exposures and changes in selected genes will be explored.

Who can participate?
Adults resident in Nigeria and attending clinics at the participating centres who have been diagnosed with dementia or parkinsonism, and healthy volunteers

What does the study involve?
Participants will spend about 2 hours in the clinic and will be asked questions to confirm their diagnosis, undertake a clinical examination and review of any tests they have done, and have a blood sample taken.

What are the possible benefits and risks of participating?
The participants will not have any direct benefit from participating. However, their participation will help find answers that may explain the reasons why people get dementia or parkinsonism. The blood sample will be taken under standard precautions to minimize the pain and risk of

infection which are both minimal. In the genetic analysis, the information will be entirely de-identified so that it cannot be linked to any individual participant, and only researchers involved in the study will be able to access the data.

Where is the study run from?
University of Lagos (Nigeria)

When is the study starting and how long is it expected to run for?
November 2019 to December 2023

Who is funding the study?
The Tertiary Education Trust Fund National Research Fund (Nigeria)

Who is the main contact?
Prof. Njideka U. Okubadejo, nokubadejo@unilag.edu.ng

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
1.0

Study information

Scientific Title
Nationwide study of environmental risk factors and candidate gene-environment interactions in neurodegenerative disorders in Nigeria

Acronym
SERGEND

Study objectives
Alzheimer disease and related dementias (ADRD) and Parkinson disease and atypical parkinsonisms (PDAP) represent the two most prevalent and burdensome groups of neurodegenerative disorders globally. Unchecked these disorders will become the leading cause of death by 2050. On account of the apparent complex inheritance for the majority of ADRD and PDAP, an interplay between heritability and environmental exposures is presumed to underpin the mechanisms leading to progressive and selective neuronal cell loss and subsequent pathological and clinical manifestations. There is a significant gap in the specifics of the genetic variability predisposing to ADRD and PDAP, and the precise environmental exposures in diverse populations are largely unknown. Elucidating environmental risk factors and a detailed understanding of the interaction with genetic factors are critical steps for understanding the mechanistic basis of ADRD and PDAP, and for driving the development of interventions to prevent, treat and reduce the unacceptable accompanying morbidity and mortality. Identifying the genetic and environmental factors responsible for variability in the risk of developing ADRD and PDAP will also help identify persons and individual characteristics that portend increased

susceptibility, and guide developing interventions to forestall such exposures, particularly if modifiable. Considering the variety of environmental exposures encountered based on geographical location, and the disparity in prevalence and incidence of ADRD and PDAP between African and more industrialized countries, it is imperative that the role of environmental exposures and potential interaction with genetic variability as protective or causative factors is explored.

The environmental risk factors and gene-environment interactions for ADRD and PDAP in Nigeria (and indeed in sub-Saharan Africa) have not been systematically studied from a national and geographically diverse and representative perspective. This study proposes to bridge this gap in knowledge by utilizing a case (affected) – control (unaffected) approach to systematically evaluate the effects of several putative environmental exposures and genetic variability in two candidate genes, on the risk of ADRD and PDAP in Nigerians. The study will explore the individual and combined effects (gene-environment interactions) of the environmental and genetic susceptibility risk factors in ADRD and PDAP risk. The candidate genes (α synuclein – SNCA and apolipoprotein E – APOE) have been selected for their prior strong association with ADRD and PDAP).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 31/03/2020, National Health Research Ethics Committee (National Health Research Ethics Committee, Department of Health Planning, Research and Statistics, Federal Ministry of Health, 11th Floor, Federal Secretariat Complex Phase III, Ahmadu Bello Way, Abuja, Nigeria; +234 (0)95238367; +234 (0)8063190328; chairman@nhrec.net), ref: NHREC/01/01/2007

Study design
Prospective observational cross-sectional multicentre study

Primary study design
Observational

Study type(s)
Screening

Health condition(s) or problem(s) studied
Neurodegenerative diseases (Alzheimer's disease and related dementias (ADRD); Parkinson's disease and atypical parkinsonism (PDAP))

Interventions
Study participants (persons with ADRD and PDAP) will be recruited from participating hospitals across the six geopolitical zones of Nigeria under the guidance of study neurologists. All dementia cases will be screened with the Intervention for Dementia in Elderly Africans (IDEA) questionnaire as an initial step, and then further evaluated with relevant components of the National Alzheimer Coordinating Centre (NACC) Unified Dementia Screening instrument (version 3.0) (UDS). Parkinsonism will be diagnosed based on the UKPDS brain bank criteria and additional features in atypical cases. Controls will be healthy (neurologically normal) age- and gender-matched unrelated persons from the same population. Standardized clinical assessments will be conducted to characterize disease, evaluate severity and document environmental risk factors (using the common data elements from the NIH environmental risk factor questionnaire.

Baseline anthropometric indices, fasting blood glucose and brain imaging (where previously available as part of the ongoing clinical consultation) will be documented. Blood samples (whole blood) will be obtained for genotyping.

Intervention Type
Mixed

Primary outcome(s)
The association between each specified environmental risk factor documented in the Environmental Risk Questionnaire (ERQ) (residential history, smoking and tobacco, alcohol use, diet, occupation, toxicants, pesticides, caffeine, head injury, NSAID and calcium channel blocker use) and genetic polymorphisms in SNCA REP1 and APOE and ADRD and PDAP will be measured by comparing the presence of the risk factor compared in cases (dementia i.e. ADRD, and parkinsonism i.e. PDAP) and controls. Specifically, the study will report on:
1. Relative risk associated with specified environmental exposures in dementia versus healthy controls
2. Relative risk associated with specified environmental exposures in parkinsonism versus healthy controls
3. Hazard ratios comparing the frequency of APOE polymorphisms in cases (dementia and parkinsonism) and controls
4. Hazard ratios comparing the frequency of SNCA REP1 polymorphisms in cases (dementia and parkinsonisms) and controls.

1. Environmental risk exposure measured using Environmental Risk Questionnaire at baseline (enrolment)
2. Genetic variability in APOE and SNCA REP1 measured using genotyping for polymorphic variability/allele frequencies at baseline (enrolment)

Key secondary outcome(s))
Combined effects (gene-environment interactions) will be analysed by comparing the combined effects of all environmental risk factors and the genetic polymorphisms (measured at baseline [enrolment]) on the risk of dementia and parkinsonism. Computational analysis will be employed as the statistical method for data analysis. The outcomes will be reported as risk ratios.

Completion date
31/12/2023

Eligibility

Key inclusion criteria
1. ADRD or PDAP diagnosed based on standardized clinical research criteria (with or without corroborating additional diagnostic information)
2. Neurologically healthy volunteers

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group

Adult

Sex
All

Key exclusion criteria
1. Non-consent
2. Unable to complete clinical assessments due to disability

Date of first enrolment
01/05/2020

Date of final enrolment
31/12/2023

Locations

Countries of recruitment
Nigeria

Study participating centre
College of Medicine, University of Lagos
Ishaga Road, Off Itire Road,
Lagos
Nigeria
-

Study participating centre
Ahmadu University Teaching Hospital
Zaria
Zaria
Nigeria
-

Study participating centre
University of Maiduguri Teaching Hospital
Maiduguri
Maiduguri
Nigeria
-

Study participating centre

University of Ilorin Teaching Hospital
Ilorin
Ilorin
Nigeria
-

Study participating centre
University College Hospital, Ibadan
Ibadan
Ibadan
Nigeria
-

Study participating centre
University of Nigeria Teaching Hospital
Ituku Ozalla
Enugu
Nigeria
-

Study participating centre
University of Calabar Teaching Hospital
Calabar
Calabar
Nigeria
-

Study participating centre
Lagos State University Teaching Hospital
Ikeja
Lagos
Nigeria
-

Study participating centre
Benue State University Teaching Hospital
Makurdi
Makurdi
Nigeria
-

Study participating centre
Federal Medical Centre
Owerri
Owerri
Nigeria
-

Sponsor information

Organisation
Tertiary Education Trust Fund (TETFUND)

Funder(s)

Funder type
Government

Funder Name
Tertiary Education Trust Fund

Alternative Name(s)
Tertiary Education Trust Fund, TETFund

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Nigeria

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analyzed during the current study will be available upon request from Prof. Njideka Okubadejo (nokubadejo@unilag.edu.ng): deidentified data including baseline demographics and summary data on the presence or absence of risk factors in the Environmental Risk Factor Questionnaire. Written informed consent was obtained from all participants. Only anonymized data will be shared.

IPD sharing plan summary

Available on request